somatosensory testing & rehabilitation

A. LEE DELLON, MD
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At the time of the first printing of this book, Dr Dellon had a proprietary interest in these: the Disk-Criminator™, the Pressure-Specified Sensory Device™, Digit-Grip™, and the Skin Compliance Device™.

At present Axogen, Inc is the company selling the PSSD, and now calls it the AcroVal system. Dr Dellon still has a proprietary interest in the Acroval system

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THIS BOOK

IS DEDICATED TO

MY SENSATIONAL TEACHERS,

RAYMOND M. CURTIS, MD,

ERIK MOBERG, MD,

AND

NEBOJSA KOVACEVIC
ACKNOWLEDGEMENTS

The presentation of crucial concepts in this book has relied upon the insights and artistry of its illustrator. The artist was carefully chosen. I have known him, and observed his work develop over the past 18 years. That artist, Glenn George Dellon, my son, did this during his senior year in high school. The illustrations have been prepared in the style of a cartoonist to convey the spirit of joy and enthusiasm that has always surrounded the subject of the peripheral nerve for me. Seeing Glenn’s unique perspective transform neuroscience has added immeasurably to the thrill of preparing this book.

I want to thank those who took the time to review portions of the text during the stages of its preparation: Pegge Carter-Wilson, OTR, CHT; Beth Wojiclechowski-Roros, OTR; Patsy Tassler, BA; John (Jack) E. Barham, Med; David Seller MBA; Stephanie Hollenback, BSN, RNFA; Oskar C. Aymann MD; and Jennifer R Berman, MD. Their time and understanding enabled me to believe that the text was both readable and relevant to its intended audience.

Finally I wish to express appreciation to the group that produced this textbook under the direction of Frances McCarrey, Director of Nonperiodical Publications and to Dianne Stamm, the editor who molded the final words.
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● THERAPIST AS RESEARCHER AND TEACHER ●

CHAPTER 20. THERAPIST AS RESEARCHER

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At the 26th Annual Meeting of the American Society for Surgery of the Hand, held in San Francisco in March 1971, Lee Dellon presented a paper, coauthored by Raymond Curtis and Milton Edgerton entitled, “Re-education of Sensation in the Hand After Nerve Injury and Repair.” His presentation was published as an abstract in the *Journal of Bone and Joint Surgery*, followed by publication of the full version in 1974 in the *Journal of Plastic and Reconstructive Surgery*. That original “little paper” changed forever the course of clinical care of the patient with an upper extremity injury to the peripheral nerve. The purpose of the paper was to present the most recent neurophysiological findings on cutaneous sensation, set a specific reeducation program, and give an appropriate timetable for that reeducation. Lee Dellon was just beginning his career as a hand surgeon, and hand therapy was in its very infancy. The only other published work describing a specific sensory reeducation program of the peripheral nerves in the upper extremity was contained in Wynn Parry’s 1966 edition of *Rehabilitation of the Hand*. Lee’s publication was unique in that it was the first time someone had attempted to increase the understanding of clinical testing by correlating the methods directly with the latest findings of neurophysiological research.

On a personal note, I was just starting my career in hand therapy in 1974. Lee’s first article on peripheral nerve evaluation and reeducation had a profound impact on me, creating an interest in sensibility that continues to this day. I was very fortunate in those early years to be able to teach with Lee at various hand symposiums across the country. He was tireless in trying to encourage therapists to expand their knowledge base in neurophysiology and their testing skills as clinicians. Throughout the years, we have collaborated, discussed, and even disagreed. Lee has always been a very patient teacher. My hope is that through his latest effort, a new generation of students and clinicians will become as fascinated with sensibility as I did over twenty years ago.

Since that modest beginning in 1971, Lee Dellon has never wavered from his concept of incorporating the basic sciences with clinical skills. In 1981, he published *Evaluation of Sensibility and Re-education of Sensation in the Hand*, an entire text dedicated to increasing
understanding of nerve physiology, evaluation of sensibility, and nerve rehabilitation. True to his nature as a teacher, Lee approached the subject in a highly personal fashion, making it accessible to the clinician. His approach created some controversy, but also provided the impetus that helped to increase interest in, and study of, the evaluation and reeducation of the peripheral nerve, both nationally and internationally. As a direct result of his publications, Lee provided the tools that enabled the therapist not only to evaluate the status of the peripheral nerve, but also to interpret the physiological meaning of the test results.

somatosensory Testing and Rehabilitation. Lee Dellon’s most recent endeavor, brings us up-to-date on both the latest findings of neurophysiological research and the technological changes in evaluation. Advances in surgical techniques, particularly in plastic surgery, create a very apparent expansion from the author’s previous work. His latest contribution is a Herculean effort that encompasses not only evaluation and reeducation of the upper extremity, but also includes the entire body extending beyond the peripheral nerve to include all aspects of plegias and cortical plasticity. Once more, he has approached his subject as a teacher, offering basic neurophysiology and anatomy, methods of quantitative testing and techniques of sensory reeducation, followed by specific applications for each area of the body. He ends by challenging the therapist to become both a researcher and a teacher by being an integral member of the research team, publishing results, and presenting those results to peers in a teaching environment. The final section of the text is an excellent teaching tool, consisting of self-administered questions and answers to help the student of somatosensory rehabilitation test his or her level of comprehension of the material.

When Lee authored his first text, he stated that his purpose “was to bridge the potential, if not actual, gap between those involved with the neurosciences and those involved with the care of the peripheral nerve.” He did that. With this latest effort, he goes beyond that to bring us abreast of not only neurophysiological research and its application in the clinic, but also the implications of changing technology. I doubt he is finished. I’m sure he will continue his journey to keep the student and the clinician current with the wealth of research knowledge and technology that in the end will give the patient the benefit of the highest quality of care both now and in the future.

Margaret S. Carter, OTR, CHT
August 6, 1995 Past President, American Society for Hand Therapy
● ● ●
Tube, or not tube . . . . . . . . . . . . . . . . . . . . . . that is the question:

Whether 'tis nobler in the mind to suffer

The stings and shooting pains of neuroma formation,

Or to take our nerve after a divisive injury,

And oppose its ends within a tube?.... To frustrate,

No more, and by entubulation will end

The pain and the thousand natural shocks

That nerve is heir to.... 'tis a consummation

Devoutly to be wish'd. To regenerate,

To rehabilitate! perchance to discriminate.... ay,

There's the sense.

HamLeet,

Act III, Scene I*

● ● ●

We all come into the world virtually devoid of sensory experience. Virtually, because perhaps, during the 9 or so months of life in utero, the physical interface between the skin and the temperature-controlled surrounding liquid environment imparts the first stimuli to the nerve fibers that subserve the transmission of sensory information to the brain. It may well be that the stimuli also have reached the brain through acoustic mechanisms, through the transmission of vibratory stimuli. Yet, certainly, these vibrations have been cushioned by their passage across the maternal body and the water interface with the tympanic membrane. And so, we all come into the world virtually devoid of sensory experience. Then, BANG!, an explosion of sensory stimuli, and the awareness of the central nervous system that it must deal with this new torrential rain of information from the periphery. Understanding the mechanisms that let us process this information in health and disease, understanding the techniques to quantitate sensibility in health and disease, and developing approaches to rehabilitate these systems constitute the subject of this book.

There was a prophet, Raymond M. Curtis, originally from Columbus, Missouri, who preached of the need to do meticulous surgery to reconstruct the injured hand, and to spend at least an equal amount of attention on the rehabilitation of that hand. In 1969, during the summer between my second and third years at the Johns Hopkins University School of Medicine, I received permission to observe Dr. Curtis in surgery at the Children’s Hospital in Baltimore on Tuesday afternoons. He operated in Room 2. It was the contrast between the precision I observed in his work with nerves and the inability clinically to be able to quantitate the function of those nerves that led to my first research with the peripheral nerve. Part of my job as Dr. Curtis’s first Hand Fellow in 1977, in his new Hand Center, was to establish research models in his lab, a converted labor and delivery room at Union Memorial Hospital. From that lab, during the academic year 1981-1982, the last year of his active practice, were initiated the basic science models that led to our understanding of chronic nerve compression, the double crush syndrome, neuroma formation, and neural regeneration through bioabsorbable conduits.
When I last visited Dr. Curtis in 1992, at his home on Gibson Island, Maryland, he was still reading the *Journal of Hand Surgery* and asking provocative questions about current research activities. His wife, Anne, was able to make him aware of this book’s dedication to him prior to his death. He died on October 9, 1994 in Seattle, Washington. He left with us the Curtis Hand Center, whose Surgery and Rehabilitation Departments radiate his preaching’s to the world. Here was another prophet in the surgical community, Erik Moberg of Gotteborg, Sweden, who preached of the essential need to quantitate sensibility. He visited Baltimore in 1969, to go sailing with Dr. Curtis. I was in my third year of medical school and, having been inspired by Dr. Curtis to study the pattern of recovery of sensation after nerve injury, was given the opportunity to present my research to Dr. Moberg. It was the beginning of a long association. I last had dinner with him in Seattle in 1989, at the meeting of American Society for Surgery of the Hand. At the last lecture I heard him give, which was in Vienna, Austria, in November 1991, he was still intent on creating a device to make better two-point discrimination measurements. Dr. Moberg died on February 14, 1993. He was singlehandedly responsible for awakening the spirit necessary to make sensibility testing available worldwide.

A third prophet has formed a bridge from the scientific community to the medical community. Born Nebojsa Kovacevic, in the village of Kovacevic, Slavonia, Yugoslavia, this survivor of World War II, and the only survivor of my Three Wise Men, helped his brother and sister become physicians, while he became an aviator. He began, in 1944 at the age of 17, by flying a homemade glider from a cliff, and later suspending it over the Danube River. From this he learned to measure the force of the wind against his wings. Perhaps as a memorial to those early experiences, he recently developed a desktop, computerized wind tunnel to teach aeronautical engineering students. He came to the United States in 1959, and since then his professional life has been devoted to the challenges of theoretical aerodynamics, especially astronautics, including a fellowship at the University of Maryland where he was involved with...
several NASA research projects. In 1970, Nebs began to expand his aeronautical engineering measurement horizons into medical applications and computer technology.

Nebs and I met in 1987 in his laboratory outside Minneapolis, where he developed state-of-the-art, computer-assisted sensorimotor testing equipment that will bring us into the 21st century. It is in recognition of the influence on me of these three prophets that I dedicate this book to Raymond M. Curtis, Erik Moberg, and Nebojsa Kovacevic (see Figures 1 & 2).

Somatosensory Testing and Rehabilitation must fill the void of texts needed to educate the new generation of therapists who will provide the essential service of quantitating sensibility and reeducating sensation. And these services will be provided not just for the hand, and not even just for the limbs, but for the entire body surface, including its mucocutaneous and mucous membrane-lined surfaces. And these services will be provided not just for hand injuries, but also for people with peripheral neuropathy, and for people who have developed the side effects of many of the modern chemotherapy agents, sensory loss in the hands and feet.

Somatosensory Testing and Rehabilitation comes at a time when the United States federal government, through Medicare, has agreed to pay for the costs of protective footwear if the referring doctor documents the need for such protection, and at a time when the American Peripheral Neuropathy Association (neurologists) has recognized that electrodiagnostic testing has limitations that can be overcome by quantitative sensory testing. This book comes at a time when the American Diabetes Association (internists, endocrinologists), through its 1988, 1993, and most recently its 1996 consensus statement, has mandated periodic testing of cutaneous vibratory and pressure thresholds to follow the sensory changes characteristic of the neuropathy that affects approximately 5 million Americans. Plastic surgeons have begun to quantitate the sensation recovered in women following breast reconstruction, and in men after penile reconstruction.

Plastic surgeons, as well as ear nose and throat surgeons, have begun to quantitate the sensation in the oral cavity after reconstruction for cancer of the oral cavity and pharynx, and in the face after craniofacial trauma. Urologists have become increasingly aware of the sensory deficits present in men with impotence. And in 1991, the American Society for the Peripheral Nerve was founded.

Yes, Somatosensory Testing and Rehabilitation is a book whose time has finally come. It is for these reasons that this book is not a second edition of Evaluation of Sensibility and Re-education of Sensation in the Hand, my first book, published in 1981, reprinted in 1984 and 1987, and translated into Japanese in 1993. The title of this new book reflects the emergence of technology for sensibility testing that will carry us into the 21st century, and the expansion of my original concepts from the hand to the entire body.

To accomplish its function as a textbook, this book is written in a user-friendly style. The language is factual yet straightforward, with an emphasis on understanding the physiology and pathophysiology. This textbook does not assume the reader has extensive basic science knowledge. This book contains information on areas of sensibility not covered in my first book. For example, there are extensive discussions of the diagnosis and treatment of pain problems (Chapter 7), as well as an entire chapter on cortical plasticity (Chapter 10), which is now understood to be the basis for the success of sensory reeducation. This new book also explains the theoretical and practical reasons that allow a unification of threshold and innervation density testing. There are no footnotes and the text is without numbered references; however, at the end of each chapter are sections of references and additional readings for those students who wish to pursue their interests further. Names that should at least become familiar to the student are included as part of the text, with some clarifying biographical comments to broaden the subject.
A series of self-administered questions, keyed to each chapter, is included in Chapter 21. They may be used by the teacher of the course or by the student for testing or continuing education purposes.

The book is organized anatomically by functional region to facilitate special interests in education, therapy, or research. Each of these anatomic regions is introduced with a review of the pertinent neuroanatomy, and contains tables that record the known normal and abnormal values for quantitative sensitivity testing for that anatomic area. To the extent that specific protocols for sensory rehabilitation exist, they are included in the pertinent regions. Where these do not already exist, techniques for rehabilitation are suggested based on general principles learned from the other areas. Clinical examples are introduced into each area to establish the relevance of the more didactic points. Application of the newest, state-of-the-art, computer-assisted sensibility testing is also included, both as a subject in its own right and as it applies to each anatomical region.

A Lee Dellon, MD
Baltimore, Maryland
July 23, 1995
SECTION ONE

basic principles
CHAPTER ONE

the neuron

• ANATOMY •

The neuron is the cell that is the most basic unit of the nervous system. In the central nervous system (CNS), the neuron is contained completely within the brain or the spinal cord. In the peripheral nervous system (PNS), the neuron is located in such a way that it communicates between the CNS (the brain and spinal cord) and the rest of the body. In the PNS, therefore, the neuron has its cell body located either within the spinal cord, for the motor neuron, or next to it in the dorsal root ganglion, for the sensory neuron. The cell process that extends from the cell body to the periphery is called the axon for both the motor neuron and the sensory neuron. The motor neuron’s distal part, the axon, is located outside the CNS, enabling the motor neuron to send an effector message from within the CNS to a motor end-organ in the periphery, like a muscle in the hand. The sensory neuron’s distal part, the axon, is also located outside the CNS, enabling the sensory neuron to transmit toward the brain a message from a sensory receptor in the periphery, like the Meissner corpuscle in a fingertip. The process that extends from the cell body into the spinal cord is called the dendrite for both the motor and the sensory neuron. The cell body for the motor neuron is located in the ventral horn of the spinal cord. The cell body for the sensory neuron is located in the dorsal root ganglion (see Figure 1.1). A ganglion is a collection of cell bodies.
Figure 1.1: The motor neuron (top) has its cell body in the ventral horn of the spinal cord, and its axon extends to a skeletal muscle. Its central process, the dendrite, communicates with the central nervous system by receiving messages that have been transmitted along the pyramidal tract directly from the motor cortex in the precentral gyrus of the brain. The sensory neuron (bottom) has its cell body in the dorsal root ganglion and its axon extends to a sensory receptor in the fingertip. Its central process, the dendrite, communicates with the central nervous system through a series of relay stations that modify the series of neural impulses in anatomic regions such as the thalamus before the final input reaches the sensory cortex in the post-central gyrus of the brain.

**Sympathetic and parasympathetic neurons** are specialized forms of motor neurons. Instead of going from the CNS to a skeletal muscle, these effector cells go to such endorgans as the sweat glands, the erector pili muscles at the base of hair follicles, and the muscles in the walls of the arteries. The difference in function between the sympathetic and the parasympathetic neurons is exemplified by penile function. In general, the parasympathetic neuron causes a relaxation or inhibition. This activity, with respect to penile function, causes vasodilatation, resulting in an increase in blood flow into the corpora cavernosa, creating an erection. In general, the sympathetic neuron causes increased activity. With respect to penile function, this causes contraction of the muscles in the prostatic urethra, resulting in ejaculation. (See Chapter 17, “The Penis,” for more information on this subject.) The cell bodies for these neurons are located just lateral to the ventral horn in the intermediate or lateral grey region of the spinal cord, or in ganglia that lie along the spinal cord (paraspinal ganglia), like the stellate ganglion in the neck or the lumbar ganglia in the back.

There are other neurons that lie within the brain that control functions outside the brain but are still considered part of the CNS. For example, the autonomic nervous system is primarily controlled by neurons that give rise to the vagus nerve, the 10th cranial nerve. These neurons are located in the brain stem, travel through the base of the skull to enter the neck, and then innervate the heart and the gastrointestinal system. Overactivity of the autonomic neurons of the vagus nerve can cause fainting (syncope) by causing an inhibition of the heart muscle. Two of the cranial nerves are contained totally within the CNS. These are (a) the olfactory nerve (smell), the first cranial nerve, and (b) the optic nerve (vision), the second cranial nerve. Even the end organs of these two cranial nerves, the retina of the eye and the olfactory lobes, are embryologically part of the CNS. Although the neurons of the rest of the cranial nerves are located within the CNS, their axons travel outside the CNS; therefore, with regard to neural regeneration, they behave like peripheral nerves and can regenerate. Thus, division of the optic nerve results in blindness.
which, so far, cannot be restored by nerve repair, whereas division of the facial nerve results in facial paralysis, which can be restored by nerve repair.

The neuron does not exist alone, but rather functions in conjunction with a host of supporting cells which, in the CNS are called glial cells. Examples of glial cells are the astrocyte and oligodendrocyte. The analogous cell in the PNS is called the Schwann cell. The axon is always ensheathed by a glial cell process. In the PNS, every axon is ensheathed by Schwann cells. The axons that conduct impulses the fastest require a form of insulation, which is myelin, a lipoprotein. One Schwann cell relates to each myelinated axon at any given site along its length. Many Schwann cells are required to ensheathe an axon along its entire length. The slower conducting axons of the PNS are not myelinated. One Schwann cell ensheathes more than one unmyelinated axon (see Figure 1.2). In the CNS, the oligodendrocyte makes a myelin protein, too, but it differs in its chemical composition.

Figure 1.2: Electron micrograph from the rat sciatic nerve, demonstrating large and small myelinated axons (MA), each of which is ensheathed by a single Schwann cell (SCN), and unmyelinated axons (ua), a cluster of which is ensheathed by a single Schwann cell (osmium stain, magnified 2000x). The large myelinated axon may range from 15 to 20 microns in diameter, the small myelinated axons may range from 2 to 4 microns in diameter, and the unmyelinated axons may range from 0.5 to 1.5 microns in diameter. The large myelinated axons subserve both muscle function and the perception of touch. The small myelinated fibers subserve the perception of pain. The unmyelinated fibers subserve the perception of hot and cold, as well a burning pain. Photo courtesy of A. Lee Dellon, M.D.

Schwann cells, in addition to making myelin, serve another critical support function for the peripheral nerve, which is to make nerve growth factor. It is this critical support function that the Schwann cell performs for the peripheral nerve, that the oligodendrocyte does not perform for the CNS, that enables the peripheral nerve to regenerate. Furthermore, it is likely that certain supporting cells of the CNS, perhaps the astrocytes, make a glycoprotein that actually inhibits the efforts of injured CNS neurons to regenerate. We know this because if a peripheral nerve is
placed into the spinal cord, the neurons of the CNS will regenerate into the peripheral nerve, where the Schwann cells create an environment hospitable for neural regeneration, whereas those same CNS neurons will not regenerate sufficiently to reestablish function in the spinal cord.

The word nerve is usually not meant to imply a neuron, but rather a peripheral or cranial nerve. A nerve is composed of hundreds, and more commonly tens of thousands, of nerve fibers, which are the axons of the neuron. A neuron is microscopic. Table 1.1 lists a classification of neurons that is based on their size and myelination. This classification by Erlanger and Gasser (1937) of Johns Hopkins University was awarded the Nobel Prize in physiology and medicine. In contrast, a nerve is composed of a longitudinal array of neurons. The word fascicle, which is commonly used to refer to such a collection, is derived from the Latin word fasciculus, meaning bundle. Each fascicle is surrounded by a serial coating or layers of connective tissue called the perineurium, which creates a unique environment for the individual neurons, which are also called nerve fibers. The space within the fascicle also contains elastic fibers and collagen fibers, and is called the endoneurium. The small blood vessels within this space are therefore called the endoneurial microvessels.

<table>
<thead>
<tr>
<th>Group</th>
<th>Myelination</th>
<th>Size</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\alpha)</td>
<td>myelinated</td>
<td>15-20 microns</td>
<td>motor</td>
</tr>
<tr>
<td>(\beta)</td>
<td>myelinated</td>
<td>10-15 microns</td>
<td>touch</td>
</tr>
<tr>
<td>(\delta)</td>
<td>myelinated</td>
<td>2-5 microns</td>
<td>sticking pain &amp; temperature</td>
</tr>
<tr>
<td>(C)</td>
<td>unmyelinated</td>
<td>0.5-1.5 microns</td>
<td>burning pain</td>
</tr>
</tbody>
</table>


The collection of fascicles surrounded by connective tissue is called the nerve, the peripheral nerve, or the cranial nerve. The connective tissue uniting these fascicles is called the epineurium. The epineurium between the fascicles is called the interfascicular epineurium, and the epineurium that surrounds the circumference of the nerve is termed the external epineurium (see Figure 1.3). The epineurium and the perineurium each contain elastin fibers (see Figure 1.4). These terms are important to define because they will be used to describe both the normal and the pathophysiologic condition of the nerve, and to describe surgical strategies to repair and reconstruct the nerve.
The most critical function a nerve fiber must be capable of performing is the transmission of an impulse that will conduct a message from one location to another. To do this, the cell membrane of the neuron is specialized to permit the passage of sodium and potassium ions through regions of its lipoprotein structure. These regions are often called channels. Energy is required to maintain the integrity of these channels which, at a biochemical level, use the energy-rich phosphate bond of adenine triphosphate (ATP) to power the so-called sodium/potassium pump. When this pump is functioning, there exists an electrical difference between the outside and the inside of the neuron’s membrane. A particular stimulus will destabilize this system, permitting potassium to flow into the neuron, initiating the chain of molecular events that result in the conduction or propagation of an electrical impulse along the axon. The speed with which this impulse travels is about 1 to 2 m/s along an unmyelinated axon.
Figure 1.4: The physiological environment established by the fascicle is due to the blood/nerve barrier that is created by the right junctions of the endothelial cells lining the perineurial arterioles. When the blood/nerve barrier is intact (A), the fluorescent dye (reddish color) remains within the blood vessels, and the endoneurial environment (green is color) is protected. When the blood nerve barrier is damaged as for example, after 8 hours of ischemia (B) or after local pressure of 400 mm Hg for 2 hours (C), then the blood vessel wall becomes permeable, and the fluorescent dye escapes into the endoneurium. The ability of the nerve to glide with adjacent joint movements, and for fascicles to glide with respect to other fascicles and respond within limits to stretch and traction injuries, is due to the viscoelastic properties of the structural proteins elastin and collagen. These structural proteins are denoted by their histochemical and ultrastructural properties. From *Nerve Injury and Repair*, by G. Ludbrog, 1988. Edinburgh: Churchill Livingstone. Reprinted with permission of the authors.

The speed of propagation is increased by having the Schwann cells arrange themselves along the length of the axon, forming myelinated rings around the axon and leaving small unmyelinated regions between one Schwann cell and the next. These regions are called the nodes of Ranvier, and the distance between them is the internodal length. If the impulse jumps from one node to the other, the conduction is called saltatory conduction, and is much faster than if the impulse moves linearly along the axon. If the myelin is thicker, this insulation layer further increases the speed of impulse conduction. Thus, a greater internode distance and thicker myelin will permit conduction velocities greater than 60 m/s, such as is found in the Group A-alpha (motor) and Group A-beta (touch) fibers. This is in contrast to the thinner Group A-delta (pain)
fibers which conduct at about 20 m/s, and the unmyelinated C-fibers, which conduct at about 2 m/s. Electrodiagnostic testing uses these properties of the peripheral nerve.

An individual nerve fiber must maintain communication between its end in the spinal cord and its end in the extremity. This distance can be more than 3 feet long for the sensory nerve fibers to the big toe. Communication is achieved by means of axoplasmic flow. Despite the stationary appearance given to the nerve by histologic sections, the axon is a dynamic environment. The microtubules within the axoplasm are composed of the protein tubulin, which acts as a transit system, using energy to transport structural proteins. These are necessary to maintain the integrity of the cell membrane and for neural regeneration, where they form the growth cone. This system is called the slow component of anterograde axoplasmic transport, and may moves these macromolecules at speeds of 2-30 m/s. The fast component of axoplasmic transport moves at the speed of 40-400 m/s, and moves smaller chemicals like the neurotransmitters. Information from the periphery, such as growth factors, can be transmitted backward to the nucleus by retrograde axoplasmic transport, also at speeds of 2-30 m/s (see figure 1.5). Many pathologic conditions, like the neuropathy of diabetes or the neurotoxic complications of chemotherapy (vincristine, cisplatin, taxol), manifest themselves through interruption of axoplasmic transport (see Chapter 14).

The group A-beta class of nerve fibers have special physiologic properties of adaptation that are useful in understanding the perception of touch. These nerve fibers are related to the skin by specialized mechanoreceptors and are, therefore, also called mechanoreceptive afferents. If these nerve fibers are isolated and individually recorded, their electrophysiology may be studied under

Figure 1.5: The relationship of the nucleus to the distant structures of the peripheral nerve is maintained by the transportation of molecules through the cell. This process is called axoplasmic transport. The transport that goes from the nucleus is anterograde, and has slow and fast components. The fast component (motorcycle) transports smaller molecules, like the neurotransmitter acetylcholine (ACh). The slow component (railroad hand cart) transports macromolecules (blocks) required for maintaining the cell membrane. These structural proteins are moved along the system of microtubules within the axoplasm. The transport that goes from the cell's most peripheral end toward the nucleus is retrograde transport, slowly transporting (rickshaw) molecules like nerve growth factor (NGF) from the Schwann cell. Drawing by Glenn George Dellon. Reprinted with permission.

The group A-beta class of nerve fibers have special physiologic properties of adaptation that are useful in understanding the perception of touch. These nerve fibers are related to the skin by specialized mechanoreceptors and are, therefore, also called mechanoreceptive afferents. If these nerve fibers are isolated and individually recorded, their electrophysiology may be studied under
conditions in which the fingertip is given well-defined sensory stimuli. This type of research work led Vernon B. Mountcastle, Professor of Neurophysiology at Johns Hopkins University School of Medicine, to classify these group A-beta fibers into slowly- and quickly-adapting fibers (Mountcastle, 1968). The slowly-adapting fibers begin to transmit impulses as soon as the fingertip is touched, and will continue to generate impulses for the entire time the stimulus remains in contact with the skin surface. During this time of stimulus contact only the rate of impulse generation decreases; that is, it adapts slowly to the stimulus. This stimulus would be perceived as constant- or static-touch. If the force applied to this constant-touch stimulus increases, which would be perceived as increased pressure, the slowly adapting fiber will increase its rate of firing. The sensory receptor associated with this type of fiber is the Merkel cell neurite complex in the glabrous (non-hairy) skin, and the Ruffini end-organ in hairy skin (see Figure 1.6).

Two subtypes of slowly-adapting fibers can be distinguished electrophysiologically. Type I does all that has just been described. Type II, in addition, has a regular spontaneous discharge and responds to lateral stretching of the skin. While Type II is called a Ruffini-type, the Ruffini end-organ has not been identified in glabrous skin, and for glabrous skin the identity of the exact receptor ending remains undefined. In contrast, the quickly-adapting fibers generate just one or two impulses and then stop firing during a constant-touch stimulus. The quickly-adapting fiber will generate another impulse when the constant-touch stimulus stops, giving rise to an “on/off” type response; that is, it adapts quickly to the stimulus. The quickly-adapting fiber will not increase its rate of firing in response to an increase in stimulus intensity and, therefore, cannot transmit information about perception of pressure. The Pacinian and Meissner corpuscles are both quickly-adapting receptors associated with the quickly-adapting fibers in glabrous skin, while the hair follicle is the corresponding receptor in hairy skin (see Figure 1.6 and Table 1.2).
The quickly-adapting group A-beta fibers are also responsible for the perception of movement and vibration. The quick response to any touch stimuli permits a series of different quickly-adapting fibers to respond to a horizontally moving touch in a sequence that corresponds to the direction of movement (see Figure 1.7B). This same physiologic property permits any given group of quickly-adapting fibers in the vicinity of a vertically varying touch stimulus, such as the oscillating end of a tuning fork, to mediate the perception of vibration. While any quickly-adapting fiber will respond to any frequency vibration, provided that the stimulus intensity is sufficiently strong, there are two major subdivisions with response to frequency. Those quickly-adapting fibers that are associated with Pacinian corpuscles are most sensitive to high-frequency stimuli, at about 256Hz (cycles per second). Those quickly-adapting fibers that are associated with Meissner corpuscles are most sensitive to low-frequency stimuli, at about 30 Hz. As will be discussed in detail in Chapter 4, regarding neural regeneration, it is easier to reinnervate a Meissner corpuscle than a Pacinian corpuscle. Therefore, these two subpopulations of fibers/receptors recover at different rates during nerve recovery. These physiologic properties have application to sensibility testing in that tuning forks of different frequencies can be used to evaluate these different subpopulations of nerve fibers (see Table 1.2).

<table>
<thead>
<tr>
<th>Nerve Fiber Type</th>
<th>Receptor</th>
<th>Perception</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slowly-Adapting I</td>
<td>Merkel cell</td>
<td>constant-touch pressure</td>
</tr>
<tr>
<td>Slowly-Adapting II</td>
<td>Ruffini end-organ</td>
<td>constant-touch pressure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>lateral stretch</td>
</tr>
<tr>
<td>Quickly-Adapting</td>
<td>Meissner corpuscle</td>
<td>movement vibration (30 Hz)</td>
</tr>
<tr>
<td>Quickly-Adapting</td>
<td>Pacinian corpuscle</td>
<td>movement vibration (256 Hz)</td>
</tr>
</tbody>
</table>

Figure 1.7 (1-i): Slowly and quickly-adapting nerve fibers. (A) The slowly-adapting fibers detect the presence of stimuli of varying pressure. The heavier the weight of the stimulus, the greater the pressure, and the more frequent the neural impulses generated. (B) The quickly-adapting fibers detect the presence of movement. These fibers send an impulse after each is stimulated. Patterns of impulses result in movement perception. Drawing by Glenn George Dellon. Reprinted with permission

This overview of sensory fiber/receptor correlations is simplified to present a theoretical framework for sensibility testing that has been clinically useful for the past 25 years. For example, because the examiner’s hand has small but real intrinsic oscillations, as does a patient’s, even a constant-touch stimulus will set off some quickly-adapting fibers. However, as will be discussed in detail in the section on reliability and validity of sensibility testing (see Chapters 5, 6, and 7), the perception by the patient is that the test stimulus is stationary, that is, not moving, at the spot being tested. This perception is due to the signal processing that occurs of the impulses generated at the periphery as they travel to the post-central gyrus through the second and third order sensory ganglia and the thalamus. An analogy would be the way the signal processing in the auditory system enables you to hear radio music by filtering out the static.

<table>
<thead>
<tr>
<th>Seddon/Sunderland</th>
<th>Pathophysiology</th>
<th>Type of Regeneration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurapraxia</td>
<td>metabolic block or demyelination</td>
<td>complete in 3 to 6 weeks</td>
</tr>
<tr>
<td>Axonotmesis</td>
<td>loss of axonal continuity</td>
<td>complete at 1 mm/day</td>
</tr>
<tr>
<td></td>
<td>3rd degree</td>
<td>incomplete at 1 mm/day</td>
</tr>
<tr>
<td></td>
<td>4th degree</td>
<td>none</td>
</tr>
<tr>
<td></td>
<td>5th degree</td>
<td>none</td>
</tr>
<tr>
<td>Neurotmesis</td>
<td>loss of continuity</td>
<td>none</td>
</tr>
</tbody>
</table>
The neuron’s response to injury depends on the nature of the injury. While it is true that if the neuron dies there will be no function of that nerve fiber, an injury may be such that the nerve fiber stops transmitting or generating impulses even though the neuron is still biologically alive. The function of a given peripheral nerve, like the median nerve, is the sum of all the individual nerve fibers it contains. The ability to evaluate the sensibility of skin supplied by the median nerve will depend, therefore, on understanding the effect on the neuron of various degrees of injury, and on the connective tissues that support the tens of thousands of nerve fibers within the peripheral nerve. The ability to understand the basis for a patient's symptoms and signs, and the ability to devise an appropriate rehabilitation plan, also will depend on understanding the peripheral nerve’s response to injury.

At the neuron level, it is well documented that the response to complete transection of the axon is for the distal portion of the nerve to die. These observations were made by August Waller in 1850 in the glossopharyngeal and hypoglossal nerves of the frog, and are still referred to as Wallerian degeneration. The axoplasm degenerates and the Schwann cell ingests the myelin. The basement membrane that surrounds the Schwann cell, and which is elaborated by the Schwann cell, remains because the Schwann cell is still alive. These basement membrane profiles surrounding the Schwann cell processes appear as bands or tubes depending on the histologic section, and remain indefinitely in the degenerated peripheral nerve. The perineurium remains after the nerve is divided, as does the connective tissue of the epineurium and the endoneurium; therefore, the degenerated peripheral nerve remains unchanged in its clinical appearance from a normal nerve. As will be discussed in Chapter 4 on neural regeneration, this condition of the distal nerve is ideal because there is no fibrosis or scarring within the nerve distally to impede the regenerating axon. If the nerve division is repaired, peripheral nerve function can be recovered to some degree once the nerve fibers have regenerated to the periphery (at about 1 mm/day or 1 in. /month).

In contrast, if the peripheral nerve is injured by a stretch/traction type of injury, or a severe crush, then the nerve fibers can also be completely disrupted, and Wallerian degeneration will occur just the same as if the nerve had been sharply divided. However, in the case of stretch/traction or crush mechanisms of injury, the connective tissue components of the nerve are injured over a given length, and respond to that injury with varying degrees of increased collagen formation. This collagen creates a scar blockade that may completely prevent axonal regeneration through the injured region if the divided ends of the nerve are repaired. In another mechanism, the nerve fibers may remain anatomically completely intact, but cease to function. This can occur from lack of oxygen (ischemia) or chemical mechanisms (ionic block, like a local anesthetic). In this situation, no Wallerian degeneration occurs because the connection of the distal axon to the nucleus (and axoplasmic flow) remains intact, and complete nerve function can be recovered quickly when this temporary biochemical situation is reversed biochemically. These concepts regarding the mechanism of injury, response to injury, and clinical recovery have been described by both Seddon (1975) and Sunderland (1978). These concepts remain conceptually valid and clinically useful and are correlated in Table 1.3 and Figure 1.8.
The response of the central portion of the neuron to injury is to prepare for repair. This occurs within the nucleus by changes that reflect increased amounts of messenger RNA activity designed to produce the structural proteins and meet the energy requirements for axonal sprouting and elongation. However, if the level of nerve fiber transection is sufficiently close to the cell body in the spinal cord or dorsal root ganglia, then the loss of cell volume resulting from Wallerian degeneration appears to be too severe, and a percentage of the neurons will die. In those neurons that survive, the portion of the axon just proximal to the site of transection will have axonal loss for just the first internode length. The portion of the axon just proximal to this will be the site of growth cone formation within the first 12 to 18 hours after injury.

The response of the sensory receptors to injury is described in Chapter 2.
**REFERENCES**


Waller, A. Experiments on the section of the glossopharyngeal and hypoglossal nerves of the frog, and observations of the alterations produced thereby in the structure of their primitive fibers. *Philosophical Transactions of the Royal Society of London* 140:423-429, 1850.

**ADDITIONAL READINGS**


CHAPTER TWO

Cutaneous Sensory Receptors

- CRETACEOUS PARK AND GLABROUS SKIN -

The cutaneous sensory receptors, the “encapsulated” structures in the dermis, the Meissner corpuscles, Pacinian corpuscles, and the Merkel cell neurite complexes, must be organized to transmit stimuli from the skin to the central nervous system. The stimulus is presented to the skin as some form of energy which must be transduced into a neural impulse. For example, the perception of heat occurs because the energy that is transferred from the hot stimulus through the skin initiates a neural impulse. This impulse travels to the dorsal column of the spinal cord, and is then relayed through specific pathways to the opposite side of the brain that enable the sensory cortex to interpret those impulse patterns as being due to a stimulus whose temperature is greater than that of the skin it stimulated.

Because skin all over the body must be able to perform this particular protective sensory function, no unique skin modification and no unique sensory end-organ developed. Furthermore, the earliest forms of life needed to detect temperature changes. Therefore, the sensory receptor that mediates the perception of temperature is the simplest: the “free” nerve ending. (Free nerve endings do not relate to specific receptors.) The same general considerations apply to the perception of pain, which is also mediated by free nerve endings, or terminals. The diffuse layer of thinly myelinated and unmyelinated nerve networks in the dermis, and the free nerve endings in the base of the epidermis, are the physical manifestations of these receptors, and they are uniformly represented throughout the body surface area. These neural nets were surely present in the vertebrates that existed in the Jurassic period of geologic time, about 135-180 million years ago.

In the Cretaceous period, which was the most recent period of the Mesozoic era, from 70-135 million years ago, the dinosaurs were gone. Animals like the duck and the goose, with more
specialized skin regions, such as the bill, originated. These animals did not have fingers and toes, but rather used their bills to search beneath the water for food. The neural network is still present in the animals of this time period, but now their bills contain an encapsulated end-organ, the Herbst corpuscle, which is analogous to the Pacinian corpuscle and the quickly-adapting fiber/receptor system. Their bills also contain an expanded-tip ending of the nerve in close approximation to an epithelial cell, originally described by Grandy (1869), which is analogous to the Merkel cell neurite complex and the slowly-adapting fiber/receptor system.

Mammals of the Cretaceous period had other unique nasal skin modifications that helped their survival. The mole, for example, is blind and must rely on the sensory apparatus in its snout. This snout sensory organ was described by Eimer (1871), and contains an encapsulated end-organ and an expanded tip-ending in conjunction with an epithelial cell. The opossum, in the geologic transition time between the Cretaceous and the more recent Eocene period, has Pacinian and Merkel cell neurite complexes in its snout. It is not, however, until we reach the mouse, one of the earliest rodents, that we find the forerunner of the first Meissner corpuscle, an encapsulated sensory end-organ with more than one nerve entering it, and a lobulated appearance, quite different from the Herbst corpuscle of the birds. Finally, all suborders of primates, including humans, have the specialized skin at the fingertips that contain the definitive arrangement for transduction of mechanical stimuli. This arrangement, as depicted in Figure 2.1, arose between 35 and 55 million years ago.

The specialized relationship between the Merkel cell neurite complex and the papillary ridge maximizes the transduction of vertical forces against the skin into impulses to mediate the perception of constant-touch of varying intensity, or pressure. So, too, does the location of the Meissner corpuscle on either side of the intermediate ridge in the dermal papillae. A movement across the fingertip will transfer its horizontal component of force to the papillary ridge, causing it to move within the space bounded by the limiting ridges (see Figure 2.1), much like a pendulum. The movement of the intermediate ridge causes direct stimulation of the Meissner corpuscle. This is similar to what you experience when you ride across railroad tracks in your car; your horizontal motion is transformed into a vertical, oscillatory motion by the tracks. This low-frequency perturbation, or vibration, is what the Meissner afferents, quickly-adapting group A-beta fibers (see Chapter 1) are best at mediating.
Figure 2.1: The fingertip is hairless skin that has been modified by the presence of papillary ridges, or fingerprints. Directly beneath that is the intermediate ridge of dermis into which sweat glands (SG) send their ducts (SD). The Merkel cells are located about the intermediate ridge in proximity to the sweat ducts (MD), and are innervated by a Slowly-adapting nerve fiber to form the Merkel cell-neurite complex. The Pacinian corpuscle is located in the subcutaneous layer (PC), and is innervated by a single quickly-adapting fiber. The Meissner corpuscle (MC) line the dermal papillae on either side of the intermediate ridge, and are each innervated by more than one quickly-adapting fiber. In this view a portion of the epidermis has been removed to demonstrate the array of sensory corpuscles organized with respect to the papillary ridges. Note that the intermediate ridge is free to swing pendulum-like in the dermis within the space bounded by the limiting ridge’s collagen attachment to the deeper tissues. From Evaluation of Sensibility and Re-education of Sensation in the Hand, by A. L Dellon, 1981. Baltimore: Williams & Wilkins. Reprinted with permission of the author.

Electron microscopy has clarified the fact that the “encapsulated” end-organ, like the Meissner corpuscle, is not really bounded by a capsule. The myelinated nerve fiber loses its myelin upon entering the corpuscle. The Schwann cell processes continue to ensheath the axons, and the Schwann cell nucleus represents the supporting cell and its nucleus of the corpuscle. The space between the cell processes is contiguous with the extracellular space of the
dermal papillae. In contrast, the Pacinian corpuscle represents one axon that is completely bounded by *concentric lamellae* of supporting structures. This large corpuscle is exquisitely sensitive to mechanical stimuli. For example, it is the Pacinian corpuscle that mediates the perception of the very gentle stimulus of a breeze blowing against the skin. The Merkel cell is a clear cell histologically, which ultrastructurally contains granules that contain an as yet unidentified neurotransmitter.

The relationship between the sensory end-organs and the myelinated nerve fiber is critical to understanding the order of sensory recovery during neural regeneration (see Chapter 4). Table 2.1 lists the ratio of nerve fibers innervating the end-organ to the end-organ. From this calculation it is clear that the Meissner corpuscle will be the easiest to reinnervate because any of 9 different nerves may innervate it, and from any direction. In contrast, the football-shaped Pacinian corpuscle may only be reinnervated by a single nerve fiber entering it at precisely one of its tapered ends. The Merkel cell neurite complex is also hard to reinnervate, in that one nerve must make contact with more than one Merkel cell. Since transduction of constant-touch probably still occurs even if all the Merkel cells are not reinnervated, achieving function of the high-frequency, quicklyadapting fiber/receptor system is the most difficult. For the reinnervated Merkel cell neurite complex, recovered function will be with a lower than normal innervation density and a higher than normal threshold for stimulation. For the Pacinian, reinnervation may not occur at all. The Meissner afferents have the potential to achieve near-normal innervation density with close to a normal threshold for stimulation. These theoretical formulations have been observed during single-unit nerve fiber recordings in baboons following median nerve repair by Terzis, Dykes, and Hakstian (1976), and by many clinicians in observing patients following nerve repair if they test their patients with 30 and 256 Hz tuning forks, and with two-point discrimination testing.

**• NON-GLABROUS SKIN •**

The sensory receptor of the hairy skin is the hair follicle. The same four types of group A-beta fibers that exist in *glabrous* skin are present in hairy skin. When these fiber types grow toward the skin from their *dermal plexus* they encounter, instead of various epidermal ridges, hair follicles. The quickly-adapting fibers form *lanceolate endings* around the base of the hair follicles. The slowly-adapting fibers form expanded-tip endings in relationship to the hair follicle, as well as the Ruffini end-organ (see Figure 2.2). Similar structures have been identified in animals, and direct recordings of them made. It is clear that while the number of nerve fibers in a given area of hairy skin is less than in a given area of glabrous skin, hairy skin is able to transduce all the same stimuli as nonhairy skin.

### Table 2.1 Numerical Relationship of A-beta Fibers to Their Sensory Receptors

<table>
<thead>
<tr>
<th>Receptor</th>
<th>Number of Fibers</th>
<th>Number of Receptors</th>
<th>Ratio (fibers/receptors)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pacinian</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Meissner</td>
<td>1-9</td>
<td>1</td>
<td>&gt;1</td>
</tr>
<tr>
<td>Merkel cell</td>
<td>1</td>
<td>4–5</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>
Figure 2.2: Hairy skin sensory receptors are the hair follicles. The lanceolate ending about the hair follicle base and shaft, as shown here, is a quickly-adapting fiber/receptor system similar to the Meissner corpuscle. The expanded tip-ending in conjunction with epithelial cells at the base of certain hair follicles (not shown) is a slowly-adapting fiber/receptor system to the Merkel cell-neurile complex. In the hairy skin, this is the Ruffini end-organ. Photo courtesy of Bryce Junger, PhD, Department of Anatomy, University of Tasmania, Australia.

**OTHER SENSORY RECEPTORS RELATED TO THE SKIN**

There are regions of the skin surface that are best considered as transition zones. The vermillion of the lip is one such zone, being a transition between skin and mucous membrane. This zone was observed by Krause (1866) to contain a rounded sensory end-organ innervated by a large myelinated fiber that became known as the *Krause end-bulb*. Krause end-bulbs were identified by Krause in the conjunctiva of the eye and in the tip of the penis. No one has identified them in the glabrous skin. Von Fry (1896) assigned the Krause end-bulb to be the sensory receptor for the perception of cold. This is now known to be incorrect; as described in Chapter 1, the free nerve ending of the thinly myelinated fibers subserve the perception of cold. Krause end-bulbs are best considered as quickly-adapting receptors whose supporting cells differ from those of the Meissner corpuscle due to the nature of the skin covering itself. These are best termed the mucocutaneous end-organ, and should be considered in the series midway between
the Meissner corpuscle of glabrous skin and the lanceolate ending of the hairy skin. A histologic example of the mucocutaneous end-organ from the penis is given in Figure 17.3.

![Figure 2.3A: Response of Meissner corpuscle to progressive denervation and reinnervation over 9 months. The Meissner corpuscles in the finger-tip skin of the monkey and are surrounded by the normal dermis (photomicrographs [160 x1]). Silver stain stains axons black.]

The sensory receptors related to muscles and joints will be discussed in Chapter 3. Among these are the Ruffini spray endings. As indicated above for the Krause end-bulb, von Fry (1896) ascribed the perception of heat to the Ruffini ending. This, too, is now known to be incorrect. The Ruffini end-organ is a slowly-adapting, large, myelinated fiber/receptor which mediates information regarding stretching for the joints, as it does for the skin.

- **DENNERVATION AND REINNERVATION**

The transection of the nerve to cutaneous sensory receptors initiates a predictable and well-documented series of events that has critical clinical importance. Wallerian degeneration (see Chapter 1) occurs in the axon. For the thinly myelinated A-delta fibers and the unmyelinated C-fibers that mediate the perception of temperature and pain, this is the whole story because they have free nerve endings; that is, they do not relate to specific receptors. At any length of time after the nerve division, the nerve fibers can (a) be reconstructed by any known and accepted technique (see Chapter 4), (b) be expected to regenerate distally, (c) reinnervate skin, and (d) reestablish perception of temperature and pain. For the large, myelinated A-beta fibers that mediate the perception of touch, the response of their specialized end-organs to denervation is to undergo various degrees of degeneration based on their unique connective tissue components.

The onion-bulb-like concentric layers of the Pacinian corpuscle are most resistant to change following denervation. Examples of virtually unchanged, although axonless, Pacinian corpuscles have been documented years after proximal nerve injury. The reason it is difficult to reinnervate the Pacinian afferents after nerve reconstruction is not because the end-organ is no longer present, but because, as was discussed above, it is difficult for a regenerating axon to directly contact the opening at one end of this large (up to 4 mm in size) structure.
The response of the more loosely knit lobular structure of the Meissner corpuscle to denervation also has been well documented (see Figures 2.3 A and 2.3 B). There is progressive shrinkage of the connective tissue components following denervation, but the lamellar cells, which are modified Schwann cells, remain alive, and can form relationships again with regenerating axons, giving the appearance that the Meissner corpuscle can be reinnervated. The same sequence is expected for the Merkel cell neurite complex as for the Meissner corpuscle. Studies similar to those illustrated in Figure 2.3 for the Meissner have been done for a Merkel cell-related structure in the cat, the touch dome, which is a slowly-adapting fiber/receptor system. These studies, by Burgess and Horch (1973), demonstrate complete disappearance of the touch dome after denervation, but reappearance of it in the same location after reinnervation. This is predictable, given that the Merkel cell is an epithelial cell not dependent on the axon on survival, but only for some trophic interaction that may result in its size and appearance. The epithelial cell will remain in its unique position in the dermis, and be available for reestablishing the expanded-tip/epithelial cell interaction that creates the unique slowly-adapting mechanoreceptor properties.

Figure 2.3B (A) is the normal appearance of the corpuscle. After division of the median nerve, the complete loss of axons is noted in (B) 480 hours after nerve division, and (C) after 6 weeks, when Wallerian degeneration has been completed. Note the progressive decrease in size of the corpuscle’s connective tissue components following Wallerian degeneration. The median nerve was primarily repaired at the wrist level in this monkey, and the earliest axons to reinnervate the corpuscle are apparent with silver stain at (D) 3 months after repair there is progressive reinnervation during the (E) 6-

It may be hypothesized that the denervated lamellar cells of the Meissner corpuscle, and the denervated Merkel cell, being Schwann cell analogues, have the capacity to respond to loss of neurotrophic interaction with the axon following denervation by upregulating the genes that produce nerve growth factor. It may be the release of nerve growth factor by these supporting cells in the dermis that permits the regenerating axon sprouts to find their way back to these potential end-organ sites (see Figure 2.4). This implies that at any time following nerve injury, it is possible to recover some degree of touch sensation by nerve reconstruction (see Figure 2.5).

**Figure 2.4:** The regenerating sensory axon leave the subdermal plexus and begin their approach to the dermis, most likely following the chemical gradient of neurotrophic substances, like nerve growth factor (NGF, symbolized by filled circle and hollow squares). The NGF is probably synthesized and released by the former connective tissue components of the Meissner corpuscle (filled circles) or the former epithelial cell component of the Merkel cell-neurite complex (hollow squares) at precise locations along the base of the epidermis (see Figure 2.1). It is likely that a degree of misconnection will still occur, such that the quickly-adapting fiber that formerly innervated a Meissner corpuscle or a Pacinian corpuscle will now enter the complex of Merkel cells. The resulting abnormalities in threshold and innervation density provide the need for sensory rehabilitation. Drawn by Glenn George Dellon. Reprinted with permission.

**Figure 2.5:** Effect of delay in nerve suture upon the final degree of sensory recovery. Using the British classification system, S4 is a normal degree of sensation, S3+ has “some” two-point discrimination, S3 has touch perception without hyperalgesia, and S1 and S2 are of just sufficient sensibility to provide protective function. These studies, published in the late 1950s on patients with median nerve injuries, demonstrate that if more than 6 month elapsed after nerve injury, protective sensation can always be recovered, but functional sensibility may not be recovered. It should be noted that in interpreting these graphs, none of the patient in the early studies had the benefit of sensory reeducation. From Evaluation of Sensibility and Re-education of Sensation in the Hand, by A. L. Dellon, 1981, Baltimore: Williams & Wilkin. Adapted with permission of the authors.
This is clearly different from the situation with muscle in which, if the regenerating axon does not reach the muscle by about 1 year following denervation, the muscle cell, though still alive, no longer produces the acetylcholinesterase (AchE) receptor necessary to reestablish the motor endplate and, therefore, cannot be reinnervated. The reinnervation of the Meissner corpuscle in Figure 2.3 appears normal; however, it is not clear that after a prolonged period of time the reinnervated corpuscle or the reestablished Merkel cell neurite complex is capable of achieving normal thresholds, and it is unlikely that the complex events of regeneration will permit normal innervation density (see Figures 2.3 & 2.4). Furthermore, the nerve growth factor may attract a slowly-adapting fiber that used to relate to a Merkel cell to reinnervate a dermal papilla and interact with the lamellar cells of a former Meissner corpuscle. The net effect of this inappropriate reinnervation is unclear. These types of abnormal reinnervation patterns among the cutaneous sensory receptors create the need for sensory rehabilitation, which will be described in Chapter 12.

Finally, it is appropriate now to consider a study that correlates much of the information in these first two chapters. Because the innervation density in normal skin is high, biopsy of normally innervated fingertip skin would yield too many receptors to correlate with any measurements of sensibility. However, fingertip biopsy of the middle finger of a patient about 6 months after median nerve repair at the wrist permitted careful sensibility testing of this small region of skin, which then could be biopsied. Serial sections of this specimen permitted a correlation of the reinnervated sensory receptors with the clinical measurements (Dellon & Munger, 1983). The results of that study confirmed in humans the electrophysiological studies done in animals, and the theoretical considerations that went into the correlations in Table 1.2. This type of clinical research has provided the basis for the approach to evaluating sensibility that will be described in Chapters 6 and 7.

REFERENCES

• ADDITIONAL READINGS •


proprioception

• CONTRIBUTION FROM JOINTS •

Proprioception is our awareness of the position of our joints. If you have a person shut their eyes and then move their finger so it is either flexed or extended, the person can you tell you correctly whether it is flexed or extended. In fact, a person can usually tell correctly within a few degrees the position of the extremity of a joint. It seems only reasonable that this should be a function of the joint receptors. And there are, without any doubt, well-documented Pacinian corpuscles and Ruffini end-organs within joints. They are located within the ligaments and within the capsules of joints. These two sensory receptors are related to the same quickly-and slowly-adapting fibers as their counterparts in the fingertips and in hairy skin. Classical neurology teaches that an injury to the posterior columns of the spinal cord causes loss of proprioception. It seems perfectly straightforward, then, that proprioception is due to the sensory afferents coming from the joint structures. However, this is not clinically true.

Moberg (1984) made observations that argued against proprioception being due primarily to joint receptors. These observations have been confirmed by direct basic and clinical research by others, and should be taken as true.

These observations include:

1. Injection of local anesthetic into a joint, which anesthetizes the joint receptors, does not cause loss of position sense.

2. Following a surgical procedure to replace a joint, like the hip, with an artificial joint, the patient can still identify the position of the joint within 5-10 a (Grigg, Finerman, & Riley, 1973).

3. Direct recording of the afferent nerves from a joint in the cat demonstrated few if any impulses during the normal range of motion of that joint, but showed rapid impulse
generation as the extremes of joint range of motion are reached (Clark & Burgess, 1975; Grigg & Greenspan, 1977).

4. Direct recording of the afferent impulses from the human in whom the finger was taken through a range of motion, demonstrated almost no activity from nerve fibers that had no cutaneous receptive field (Clark, Horch, & Bach, 1979).

**CONTRIBUTION FROM MUSCLE**

A muscle sense has been described in humans (Gelfan & Carter, 1967). This implies that humans are conscious of the movement of the muscles themselves and, therefore, that the movement of the muscles that cause movement of a joint may be responsible for proprioception.

This premise has been directly tested and found not to be true. For example, during surgery to decompress the carpal tunnel in humans, just the skin for the incision can be anesthetized. With the patient’s eyes covered, all the flexor tendons at the wrist level can be pulled, simulating what would occur if the muscle contracted. Similarly, the tendons can be pulled distally, as they would be if the finger were extended. When this is done, the patient is not aware that the finger has moved at all, until the muscle is stretched sufficiently to cause movement of the overlying skin.

There are an enormous number of sensory receptors within the musculotendinous system. The names for these are the muscle spindle, located within the muscle, and the Golgi tendon-organ (see Figure 3.1 on next page). These sensory receptors, which will not be the subject of much discussion in this textbook, are organized so that their impulses travel to the cerebellum, not to the cerebral cortex. Thus, all the sensory input from the muscle and tendon goes to a subconscious level. Imagine if we were aware of all the different tensions within every muscle of our body every second of the day! It is safe to conclude that muscle sense is not related to proprioception.

It is likely that in the future, as we begin to appreciate the availability of sensory receptors within muscle, a cutaneous sensory nerve may be sutured to a motor nerve in the hope of restoring sensibility to areas difficult to reconstruct by traditional techniques. Up to one-third of the fibers in a so-called pure motor nerve are sensory and not motor, representing the sensory nerve fibers from the muscle spindles and tendon-organs. Chang, DeArmond, and Buncke (1986) observed, for example, that if the sural nerve was sutured to the motor branch (thoracodorsal nerve) of the latissimus dorsi muscle being transferred to a microvascular free flap for heel coverage, the patient appeared to recover the ability to perceive sensation through the skin-grafted muscle. These motor afferents previously reported to the cerebral cortex. However, I hypothesized in 1991 that with regeneration of the cutaneous afferents into the muscle sensory receptors, so that they innervate the muscle spindles or Golgi tendon-organs, touching the muscle would transmit sensory impulses to the conscious level, permitting perception of sensation in a reconstructed foot (see Figure 3.2).
Figure 3.1: The normal muscle spindle, (A) Pattern of toluidine blue-stained muscle spindles (dark spots) in three sections of a hamstring muscle from the cat, at 10x magnification (B) Transection of a muscle spindle at its widest zone lying next to muscle fibers, at 400x magnification. (C) Electron microscope image of the mitochondria-filled sensory axon within the muscle spindle, immediately adjacent to the intrafusal actin/myosin muscle filaments, at 10,000x magnification. Photos Reproduced with permission of the Mark DeSantis (1990), University of Idaho.
**CONTRIBUTION FROM SKIN**

There were some very early observations that suggested a relationship between cutaneous sensibility and proprioception. For example, Fox and Klemperer (1942) noted that among a series of patients they were testing, there were some who had lost proprioception and who also had lost vibratory perception. Moberg (1972) carried out a series of anesthetic blocks to areas of skin, and tested proprioception in patients who had lost sensibility in various areas of skin due to nerve injuries. He noted that if the patient had lost cutaneous sensibility in the area of skin that would be stretched by movement of the underlying joint, then the patient also lost proprioception for that joint. Moberg also directly noted that proprioception for the proximal interphalangeal...
joint of the finger was most directly related to static two-point discrimination in the fingertip of that finger (Moberg, 1976).

These observations, taken in conjunction with the observations given above for joint receptors and for muscle sense, lead me to conclude, as did Moberg, that:

The musculotendinous afferents which affect primarily synergistic/antagonistic muscle balances and report to the subconscious are not responsible for proprioception.

The joint receptors, which appear to begin entering the conscious level only as potentially injurious joint activity (extremes) is approached, are not responsible for proprioception.

The large myelinated nerves subserving cutaneous sensibility are responsible primarily for our awareness of joint position (proprioception) in the normal range of motion.

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● REFERENCES ●


Moberg, E. Fingers were made before forks. Hand 4:201-206, 1972.


● ADDITIONAL READINGS ●


A
n injured peripheral nerve will attempt to repair itself through the process of neural regeneration. Individual neurons have their nucleus in the dorsal root ganglion or in the ventral horn of the spinal cord, and most of these nuclei survive an injury as long as it occurs within the extremity. As discussed in Chapter 1, if the injury to the nerve is quite proximal, for example, within the brachial plexus, many more of the nuclei die as a direct result of the mechanism of injury itself. This greatly reduces the ultimate possibilities for functional recovery because there are fewer neurons to regenerate.

The process of neural regeneration begins with receipt by the nucleus of an injury message. While it is not clear what the exact mechanism is, it is most likely that an influx of extracellular calcium into the damaged nerve initiates a series of molecular events that alerts the nucleus to the injury. For example, a calcium influx causes certain protein complexes to alter their function. The nucleus, geared to receiving certain trophic messages from the periphery by retrograde axoplasmic transport, recognizes that something has changed distally. The nucleus responds by preparing to rebuild its damaged cell membranes and to extend its axon toward the periphery in an attempt to reestablish communication with its motor and sensory end-organs. Within 12 to 18 hours after disruption of the axon, the nucleus has responded sufficiently to its changed message pattern that the injured distal end of the axon has been transformed into a growth cone. Each injured axon will produce up to 15 axon sprouts, each of which will have its own growth cone (see Figure 4.1).
Figure 4.1: (A) Neural regeneration may be visualized by observing the events that occur proximally to the end of the individual nerve fiber after nerve transection. (B) There is a retrograde loss if at least the first node of Ranvier, and perhaps more if the mechanism of injury is more forceful. From the internode just proximal to this, the axon will form up to 15 sprouts (C) Each of these will regenerate distally, spearheaded by its growth cone. The growth cone has numerous filopodia that seek out trophic factor and contact guidance cues from the environment. The basement membrane serves as the most important contact guidance cue. Schwann cells will migrate distally with the regenerating axon. (D) Finally, a regenerating unit is formed containing many sprouts from the same axon, ensheathed by the same Schwann cell. Once one growth cone makes the appropriate contact with its target organ, the remaining sprouts will be recalled, or pruned. From Surgery of the Peripheral Nerve, by S. E. Mackinnon & A. L. Dellon, 1988, New York: Thieme Publishing, Reprinted with permission of the authors.

The growth cone is a highly active site for exploration of the environment. The goal of that exploration is to regenerate distally toward the appropriate site, that site being the previously innervated skin or muscle. This goal is achieved by the active extension of small, feet-like projections called filopodia into the adjacent environment. The membrane of these feelers responds to chemical gradients that might signal an appropriate distal target. Such chemicals have been called neurotrophic factors. The first to be identified was nerve growth factor (NGF). Rita Levi-Montalcini was awarded the Nobel Prize for the discovery of NGF in 1952. Many trophic factors have since been isolated, each of which has its own unique set of nerve fiber types that it will stimulate, as well as other cells that it can stimulate.

Trophic factors are proteins that are regulated by genes. They are probably all expressed, or upregulated, in a particular sequence during embryonic development and growth, and then are
downregulated once that growth has been achieved. Nerve injury appears to resequence embryonic events, causing upregulation of these growth factors. It is clear now that Schwann cells in the distal portion of the injured nerve, in response to Wallerian degeneration, undergo changes that permit them to phagocytose myelin, and to upregulate the production of NGF. Thus, the growth cone, as it extends distally into its new environment, has an increasingly strong gradient of NGF it can follow in an attempt to find its former distal end. It is possible that the end-organs themselves, the muscle cell, or the supporting cells of the sensory corpuscles also make certain neurotrophic factors that become significant once the growth cone has reached the end of its journey.

The growth cone can also respond to directional cues given by proteins in its immediate environment. The growth cone is attracted particularly to negatively charged proteins. The basement membrane is composed of three proteins that have the highest ability to attract the growth cone. These proteins are laminen, fibronectin, and type IV collagen. Researchers such as Letourneau (1983) have spread a trail of laminen onto a culture dish and observed the growth cone to track only along its surface. Once the growth cone touches basement membrane, its filopodia attaches based on the charged molecules. The growth cone contains the contractile protein actin, the same protein present in muscle. Upon attaching to basement membrane, the filopodia contract in response to the actin, pulling the proximal end of the nerve distally. This is the process known as axonal elongation. This process requires a great deal of energy and transport of structural proteins. Time-lapse movies of the regenerating nerve demonstrate the growth cone to be highly active (see Figure 4.2). The net result of all this activity is the regeneration of the injured nerve at the rate of about 1 mm/day.


The concepts of neural regeneration just reviewed will clarify one traditional teaching that is incorrect, and will resolve two traditional controversies. The traditional teaching was that regenerating axons take about 3 weeks to cross the suture line, and another 3 weeks at the distal end, once they reached the skin or muscle, to reestablish function with their end-organs. It is clear from the above discussion, however, that such a set of delay periods does not occur. This has direct application for the length of time required for postoperative immobilization of the reconstructed nerve.
The first controversy was whether any segment of nerve could be the source for neural regeneration (Dellon & Dellon, 1993). This led to studies in which fragments of sensory nerve were placed between ends of motor nerves, and vice versa. That 19th century controversy was resolved with the realization that neural regeneration had to proceed from the central neuron distally, regardless of whether it was a motor or sensory nerve. The second controversy was between neurotropism and contact guidance. This led to studies in which various substances were plated in tissue culture to evaluate contact guidance, and to studies in which various straight and y-shaped tubes were placed between two ends of nerves. That 20th century controversy was resolved with the realization that both neurotropism and contact guidance occur during neural regeneration.

Lundborg’s group, in Malmo, Sweden, have been leaders in elucidating the process of neural regeneration in silicone chambers (Lundborg, 1988). Brushart and Seiler (1987) conduct research to study whether the specificity of the regenerating nerve is controlled by unique molecules in
the basement membrane of motor fibers that are not present in sensory fibers, and to study central mechanisms by which axons that have regenerated to an inappropriate place are recalled, or pruned back, once one of their sibling sprouts reaches the appropriate target endorgan (see Figure 4.3). These strategies are of value in choosing surgical techniques for nerve reconstruction: for example, whether to use a bioabsorbable nerve conduit to reconstruct nerve gaps of up to 3 cm.

The events related to neural regeneration described above occur without exception and for all nerve fiber types. The thinly myelinated, large myelinated, and unmyelinated nerve fibers all develop growth cones and axon sprouts, respond to neurotrophic factors, and have contact guidance. The rate of axonal regeneration is enzymatically controlled, and theoretically all these fiber types should regenerate at the same rate. However, it has been observed clinically that this is not the case (Dellon, 1981). The perception of pain and temperature occurs before that of the touch submodalities. It may be that this is related to the size of the volume of the axoplasm that must be regenerated for each of these fibers the unmyelinated and thinly myelinated fibers would require much less volume of axoplasm than would the much larger diameter touch fibers. If a given nucleus can produce axoplasm at a given rate, then the larger diameter touch fibers would be the last to recover function if their thin axon sprouts were to arrive at a point similar in time to the pain and temperature fibers (see Figure 4.4). This clinical finding is important in devising a strategy for testing sensibility in the nerve following reconstruction.

**Figure 4.4:** During regeneration the nucleus of the neuron must assemble the building materials necessary for axonal elongation. The rate for this is fixed biochemically. The nucleus for the thin fibers must produce axoplasm and cell membrane components at the same rate as the nucleus for the large myelinated fibers. Regardless of their ultimate nerve fiber diameter all regenerating sprouts are about the same size, which is thin. Clinically, however, regeneration is observed to occur first for those nerve fibers which ultimately will have small diameters that is, those that detect pain and temperature, whereas those with large diameter nerve fibers, that is, those that detect touch, are the last to recover it is as if there were a pump in the nucleus producing at a fixed rate; therefore, it is easier to fill the volume required for the smaller fibers than it is for the larger ones. Drawing by Glenn George Dellon. Reprinted with permission.

**NEUROMA**

When neural regeneration is proceeding without interference, there are often sensations perceived by the patient that are disturbing. They may feel sharp shooting pains, hot or cold flashes, water running down their arm, buzzing, tingling, numbness, or sometimes nothing at all. During regeneration, these perceptions are expected, and the patient should be made aware prior
to nerve reconstruction that they will occur. The treatment for the patient who is uncomfortable during this time is discussed in Chapter 12 under desensitization. However, when the expected course of regeneration is blocked by scar, by disruption of nerve reconstruction, or by some other misfortune, the result is that regenerating sprouts become trapped in the wrong environment and are thwarted in their attempt to regenerate distally.

These sprouts become surrounded by connective tissue and are, by definition, therefore, termed a neuroma (see Figure 4.5). However, a neuroma is not by definition painful. If the neuroma is in an environment related to tendon movement or joint motion, then the entrapped distal end of failed regenerating units will signal painful messages whenever the neuroma is stimulated by movement of the adjacent soft tissues. Clearly, direct pressure on the neuroma will stimulate it, too. Often, these neuromas are in an environment in which adjacent nerve fibers that would not normally communicate with each other do communicate with each other. This cross talk is the result of an abnormal or ephaptic conduction, which is an interneuron communication without a normal synapse. This has been documented between the various Adelta and C-fibers in neuromas in rats as well as in monkeys, and may represent the pain generator site within the neuroma (Meyer et al., 1985).

If the neuroma is on a motor nerve, like the posterior interosseous nerve, the sensory fibers within that nerve that carry impulses from the joints that are also innervated by that nerve, can signal aching or pain from that joint. This, for example, can be the source of wrist pain from wrist sprains, from healed distal radius fractures, or even from a fused wrist (Dellon & Horner, 1993). The best technique to demonstrate that pain is due to a neuroma of a particular nerve is to block that nerve with a local anesthetic (see Figure 4.6). If the patient’s perceived pain is relieved by the injection of xylocaine or marcaine into the tissues adjacent to the nerve, the source of the pain signal has been confirmed. The nerve itself should never be directly injected with anything, since this interfascicular injection, in and of itself, could injure the nerve and create another source of pain. The nonsurgical techniques to treat a painful neuroma include desensitization and splinting by the therapist, injection of steroids into the vicinity of the neuroma by the physician, steroid iontophoresis by the therapist and, ultimately, resection of the neuroma by the surgeon.
Figure 4.6: Nerve blocks with a local anesthetic are the best technique to demonstrate that a particular nerve is the source of pain. This is illustrated here by the technique to block the anterior and posterior interosseous nerves just proximal to the wrist in evaluating the source of wrist pain. From “Partial Wrist Denervation,” by G. Horner & A. L. Dellon, 1993, in Problems in Plastic and Reconstructive Surgery: The Wrist, S. Levin, Editor, Philadelphia: Lippincott. Reprinted with permission of the authors.

The treatment of neuroma pain by the surgeon requires (a) the ability to determine precisely which nerve or nerves are the source of pain, and (b) a strategy to treat the end of the nerve from which the neuroma has been resected, so that another painful neuroma does not develop as the nerve again goes through the natural sequence of neural regeneration. Nerve blocks are the most sure technique to prove the source of the pain. A nerve should not be resected for the treatment of pain unless such a block relieves the pain and the patient agrees to accept the degree of sensory loss that will inevitably follow such a resection.

More than one nerve may be involved in the pain problem. For example, about 75% of patients have both the lateral antebrachial and the radial sensory nerve overlap in providing axons to the dorsoradial aspect of the wrist. A very small percentage may even have a third nerve, the palmar cutaneous branch of the median nerve, supply fibers to this area at its volar border, or the dorsal cutaneous branch of the ulnar nerve of the posterior cutaneous nerve of the forearm may supply fibers to this area at its dorsal border.

This emphasizes the importance of diagnostic nerve blocks. The surgical strategy for treatment of a painful neuroma must include resection of the neuroma to remove the pain-generating source, and then relocating the proximal end of the nerve into a site away from movement, direct pressure, and sensory neurotrophic stimuli (see Figure 4.7). These requirements for the new location are best met by implanting the end of the nerve into a large muscle which has relatively little excursion. The commonest neuromas that cause pain in the upper extremity are those over the dorsum of the hand, and the usual approach requires resection of both the lateral antebrachial cutaneous nerve and the radial sensory nerve, and implantation of
both of these nerves into the brachioradialis muscle (see Figure 4.7) (Dellon & Mackinnon, 1986; Mackinnon & Dellon, 1987).

Figure 4.7: Example of the treatment of a painful neuroma of the dorsoradial aspect of the hand. (A) Nerve blocks identify the 3 appropriate nerves. (B) Both the lateral antebrachial cutaneous nerve and the radial sensory nerve have had their neuroma resected. (C) The proximal end of each nerve is implanted into the deep surface of the bradioradialis. (D) Clinical example of painful neuroma of palmar cutaneous branch of median nerve, identified by nerve block. A block in the forearm, at the radial sensory nerve, did not relieve pain. (E) This patient also had a neurolaxis of the median nerve for recurrent carpal tunnel syndrome. Note the palmar cutaneous nerve between the retractor which, in (F), is implanted into the pronator quadratus muscle. (A) (B) (C) from “results of Treatment of Recurrent Dorsoradial Wrist Neuromas,” by E. E. Mackinnon & A. L. Dellon, 1987, Annals of Plastic Surgery 19:54-61. With permission of Lippincott-Raven Publishers. (D) (E) (F), from “Implantation of Palmar Cutaneous Branch of the Median Nerve into the Pronator Quadratus for Treatment of Painful Neuroma,” by G. R D Evans & A. L. Dellon, 1994, Churchill Livingston Journal of Hand Surgery 19A: 204-205. Reprinted with permission of the authors.

**REFLEX SYMPATHETHIC DYSTROPHY**

Reflex sympathetic dystrophy, or RSD, is a well-defined, if still poorly understood, clinical problem. Because the patient’s complaints are those of diffuse pain, many clinically painful
conditions are misdiagnosed as RSD. Today, the diagnosis of RSD should be given for a clinical pain problem only when the following criteria are satisfied (Mackinnon & Holder, 1984):

1. There is a region of diffuse pain not in the distribution of a single peripheral nerve;
2. There is swelling and/or stiffness of the region that is affected by the pain;
3. There are signs of sympathetic overactivity, for example, sweating, coldness, or color change;
4. There is impaired function of the affected part.

It should be clear from the above criteria that RSD can be applied to parts of the body other than the hand, such as the foot. While the region affected by RSD can be extensive, it almost always begins distally, and extends proximally. This means that a part of the body affected with RSD is not in the middle of two uninvolved areas; that is, if there is a problem with the elbow, but the hand and shoulder are normal, the criteria for RSD have not been met. RSD also is not burning pain in the distribution of a single peripheral nerve, for example, in the index finger and thumb. This type of pain was described by Silas Weir Mitchell (1872), a neurologist, during the Civil War. He observed soldiers injured by musket ball fire, and called this pain “causalgia.”

The best conceptual framework in which to understand diagnosis and treatment strategies for RSD is one in which a normal reflex continues to occur. The most well-known reflexes are the knee-jerk and the blink. With a blink, a sensory stimulus, which is visual, occurs, is processed in the brain, and a motor response, the rapid closure of the eyelid, occurs. With the knee-jerk, a sensory stimulus, which is the perception that the quadriceps tendon has been stretched, occurs, is processed in the spinal cord, and a motor response, knee extension, occurs (see Figure 4.8). With any pain stimulus, there is normally a response mediated through the spinal cord that prepares the body for emergency. The sympathetic nervous system is the motor system (see Chapter 1) for this normal response to pain. Thus, the normal reflex is for a sensory stimulus, pain, to occur, for this to be processed in the spinal cord and, finally, for the motor response (hair stands up, sweating occurs, blood vessels constrict) to occur. Note that normally a sympathetic response is not painful.

Figure 4.8: The classic reflex involves a sensory stimulus that is transmitted through the spinal cord and causes a motor response in the periphery, this is typified by the knee-jerk. The response of the stretch receptors to the quadriceps tendon being percussed is to generate neural impulses that are processed through the dorsal root entry zone of the spinal cord. Through an intermediary neuron, the motor neuron in the ventral horn of the spinal cord causes a contraction of the quadriceps muscle, resulting in the knee jerk. Drawing by Glenn George Dellon. Reprinted with permission.

A hypothesis that seems plausible to explain pain associated with sympathetic activity is that the pain reflex continues to occur because there is a continuing source of pain, for example, an injured intact nerve, such as a neuroma-in-continuity, or one or more disrupted nerves. The
spinal cord, then, in response to a continuous input of pain impulses, alters its usual firing pattern in the dorsal root entry zone. Intermediary neurons begin continually to relay and stimulate the sympathetic neurons to fire. This much has been demonstrated in animal experiments. The mechanism by which the release of the normally nonpain-producing norepinephrine neurotransmitter from the sympathetic ending elicits the perception of pain is still conjectural. It is possible that the C-and A-delta fibers upregulate norepinephrine receptors as a response to pain or persistent pain, that these transmitters are transported to the periphery, and in that location the norepinephrine released by the sympathetic nerve endings can give rise to a pain stimulus. What is clear from this conceptual framework is that RSD must be approached by strategies that attempt to eliminate the continuing source of pain impulses arising from injured peripheral nerves, as well as by strategies that attempt to block sympathetic activity (see Figure 4.9).

Figure 4.9: (A) Hypothetical reflex arc of reflex sympathetic dystrophy (RSD). The response of the C- and A-delta pain fibers to a pain stimulus, such as a crush injury, is to generate neural impulses that are processed through the dorsal root entry zone of the spinal cord. Through a relay neuron, the sympathetic neuron in the intermediate grey of the spinal cord is stimulated, and generates a sympathetic response in the periphery. This is due to release of the neurotransmitter, norepinephrine, whose alpha-adrenergic stimulation causes hair follicle erection, sweat production, and arterial vasoconstriction. None of these normal sympathetic responses is painful. In RSD, the entire hand or foot (B and C), not just the injured part, will be painful, swollen, and stiff. It is possible that in response to persistent pain, C-and A-delta fibers develop a norepinephrine receptor, or else they always have such a receptor but it is inactive. In RSD, this norepinephrine receptor on the C- and A-delta fibers can respond to the norepinephrine released during the sympathetic stimulation. This conceptual framework suggests that strategies to treat RSD should include plans to eliminate the source of the pain signal from the original injury, as well as to eliminate the sympathetic discharge. Illustration (A) by Glenn George Dellon. Illustrations (B) and (C) copyright A. Lee Dellon. Reprinted with permission.

The therapist is often the first person involved in the patient’s care to note the onset of RSD. RSD evolves from an acute stage, when it can be most successfully treated, to more chronic
stages, when secondary problems, such as joint stiffness and drug dependence, greatly diminish the chances for a successful outcome. In the earliest stage, the therapist will note that the hand is cool, sweating, and swollen even at the start of therapy. If these signs develop during therapy, the therapist must carefully note this and inform the referring physician. For reasons that are unclear, too much activity appears to set off RSD. This may be due to chemical mediators of the inflammatory process, like prostaglandins and interleukins, that are released into the soft tissues by the already inflamed and/or damaged connective tissues and ligaments from the original injury.

The therapist must learn to gauge the capacity of each individual hand for therapy. Measurement of hand volume with the traditional water displacement methods should occur before and after each treatment session. Measurement of skin compliance at selected sites of the hand may be found to give another aspect of quantitation of edema, hardness, or stiffness that is either complimentary to, or may replace, the volumetric measurement. Skin compliance may be checked easily during therapy, and if the measurements demonstrate increased hardness (decreased compliance), therapy may be altered or the session curtailed for that day (see Chapter 21, “Potential Research Projects for Therapists”).

At this earliest stage, the most appropriate diagnostic test is a 3-phase flow study. This radiographic imaging is often called a bone scan, uses Technetium 99, and in the third, or 3-hour phase of the scan will demonstrate increased uptake of nucleotide diffusely throughout all the joints of the fingers and wrist. If the 3-hour, or delayed phase, of the bone scan is normal, it is highly unlikely that the patient has RSD. The delayed phase of the bone scan is almost always positive in a patient with the acute stage of RSD.

The initial treatment of RSD by the physician should include referral for a stellate ganglion block for the upper extremity, and for a lumbar sympathetic block for RSD of the lower extremity. A series of blocks is often required. For a block to be successful there must be a decrease in the patient’s pain without loss of sensation in the limb that is blocked. If the anesthetic agent spills over from the sympathetic ganglia to the roots of the brachial plexus, then the patient might experience pain relief in the hand because the pain impulses from the periphery were blocked on their way to the cortex, and not because of the decreased sympathetic activity.

During a successful sympathetic block, the extremity becomes more pink, and warmer. Associated with the stellate ganglion block is Homer’s syndrome, during which the patient will experience on the same side as the block narrowing of the pupil (miosis), drooping of the upper lid (ptosis), and dryness of the eye (anhydrosis). This is due to disruption of the sympathetic fibers to the eye. For the upper extremity, a more distal blockade of the sympathetic nervous system may be tried, such as an axillary block. Another regional anesthetic technique useful for treating RSD is a Bier block. A Bier block replaces all the blood in the extremity with a local anesthetic agent, with or without a drug to inhibit the sympathetic nervous system, like reserpine (which depletes the terminals of norepinephrine), or guanethidine (which blocks the transmitter). If there is stiffness in the extremity, steroid may be added to the solution that is infused into it.

The duration of pain relief from a successful initial sympathetic block may range from hours to permanent relief. If there is only brief relief, it is appropriate to repeat the block. If the hand is quite stiff, but has been too painful for therapy, the therapist should be called in during the time of the block to begin active and passive range of motion as soon as possible. This may be started even in the anesthesia induction room, where the Bier block is often done. This therapy may even be required on an inpatient basis. Sometimes an indwelling axillary block catheter can be placed for the upper extremity, or an indwelling catheter left in the epidural space for the lower extremity. This technique permits daily inpatient therapy with good pain control.
Once interruption of the pain generating nerve(s) has occurred, it is appropriate to institute rehabilitation at a pace geared to each individual. We have no way to measure the degree of therapy that will be tolerated for any given individual. Unfortunately, this means that at some point in therapy, even if geared to the individual’s level of discomfort and with monitoring of extremity swelling, there may come a time when there will be a flare-up of the dystrophy. If this occurs too frequently, repeated stellate or lumbar blocks may be required, and if so, this may identify the individual who will require a sympathectomy in addition to the interruption of peripheral pain pathways. Prior to a surgical sympathectomy, it is reasonable to test the patient’s response to an intravenous sympatholytic agent, like propranolol. Pain relief, in response to this chemical sympathectomy, as described by Raja, Treede, Davis, and Campbell (1991), identifies a patient with sympathetically maintained pain.

If the patient fails to achieve pain relief from sympathetic blocks, whether intravenous or regional, then the possibility of a central nervous system pain-generating mechanism must be considered. Such individuals become candidates for implantation by neurosurgeons of dorsal column stimulators. While implantation of such stimulators along more proximal aspects of the peripheral nervous system have been suggested for pain control, such a peripheral source of pain control can be confirmed by regional anesthetic blocks of these peripheral nerves. Interruption of nerve function at such a location is probably more predictable than implantation of peripheral nerve stimulators, since the silicone sheaths that attach even the most sophisticated implantable neural stimulators can themselves become a source of chronic nerve compression and pain. Although reflex sympathetic dystrophy can be a devastating problem, cautious optimism may be displayed by those involved in the patient’s care. Appropriate use of radiographic imaging, local anesthetic, and intravenous sympatholytic agents for diagnosis will assure all those involved that the diagnosis is correct. Specific therapy can be determined again by local and regional anesthetic blocks for therapy, leading to strategies to interrupt peripheral nerve pain generating signals, to regain control of the sympathetic overactivity. Rehabilitation efforts must be an integral part of the overall treatment plan from the very beginning. This approach can salvage many patients with RSD, returning them to productive lives. (see Figures 4.9 & 11.10)

Figure 4.10: Nerve graft nomenclature (A) an autograft is a nerve from one person put into that same person, in contrast to an allo-graft, which is a nerve from one person placed into another person, or a xenograft, which is a graft from one species placed into another species. (B) a trunk graft was an entire large diameter nerves used as the graft. These are poorly vascularized and result in poor nerve function (C) the cable graft referred to several nerves twisted together. This also results in poor vascularization [see next page] (D) the best nerve graft results are obtained with the Millesi’s approach, that is, several small diameter grafts placed alongside each other to obtain optimal vascularization. From “Management of Peripheral Nerve injuries: Basic Principles of Microneurosurgical Repair”. By A. L. Dellon, 1992, Oral Maxiofacial Surgery Clinics—North America 4:393-403 Reprinted with permission of the author. [cont’d next page]
Nerve repair is the appropriate terminology for the surgical technique that joins two nerve ends together. These two ends can be from the same nerve, such as in repairing a divided digital nerve, or from two different nerves, such as in reinnervating the tip of the median nerve-supplied index finger by rerouting a digital nerve from the ulnar-supplied ring finger (see Chapter 13). When a segment of one nerve is interposed between two ends of another nerve, and the ends of the interposed nerve segment are joined to the ends of the other nerve, the interposed segment is termed a nerve graft. The technique of joining the ends of the nerve in a nerve graft may be the same as those used for a nerve repair, but traditionally a nerve repair does not refer to a nerve graft. When nerve ends are joined it is correct to speak of repairing them, connecting them, reconstructing them, or of a nerve juncture, but the term anastomoses is not correct. Anastomoses refers to the joining of two hollow structures, like blood vessels.

Suturing is not the only technique for repairing a nerve. Because it requires time for the surgeon to do a nerve repair by placing sutures, and because the suture material itself may serve as a source of scarring, techniques other than suturing have been developed. The two ends of a nerve may be safely connected by the means of a glue. Fibrin, a natural protein contained in blood, has been separated from blood, then separated from possible blood-born infectious agents, such as HIV virus. It is available, at least in Europe, for use in the operating room to place between the ends of nerve. Neural regeneration proceeds normally through a fibrin interface. Laser has been used to weld together two ends of a nerve by forming a heat-induced coagulum between the nerve ends, and this, too, does not impede neural regeneration.

The two ends of a nerve can be brought together by wrapping something around the nerve, again using a strategy that is designed to remove any suture material from within the nerve. Nerve wrapping, or entubulation, also offers the theoretical advantage of confining the regenerating axon sprouts to prevent them from growing into surrounding tissues. This provides the benefit of guiding the axons distally and minimizing the extent of a suture line, in-continuity neuroma. Such neuromas, which form in some degree at most nerve repair sites, may be a source of postoperative pain. The wrapping technique has a disadvantage, which is that if the wrapping material is nonabsorbable, such as silicone, it will remain around the regenerated nerve and may become a site of chronic nerve compression or irritation.

A final variation on nerve repair is related to techniques that minimize tension at the repair site and minimize damage to the neural tissue itself. A technique employing freezing the ends of the nerve prior to trimming them, bathing the nerve ends in a chemical solution that minimizes
calcium ion shifts, and suturing the nerve to a background sheet of material at a distance from the actual nerve repair site has been investigated by deMedinacelli, Wyatt, and Freed (1983).

The exact connective tissue site within the nerve, and the timing of the nerve repair with respect to the time of injury, are two other classic points for discussion about nerve repair technique. In general, if the nerve subserves a single function, such as sensory to the index finger, simply placing two 8-0 or 10-0 nylon sutures through the epineurium is sufficient for the nerve repair. In a nerve with multiple fascicles, which subserve many different functions, such as the median nerve at the wrist, it is ideal to do an interfascicular dissection proximally, identify the different fascicles distally, and do individual fascicular repairs, with two 8-0 or 10-0 nylon sutures for the motor fascicle to the thenar muscles, the common volar digital nerve to the middle/ring web space, the common volar digital nerve to the index/middle web space, and the sensory fascicles to the thumb and the radial side of the index finger. These sutures may be placed into the perineurium. Care to avoid too much intraneural scarring due to dissection is required. In a multifascicular nerve in which the function subserved by each fascicle is not known with any degree of certainty, such as in the median nerve in the upper arm, the best strategy is to do an epineural repair of the entire nerve. If several groups of fascicles are readily identified, a grouped-fascicular repair should be done, in which case the sutures may actually go through both the inter-fascicular epineurium and the perineurium.

With respect to the timing of a nerve repair it is best to repair the nerve as soon after it is injured as possible, as long as certain other considerations are met. These considerations include the wound being clean, the nerve injury being relatively sharp, the patient’s physical condition permitting, and the availability of appropriate operating facilities and a surgeon trained in microsurgery.

A nerve repair performed soon after the injury occurs is called a primary nerve repair. If the nerve cannot be repaired for the first few days, the repair is termed a delayed primary. If the repair is done after about 3 weeks, it is best to call this a secondary nerve repair. After 3 weeks, the injured ends of the nerve will have formed thickened, rounded ends, called the proximal neuroma and the distal glioma. These will require resection back to normal, nonscarred nerve for the nerve repair to be successful. Usually, such a resection creates a gap between the nerve ends that cannot be closed without creating too much tension at the nerve repair site. This tension would prevent good neural regeneration and, in this situation, a nerve graft would become the preferred technique for nerve reconstruction, rather than a nerve repair. The results of nerve repair for various nerves are given in Chapter 11.

NERVE GRAFT

A nerve graft is a technique which places a nerve segment from one nerve into a nerve defect in another nerve. The simple division of a peripheral nerve creates a gap between the two ends of the nerve due to the nerve’s inherent elastic properties. While there is some tension placed on a suture line that reconnects the two ends of such a divided nerve, this tension has little effect on the amount of scar tissue formed by the fibroblasts in the nerve during neural regeneration. However if a piece of nerve is removed, either by the injury itself or by the surgeon excising scarring from the injured nerve, then there is a true deficiency of nerve tissue, called a nerve defect. If the ends of the divided nerve are united by a suture when there is a nerve defect, then there is sufficient tension at the suture line to cause an increase in the amount of collagen deposited at the site of nerve healing. This collagen is type I collagen and creates a barrier for the
regenerating axon, as opposed to the type IV collagen normally present in basement membrane, which is useful for contact guidance neural regeneration (see above). Thus, tension is to be avoided at the nerve repair site. For this reason, the results of repairing a nerve defect by direct nerve repair have been unsuccessful. Indeed, it is because the results of repairing a nerve defect by flexing adjacent joints and hauling the ends of the nerve together with large sutures has been so unsuccessful that surgeons, under the leadership of Hano Millesi, began in the mid 1970s to return to nerve grafting as a technique for nerve reconstruction (Millesi, 1972).

The practical objection to nerve grafting was that the nerve grafts that were used during World War I simply did not work. Reevaluation of that technique by Millesi (1974) led to the realization that the nerves used for the graft were large diameter, or trunk grafts (see Figure 4.10). These grafts required revascularization for survival as a tissue, as do all nonvascularized tissue transfers. The centers of these large diameter nerves became poorly vascularized and, therefore, fibrosed. These internally scarred nerves were then a poor conduit for neural regeneration. In addition to recognizing and then proving that nerve repair under tension resulted in increased scar at the suture line, Millesi realized using small diameter nerves as a graft would correct this problem. Finally, Millesi employed the concept of internal neurolysis to divide a large nerve into its component functional groups, as described above by the terms grouped fascicular repair or perineurial repair, and applied this to nerve grafting.

Thus came the currently accepted technique of using small diameter cutaneous nerves to reconstruct a nerve defect by placing them as interfascicular interposition nerve grafts. These grafts are laid side by side to encourage vascularization, rather than intertwining them to produce what was termed a cable graft, which would place portions of nerve centrally and discourage vascularization. The theoretical disadvantages to nerve grafting are that time must be spent harvesting the donor nerve, there is scarring at the nerve graft donor site, and there is a sensory loss at the donor site with the potential for a painful neuroma proximally at the site of nerve transection. A further theoretical disadvantage is that the regenerating nerve must cross two sites of nerve repair, giving the potential for two sites of nerve disruption and two sites for a painful incontinuity neuroma. Table 4.1 lists the commonest sites for nerve graft harvesting and the potential areas of sensory loss.

Despite the practical and theoretical disadvantages of nerve grafting, the overall results of reconstructing nerve injuries would be improved without question if more nerve grafting were done. Even when it is clear to the surgeon at the time of injury that the mechanism of injury will require a large amount of nerve to be resected due to ensuing fibrosis that will surely occur over the next 3 weeks, the surgeon more often than not will carry out a primary nerve repair rather than close the wound and return in 3 weeks to do a secondary nerve graft. The results of neural regeneration through this scarred nerve repair site are often accepted as the final result, rather than returning to the operating room in 6 months, when it is clear that functional sensibility will not be recovered. It is not surprising, then, that there has been a search to replace autogenous nerve grafting with some substitute.

The patient’s own muscle and vein have been used instead of nerve to reconstruct a nerve defect. The vein is used as a nerve conduit, simply placing one end of the nerve into each end of the vein. The nerve will regenerate through this vein, although with functional results that are not as good as those achieved with bioabsorbable conduits (see Chapter 12). Muscle must first be frozen and thawed through several cycles with liquid nitrogen. This treatment kills the muscle cells, but leaves intact the basement membrane that surrounds each muscle cell (Glasby, Gschmeissner, Hitchcock, & Huang, 1986). Remember that it is the basement membrane (plus the Schwann cells) that survive in the nerve graft. Thus, acellular muscle is essentially a
basement membrane scaffolding through or along which the nerve can regenerate. Clinical trials with freeze/thawed muscle interposition grafting have been done in England, where this technique originated. Unfortunately, however, they do not result in as good functional recovery for sensibility when used to reconstruct a mixed motor/sensory nerve as do conventional nerve grafts (see Chapter 12).

Figure 4.11: Nerve Conduit. In this series of intraoperative photo, a 3cm segment of the monkey ulnar nerve at the elbow has been reconstructed with a bioabsorbable polyglycolic acid (PGA) Neurotube™. Photos (A) and (C) are at the time of surgery, and photos (B) and (D) are 1 year later at the time specimens were obtained for histologic assessment of the results of neural regeneration. In (A) and (B), the control group used traditional interposition interfascicular sural nerve grafts in (C) and (D) are the Neurotube™ group. Note that in (B) even with microsurgical repair, there are still incontinuity suture line neuroma formed at both repair sites. Not that in (D), after the Neurotube™ has been absorbed, there is what appears to be a normal nerve bridging the original 3cm defect. From “An Alternative to the Classical Nerve Graft for the Management of the Short Nerve Gap” by A. L. Dellon & S. E. Mackinnon, 1988, Plastic and Reconstructive Surgery 82:849-856. Reprinted with permission of the authors.
Nerve grafts that are obtained from one person and put back into that same person are called autografts. As with all transplant surgery, if the nerve graft donor tissue comes from one person and is put into another person, it is called an allograft or homograft. If it is transferred from one species into another species, for example, from a dog to a monkey, it is called a xenograft or heterograft. The closer the genetic match between the transferred tissues, the less is the immune response generated by the host. Thus, there is essentially only a mild inflammatory response at the site of nerve repair, with some further reaction directed to the suture material. However, with an allograft, there is an immune response at both the humoral and cellular level that will lead to a rejection of the graft. Thus, as with kidney, heart, or liver transplants, a nerve transplant will be rejected (Fish, Bain, McKee, & Mackinnon, 1992).

There are times when the need for donor nerves is so great that there would be a value to being able to do a nerve transplant. At present, doing such a nerve reconstruction with nerve taken from another person requires immunosuppression. In contrast to the transplantation of a kidney, heart, or liver, without which life is not possible, the side effects of immunosuppression are usually considered to be too great for the potential benefit conferred by nerve reconstruction. However, in 1992 Mackinnon and Hudson reported the first successful human nerve allograft. It was used to reconstruct a 23 cm sciatic nerve defect in an 8-year-old boy providing, ultimately, sensibility to the plantar aspect of the foot. The cyclosporin A immunosuppression was stopped at the 26th postoperative month. It was possible to do this because of two unique attributes of peripheral nerve.

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**TABLE 4.1 NERVE DONOR SITES FOR GRAFTING**

<table>
<thead>
<tr>
<th>Nerve</th>
<th>Region of Sensory Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper Extremity</td>
<td></td>
</tr>
<tr>
<td>Medial anterbrachial cutaneous</td>
<td>volar and medial forearm</td>
</tr>
<tr>
<td>Lateral anterbrachial cutaneous</td>
<td>volar and lateral forearm</td>
</tr>
<tr>
<td>Posterior interosseous, terminal branch</td>
<td>dorsal wrist capsule</td>
</tr>
<tr>
<td>Radial sensory†</td>
<td>dorsal radial forearm/hand</td>
</tr>
<tr>
<td>Ulnar nerve†</td>
<td>ulnar border of hand, 4 &amp; 5 digits</td>
</tr>
<tr>
<td>Common volar digital to index/middle</td>
<td>web of index/middle fingers</td>
</tr>
<tr>
<td>Lower extremity</td>
<td></td>
</tr>
<tr>
<td>Posterior femoral cutaneous</td>
<td>posterior thigh</td>
</tr>
<tr>
<td>Sural</td>
<td>dorsolateral foot</td>
</tr>
<tr>
<td>Superficial peroneal*</td>
<td>dorsum of foot</td>
</tr>
<tr>
<td>Deep peroneal*</td>
<td>web space 1st/2nd toe</td>
</tr>
<tr>
<td>Head &amp; Neck</td>
<td></td>
</tr>
<tr>
<td>Greater auricular</td>
<td>ear lobe</td>
</tr>
</tbody>
</table>

**Note:**
- † Especially if grafting to restore radial nerve motor function.
- * Especially if grafting to reconstruct a total brachial plexus palsy; may also be taken as a vascularized nerve graft.
- * Especially if grafting to reconstruct deep peroneal nerve at knee level.
- * As a vascularized nerve graft for digital nerve reconstruction.
First, nerve is much less antigenic than skin, kidney, heart, or liver. Second, once neural regeneration has proceeded across the nerve graft and has entered regions in which it is supported by host Schwann cells, immunosuppression can be discontinued. Once immunosuppression is discontinued, even if the donor graft is rejected, the host axons transiting through the graft survive. In time, the host Schwann cells, which are the component of the nerve graft most required for regeneration across large gaps, are replaced by host Schwann cells that migrate from the proximal and distal ends of the host nerve across the region of the graft. It is possible that techniques now being developed in Mackinnon’s research laboratory, such as prolonged cold storage preservation, and specific antibodies against adhesion molecules, may sufficiently reduce the immunogenicity of nerve allografts to the point that they may be used with little or no systemic immunosuppression, opening the door to clinically practical nerve tissue banking and transplantation.

The results of nerve grafting for various nerves are given in Chapter 11.

NERVE CONDUITS

It has become clear over the past two decades of microsurgical nerve reconstruction that increasing manipulation of the nerve repair site by the surgeon has not significantly improved the results of nerve repair over and above that achieved by using small diameter cutaneous nerve grafts to minimize tension at the repair site. The ideal nerve reconstruction technique would be one that (a) eliminates tension at the nerve repair site, (b) permits immediate reconstruction at the time of injury, (c) does not require sacrifice of another functioning nerve, (d) does not create a scar at a site not already injured, (e) does not add appreciable intraoperative time, (f) does not place a foreign material permanently into the body, (g) does not create the potential for chronic nerve entrapment, and (h) permits neurobiology to enhance neural regeneration.

While the nerve allograft, described above, will meet most of these requirements if the need for immunosuppression can be overcome, it has become increasingly clear that endogenous growth factors and molecular biology, each already available to us, can be harnessed to aid neural regeneration. These trends have set the intellectual framework for the development of nerve conduits, tubes through which neural regeneration can proceed (Mackinnon & Dellon, 1988).

The following statements have been proven experimentally with regard to neural regeneration through nerve conduits: Both nonabsorbable and absorbable conduits permit neural regeneration and minimize suture line neuromas (see Figure 4.11). A silicone tube will not permit regeneration beyond 10 mm, probably because of lack of oxygen. A silicone tube can cause chronic nerve compression, and if used for a nerve conduit, clinically should probably be removed at a second operation (Soteranos & Dellon, 1995; Dellon, 1994). Bioabsorbable porous tubes will sustain neural regeneration across a 3 cm gap with the quality of that regeneration being at least as good as, and possibly superior to, that obtained by interposition interfascicular nerve grafting. Beyond 3 cm, the regenerating nerve will cross a conduit, but the number of nerve fibers reaching the distal nerve is few. If neural regeneration is to produce a good result across a gap greater than 3 cm, some support, such as cultured Schwann cells, a neurotrophic factor, or contact guidance substance like laminin, will be required (Dellon & Mackinnon, 1988).

The most successful bioabsorbable conduit has been one made of polyglycolic acid (PGA). The PGA material has been in use for two decades as an absorbable suture material. This PGA nerve conduit, called the Neurotube™, was approved by the Food and Drug Administration (FDA) for clinical field trials within the United States in 1994. This tube has
been demonstrated to be successful in reconstructing a 3 cm ulnar nerve defect at the elbow level in the monkey. In these animals, the degree of nerve regeneration 1 year after the use of the Neurotube™ was compared with the results 1 year after microsurgical interfascicular interposition nerve grafting of the same defect in the opposite arm (see Figure 4.11). The Neurotube™ results were the same or better than those of nerve grafting, with the number of myelinated axons and degree of myelination being the same, electrodiagnostic testing being the same, and with reinnervation of intrinsic muscles being better in the PGA bioabsorbable nerve conduit compared to nerve grafting. Following the success of the Neurotube™ in subhuman primates, a preliminary study investigated the results of this conduit for digital nerve defects in humans. The results are given in detail in Chapter 12, but the demonstrated results were as good or better than the historic results of digital nerve repair or grafts. The availability of a Neurotube™ in the operating room will permit the surgeon, at the time of the initial injury, to resect as much damaged nerve as is deemed appropriate based on the mechanism of injury (up to 3 cm), and to still carry out a primary reconstruction without the concerns of doing a primary nerve graft. It is anticipated that the 21st century will witness the extensive use of bioabsorbable conduits to reconstruct short nerve defects, to permit neurobiology to be effective in nerve injuries without significant loss of neural tissue and, in combination with additives to the tubes, such as growth factors or laminin, to reconstruct even long nerve defects.

Figure 4.12: Collateral Sprouting. (A) This patient is 3 years after hasting the left sural nerve for median nerve reconstruction. Theoretically, there should be no sensory function of the left sural nerve, yet there is, including two-point discrimination. The assumption that the reinnervation of the foot came from the adjacent territories of the saphenous nerve and the peroneal nerve is suggested by the elevated thresholds of these nerve, and confirmed when an anesthetic block of these nerves caused loss of sensation in the sural nerve territory.
SOMATOSENSORY TESTING AND REHABILITATION

Figure 4.12: Collateral Sprouting (B) This patient demonstrates how quickly the collateral sprouting occurs. The top two panels are 8 days after resection of the palmar cutaneous branch of the median nerve and document the expected sensory loss. The bottom two panels are measurements made on the 22nd postoperation day, and demonstrate recovery of sensation at this time the patient had no pain, but felt a “crawling” or “tingling” in the skin. Note the recovered though elevated thresholds obtained with the Pressure Specified Sensory Device™.

COLLATERAL SPROUTING

The patient must be made aware that following resection of the neuroma, the adjacent normal nerves, whose territories overlap that of the resected nerve, will attempt to send axons into the newly denervated region. This phenomenon is called collateral sprouting. Most likely the nerve growth factor released from the distal end of the resected nerve can stimulate uninjured adjacent C-fibers and A-delta fibers to grow into the denervated region (Jackson & Diamond, 1977). It is also possible that the adjacent normal nerves detect the absence of some trophic factor from the resected nerve, and that this absence may contribute to the mechanism of collateral sprouting. Proof of collateral sprouting is easily obtained, although very little has been written about it clinically (see Figures 4.12A & 4.12B).

Examination of the forearm of a patient after the harvesting of a sensory nerve, like the medial antebrachial cutaneous or the lateral antebrachial cutaneous, for a nerve graft donor, or examination of the lateral aspect of the foot after the harvesting of the sural nerve for a nerve graft donor, will reveal a very small residual area of diminished sensation by 1 year after the nerve graft harvesting. This reduction in size of the area from the original large area of anesthesia to the small area of hypesthesia is the result of collateral sprouting, and is due to peripheral nerve changes. The central nervous system changes that accompany peripheral denervation will be described in Chapter 10, under cortical plasticity, but these central changes are not responsible for collateral sprouting. Collateral sprouting, in and of itself, can generate disturbing sensations such as the feeling of crawling of the skin, tingling, or itching. If a painful
neuroma has been resected, the therapist must be able to reassure the patient that the perceptions related to collateral sprouting, a normal, compensatory mechanism, are short-lived (about 3 weeks to 3 months), can be helped by reeducation techniques (see Chapter 12), and are not the original neuroma pain returning. The desensitization techniques that the therapist will employ to treat the disturbing sensations associated with collateral sprouting help the cortical reorganization that occurs following peripheral denervation.

· REFERENCES ·


**ADDITIONAL READINGS**


