TUMORS
of the
PERIPHERAL NERVOUS SYSTEM

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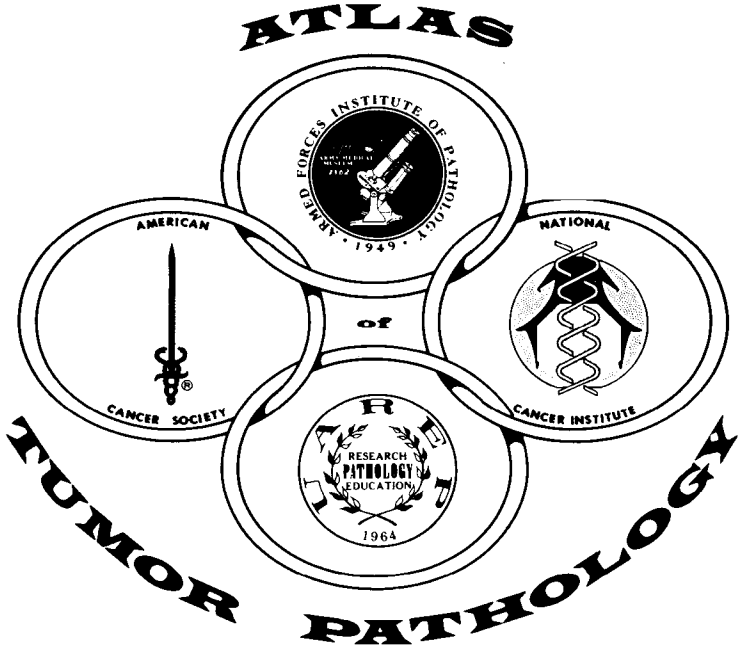

ATLAS OF TUMOR PATHOLOGY

Second Series

Fascicle 3

TUMORS OF THE PERIPHERAL NERVOUS SYSTEM

by

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ATLAS OF TUMOR PATHOLOGY

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EDITOR'S NOTE

The Atlas of Tumor Pathology was originated by the Committee on Pathology of the National Academy of Sciences—National Research Council in 1947. The form of the Atlas became the brain child of the Subcommittee on Oncology and was shepherded by a succession of editors. It was supported by a long list of agencies; many of the illustrations were made by the Medical Illustration Service of the Armed Forces Institute of Pathology; the type was set by the Government Printing Office; and the final printing was made by the press at the Armed Forces Institute of Pathology. The American Registry of Pathology purchased the fascicles from the Government Printing Office and sold them at cost, plus a small handling and shipping charge. Over a period of 20 years, 15,000 copies each of 40 fascicles were produced. They provided a system of nomenclature and set standards for histologic diagnosis which has received world-wide acclaim. Private contributions by almost 600 pathologists have helped to finance the compilation of an index by The Williams & Wilkins Company to complete the original Atlas.

Following the preparation of the final fascicle of the first Atlas, the National Academy of Sciences—National Research Council handed over the task of further pursuit of the project to Universities Associated for Research and Education in Pathology, Inc. Grant support for a second series was generously made available by both the National Cancer Institute and the American Cancer Society. The Armed Forces Institute of Pathology has expanded and improved its press facilities to provide for a more rapid and efficient production for the next series. A new Editor and Editorial Advisory Committee were appointed, and the solicitation and preparation of manuscripts continues.

This second series of the Atlas of Tumor Pathology is not intended as a second edition of the first Atlas and, in general, there will be variation in authorship. The basic purpose remains unchanged in providing an Atlas setting standards of diagnosis and terminology. Throughout this new series, the term chosen by the Committee on Tumor Nomenclature of the International Union Against Cancer is shown by an asterisk if it corresponds to the author's heading, or as the first synonym in italics if it differs from the author's first choice. Hematoxylin and eosin stained sections still represent the keystone of histologic diagnosis; therefore, most of the photomicrographs will be of sections stained by this technic, and only sections prepared by other technics will be specifically designated in the legends. It is hoped that in many of the new series a broader perspective of tumors may be offered by the inclusion of special stains, histochemical illustrations, electron micrographs, data on the biologic behavior, and other pertinent information for better understanding of the disease.

The format of the new series is changed in order to allow better correlation of the illustrations with the text, and a more substantial cover is provided. An index will be included in each fascicle.

It is the hope of the Editor, the Editorial Advisory Committee, and the Sponsors that these changes will be welcomed by the readers. Constructive criticisms and suggestions will be appreciated.

Harlan I. Firminger, M.D.

PREFACE

The encyclopedic character of the Atlas of Tumor Pathology dictated that a disease be covered in detail under the topic headings; thus general introductory comments are not made. The only exception is in the glossary which is limited to normal structures.

The fascicle "Tumors of the Peripheral Nervous System" includes topics covered in other fascicles. An attempt has been made to cover all aspects of von Recklinghausen's neurofibromatosis.

In preparation of this second series fascicle, "Tumors of the Peripheral Nervous System," the authors were fortunate to have the co-operation as well as the experience of the late Dr. Arthur Purdy Stout, author of the fascicle in the first series.

James C. Harkin, M.D.
Richard J. Reed, M.D.

ACKNOWLEDGMENTS

The authors were fortunate in having available to them the enormous amount of pathologic material provided by the Charity Hospital of Louisiana in New Orleans. We had access to all the material which includes not only the Tulane service but also the Louisiana State University service. We appreciate the co-operation of Dr. Jack Strong, Chairman of the Department of Pathology, Louisiana State University School of Medicine, Dr. Ronald Welsh, Dr. Paul McGarry, and Dr. Emma Moss, Director of the Pathology Service at Charity Hospital. Valuable assistance and generous co-operation were given by members of the Department of Pathology, Tulane University School of Medicine, particularly by Dr. Charles E. Dunlap, Chairman, Dr. William Sternberg, Dr. Herbert Ichinose, Dr. Margaret S. Skinner, Dr. Jerald Schenken, Dr. Sydney S. Schochet, Mr. Ben O. Spurlock, Mr. Raymond Johnson, photographer, Mrs. Johanna Weichert, Mrs. Marlene Matherne, and Mrs. Alice Hunt.

The photographs of gross specimens and photomicrographs were made in the Department of Pathology, Tulane University. The electron micrographic pictures were made on the Philips EM-300 and Siemens Elmiskop I electron microscopes in the Department of Pathology in connection with studies being supported by U.S.P.H.S. Research Grant NB-04330 and Research Career Development Award NB-K3-16731 (Dr. Harkin) from the National Institute of Neurological Diseases and Blindness.

Material has been available to us through our work as consultant (RJR) and by referral (JCH) from the U.S. Public Health Service Hospital in New Orleans and the Ochsner Foundation Hospital with the co-operation of Dr. G. M. Carrera and Dr. W. Mitchell, members of the Tulane University School of Medicine faculty. Co-operation and material was also provided by Tulane faculty members Dr. Charles E. Dunlap (V.A. Hospital), Dr. F. Harris and Dr. W. Harris (Flint-Goodridge Hospital), Dr. Ambrose Hertzog and Dr. Donald Bradburn (Touro Infirmary), and Dr. W. Holthaus and Dr. Ronald Padgett (U.S. Public Health Service Hospital in New Orleans).

We are indebted to the following pathologists for their co-operation in providing gross and microscopic specimens as well as clinical data: Dr. Howard B. Burch, Lafayette, La.; Dr. Robert L. Flinner, Medical and Research Hospital, Kansas City, Kan.; Dr. Hugh Williamson, Durango, Colo.; Dr. John Basone, Beaumont, Tex.; Dr. Earl Greene, Bishop Clarkson Memorial Hospital, Omaha, Neb.; Dr. Fred Shipkey, Charleston, S. C., formerly at Memorial Hospital, New York, N. Y.; Dr. E. D. Williams, Postgraduate Medical School, London, England; and Dr. John Milam, St. Luke's Hospital, Houston, Tex.

Dr. Jerald R. Schenken, Omaha, Nebraska, deserves special mention for his co-operation in furnishing histologic and clinical materials as does Dr. Bryce O. Bliss, Tulsa, Oklahoma, for his assistance in gathering material while a Resident at Charity Hospital in New Orleans and for furnishing material from Tulsa, Oklahoma.

Dr. Gordon McFarland, Ochsner Foundation Hospital, New Orleans, kindly made material in the Bone Pathology Laboratory available for review.

To our teachers, some of whom were our co-workers, we owe much of our knowledge of the subject. We do not hold them responsible for the errors. Particularly we wish to mention the following doctors in addition to our colleagues in New Orleans: Lauren V. Ackerman, Wallace C. Clark, Edward W. Dempsey, Emmanuel Farber, W. Stanley Hartroft, Simon Koletsky, Harrison Latta, Sarah A. Luse, Herbert Z. Lund, Robert C. Mellors, John E. Moossy, Alan R. Moritz, J. Lowell Orbison, James W. Reagan, J. Rudolph Schenken, Margaret G. Smith, Harlan Spjut, Fred Stewart, Robert D. Terry, J. Perry Tollman, A. G. M. Weddell, and Harry M. Zimmerman.

Five illustrations from the fascicle "Tumors of the Peripheral Nervous System" by Dr. Arthur Purdy Stout, first series of the Atlas of Tumor Pathology, are included in the present fascicle. We appreciate the co-operation of Dr. Stout. Our thanks to Dr. Harlan I. Firminger, Editor of the Atlas of Tumor Pathology.

Permission to use a copyrighted illustration has been granted by Peninsula Press, 1946, for our figure 63.

All other illustrations are the authors' own. The A. F. I. P. Atlas numbers are for identification of negatives at the Armed Forces Institute of Pathology.

James C. Harkin, M.D.
Richard J. Reed, M.D.

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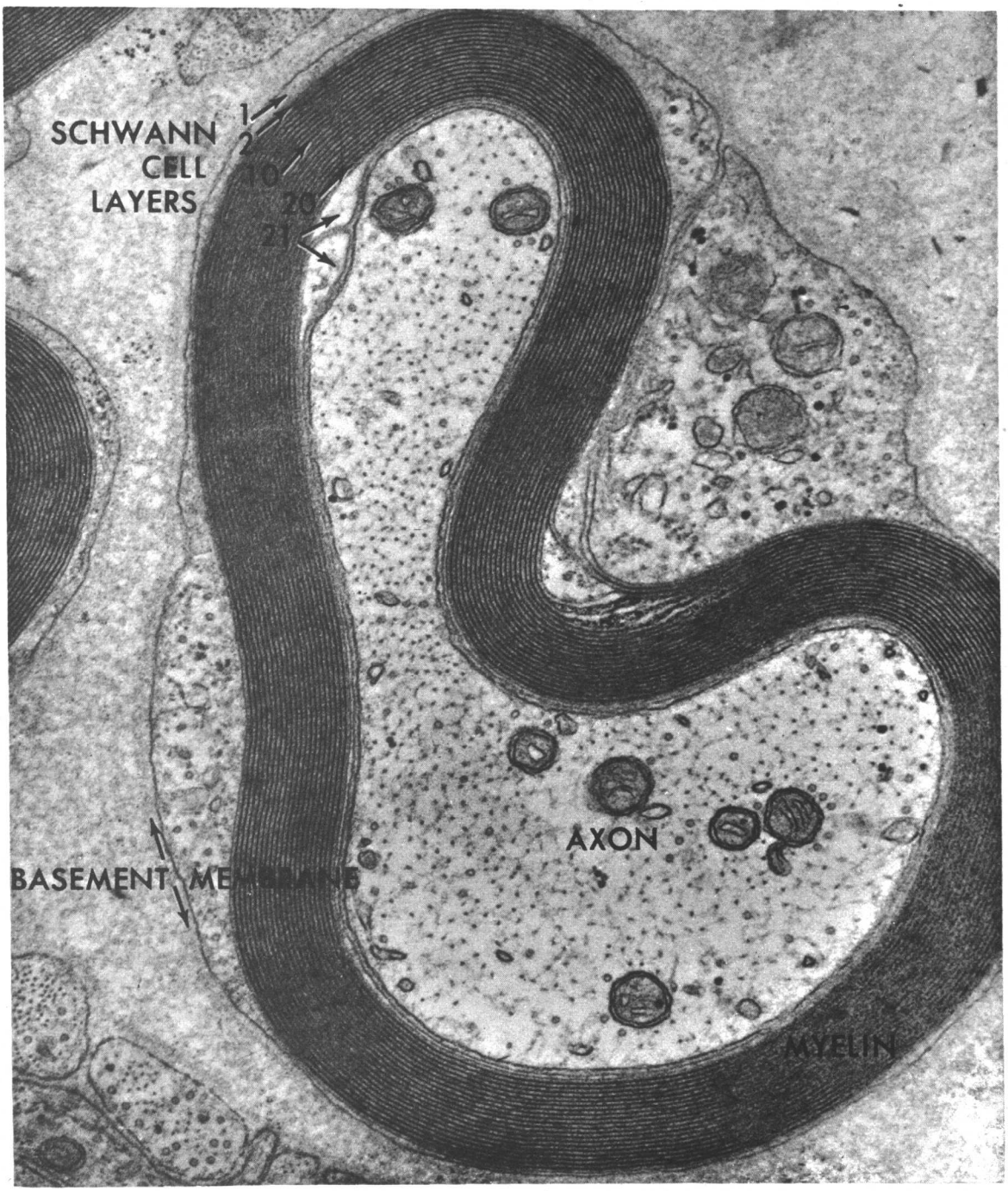


Figure 1. This electron micrograph depicts normal axon and myelin in cross section. The axon has a cell membrane. The Schwann cell has an indentation in the outer cell membrane which is continuous through the entire spiral wrap, terminating at the innermost loop, number 21. Layers 2 through 20 are each compacted into a myelin membrane. The extracellular region or endoneurium contains a basement membrane paralleling the Schwann cell membrane and collagen fibrils. × 50,000. A.F.I.P. Atlas No. 67-2-242.

TUMORS OF THE PERIPHERAL NERVOUS SYSTEM

GLOSSARY

Some normal structures mentioned in the text are defined so that the reader can clearly understand the authors' terminology. The definitions are not new. They vary somewhat depending on the technics used for defining the morphologic characteristics.

Axon: A prolonged extension of the cytoplasm of a neuron (figs. 1, 2). Axons may branch . The definition is based on structure (Bodian); the axon can function in transmission of afferent or efferent impulses. In tissue sections stained with hematoxylin and eosin (H & E) small axons are not readily seen, but large axons may be visible as eosinophilic cylinders surrounded by myelin (fig. 3). Most axons of myelinated and nonmyelinated nerves are easily seen in tissue treated with silver stains such as Bodian's stain. Some tiny axons are of such small diameter that they cannot be seen with the light microscope and require an electron microscope for study.

Basement membrane: An extracellular condensation of material paralleling the cell membrane in sites where the cell abuts a different type of tissue. The basement membrane forms a continuous sheath over adjacent cells of the same type. In tissue sections examined with the light microscope, the basement membranes of Schwann cells are seen as a network of fibers (Wilder's reticulum stain). By electron microscopy the basement membrane of a Schwann cell is an extracellular, loose but regularly arranged condensation of electron-dense material (fig. 1). The basement membrane surrounding Schwann cells is a continuous sheath over abutting Schwann cells at nodes of Ranvier (fig. 5). Basement membranes also may be found extending away from the cells into the endoneurium.

Collagen: The extracellular connective tissue fibrils of white fibrous tissue, further characterized by conversion to gelatin after being boiled in water and chemically by a relatively high content of hydroxyproline. In a tissue section examined by light microscopy, collagen is seen as coarse bundles that subdivide into parallel unbranched fibers 0.3 to 0.5 microns in diameter. Collagen is strongly eosinophilic and stains with acid aniline dyes. With Wilder's reticulum silver stain collagen appears yellowish brown. By electron microscopy and diffraction methods collagen fibrils have regular cross banding or periodicity at intervals of approximately 700 (640-710) Angstroms (fig. 36). The collagen fibers seen by light microscopy are composed of many collagen fibrils. Collagen is strongly birefringent when examined under polarized light if the fibrils are densely packed and in parallel array. The basic structural unit of collagen is approximately 2800 Angstroms long. The basic units are staggered at 700 Angstrom intervals in the collagen fibril.

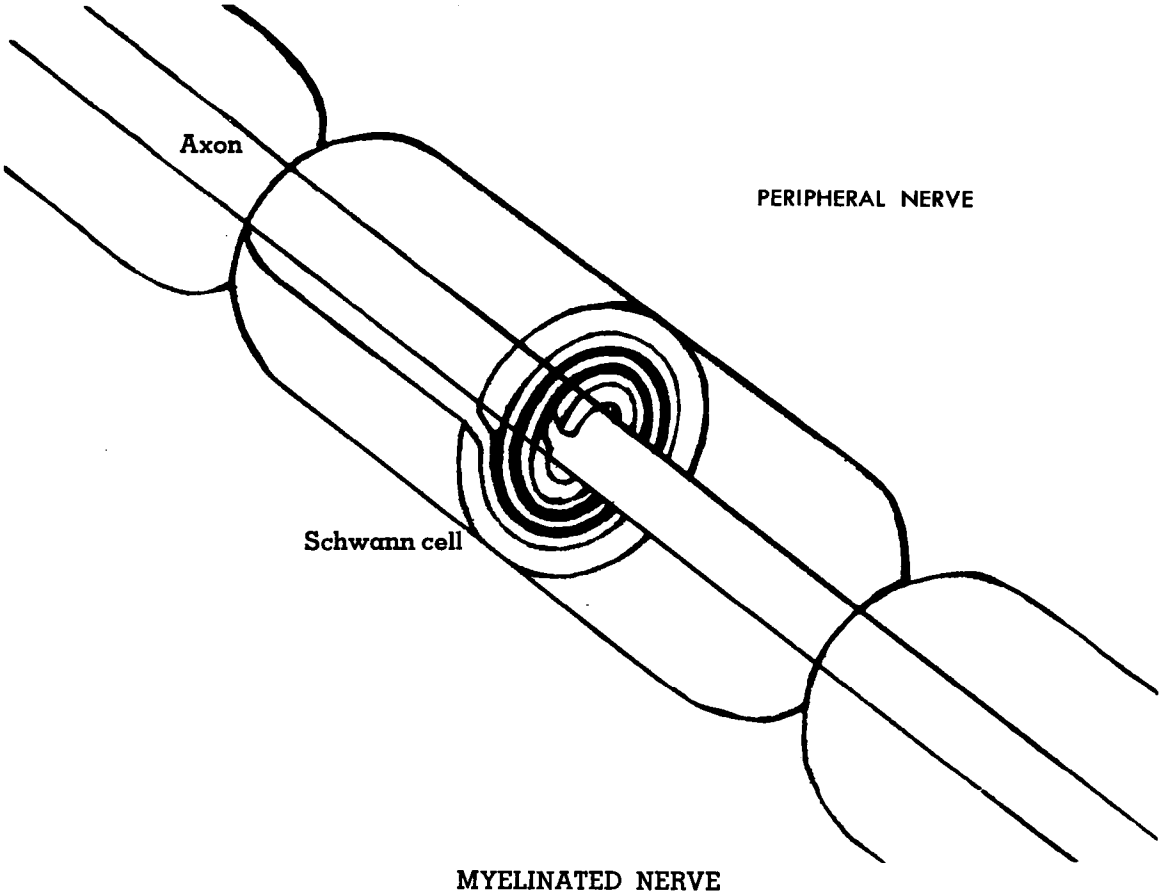
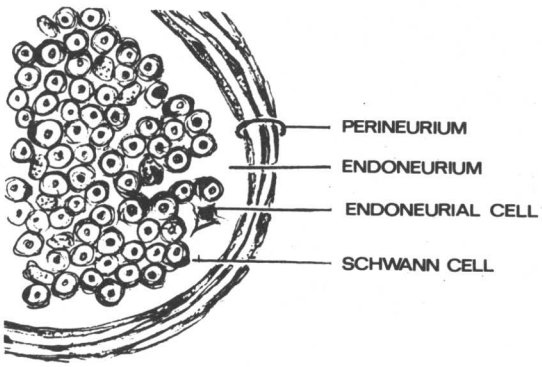


Figure 2. A three-dimensional diagram illustrates the axon and Schwann cell sheath of a myelinated nerve. Each longitudinal segment of the axon is encased by one Schwann cell. A cross section of the spiral Schwann cell myelin sheath is illustrated. The outermost layer, number 1, contains Schwann cell cytoplasm as does the innermost layer, number 4. In the other layers of the spiral sheath, plasma membranes of each layer are fused or compacted creating a "myelin membrane." A.F.I.P. Atlas No. 67-2–241.

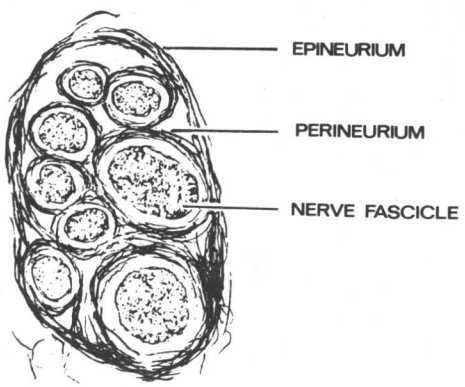
Endoneurium: The zone between Schwann cells and the perineurium, principally an extracellular region of unorganized material and collagen fibrils. Scattered fibrocytes termed endoneurial cells are found in the endoneurium (fig. 3). The basement membranes of Schwann cells can be considered part of the endoneurium. In many nerves, particularly myelinated nerves, the endoneurial space contains material that stains with alcian blue for acid mucopolysaccharides. Even if the endoneurial space is poorly developed, the zone stains with alcian blue.

Epineurium: The encasing dense fibrous sheath which surrounds several nerve fascicles (fig. 4). In large peripheral nerves it does not resemble the perineurium and is principally mesodermal rather than neuroectodermal in origin. In very small nerves, epineurium and perineurium are the same. The epineurium appears to be a prolongation of the dura mater along a peripheral nerve and is absent in the subdural space.



PERIPHERAL NERVE

Figure 3. This diagram is a cross section of a peripheral nerve fascicle. The perineurium is a sheath composed of alternating layers of perineurial Schwann cells and collagen which surrounds: (a) the endoneurium, principally an extracellular zone, but containing scattered endoneurial cells which resemble fibrocytes, and (b) axons and their Schwann cell sheaths. In this diagram, an axon appears as a dot and the myelin as a clear zone surrounding the axon. Schwann cell nuclei can be seen at the periphery of the myelin. A.F.I.P. Atlas No. 67-2–244.



PERIPHERAL NERVE

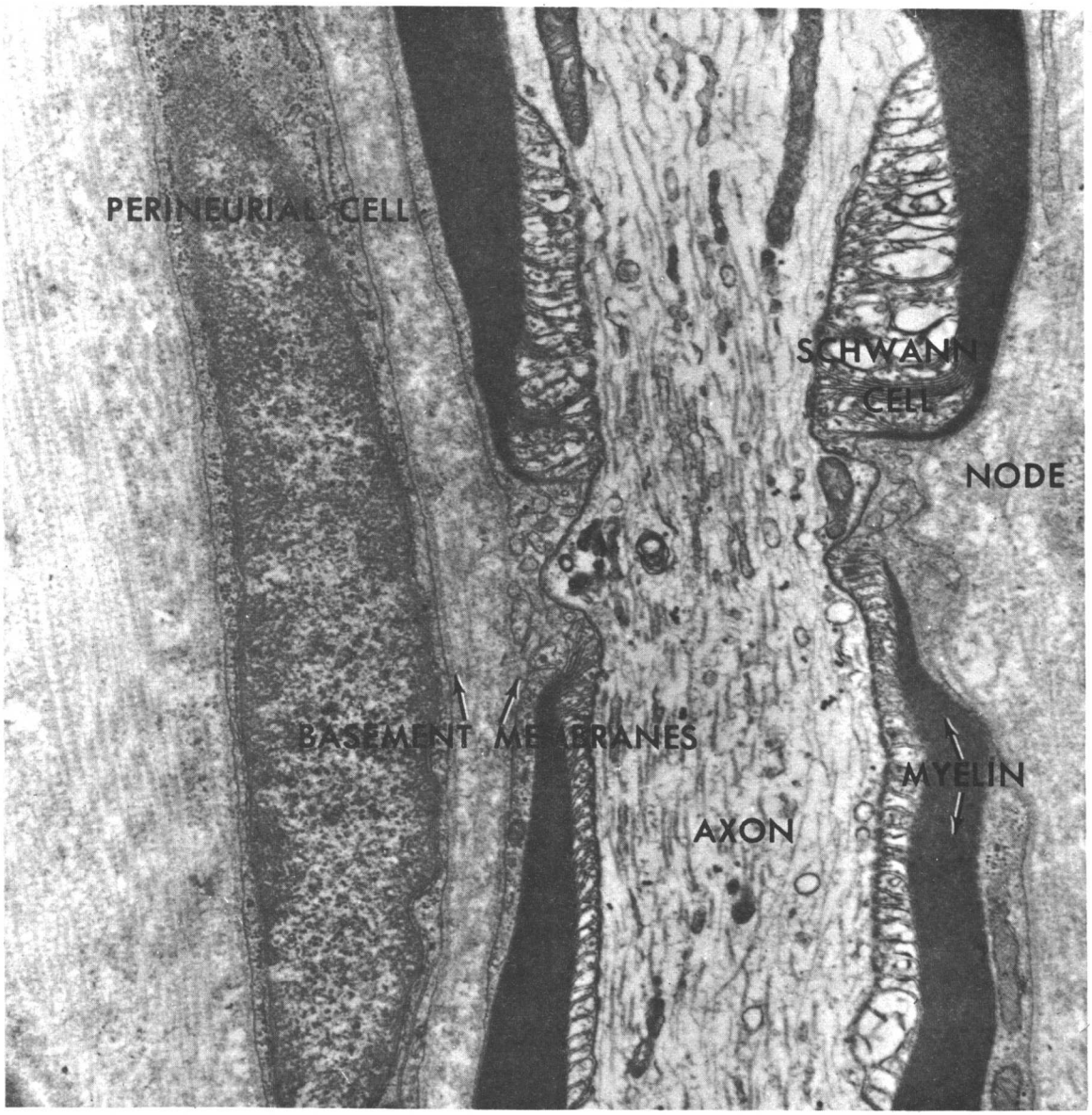
Figure 4. In this diagram of a peripheral nerve cross section, the epineurial sheath is continuous with the adjacent tissue. Each nerve fascicle is surrounded by perineurium. Part of one fascicle is seen in figure 3. A.F.I.P. Atlas No. 67-2–243.

Fibrocyte: A mesodermal cell capable of producing collagen and, under proper stimulus, mucoid or myxomatous extracellular matrix (ground substance). The cell does not have a basement membrane.

Ganglion cell: A neuron which has its nucleus located in a ganglion of spinal and cranial nerves or a ganglion of the autonomic nervous system. The normal cell contains Nissl granules concentrated adjacent to the nucleus. By electron microscopy the Nissl granules correspond to the ribonucleoprotein particles (ribosomes), some of which are arranged as polyribosomes and some of which are components of the rough-coated endoplasmic reticulum. The ganglion cell has a pale staining nucleus with small chromatin clumps and a prominent central nucleolus.

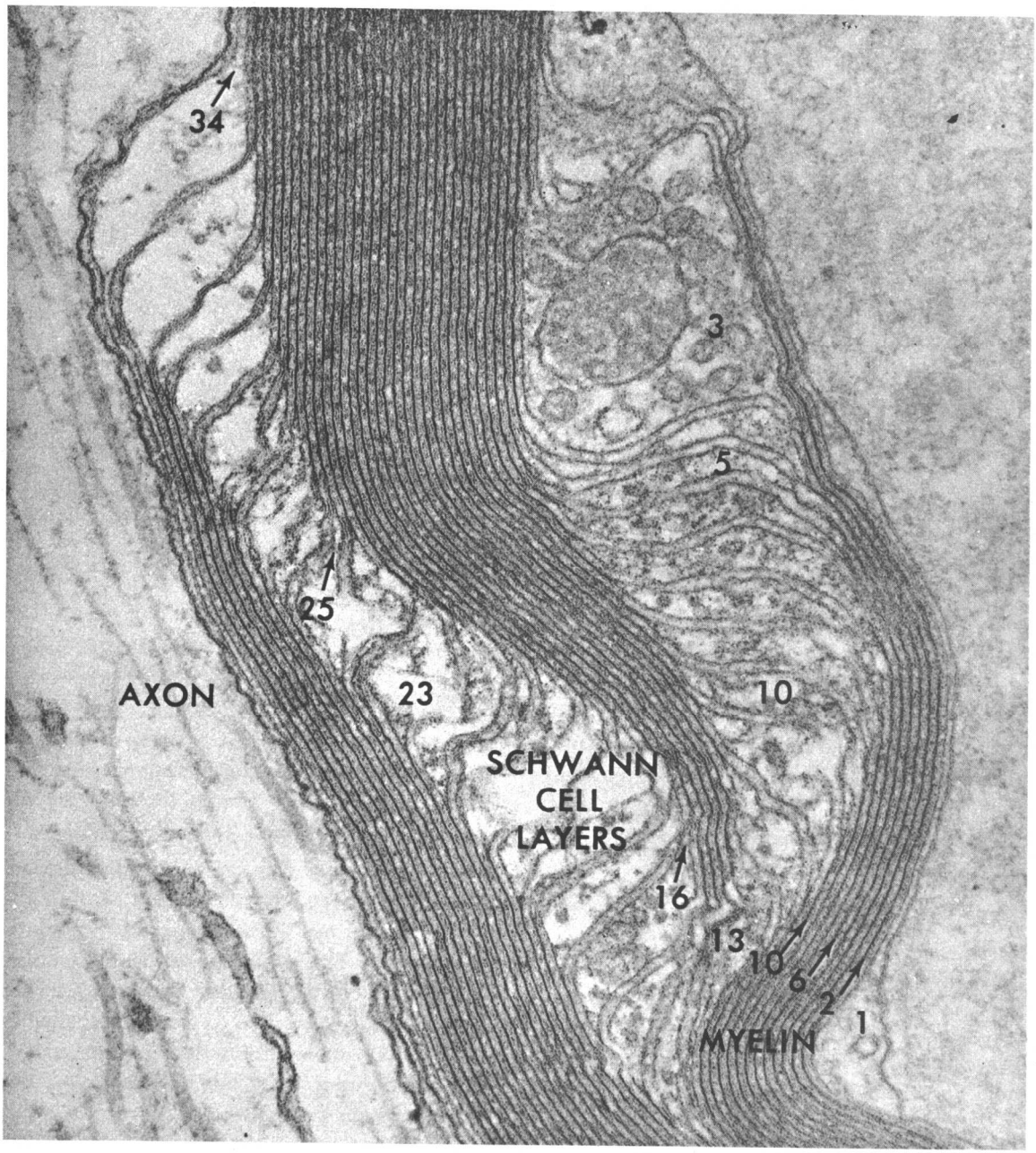
Myelin: The lipid sheath encasing longitudinal segments of large axons. In the peripheral nervous system, myelin is a spiral wrap by a Schwann cell (figs. 1, 2). Myelinated nerves are characterized by a 1 to 1 ratio between axon and the ensheathing Schwann cell for each longitudinal segment. With light microscopy in dehydrated specimens, the myelin sheath appears as a vacuolated zone between the axon and the cytoplasm and nucleus of the Schwann cell. The Schwann cell cytoplasm may not be recognized. In the long axis the myelin of each Schwann cell has v-shaped partitions, the Schmidt-Lanterman incisures (fig. 6). By electron microscopy the incisure is seen as a spiral tongue of Schwann cell cytoplasm. The gap between Schwann cells along an axon where the myelin sheath is interrupted is a node of Ranvier (figs. 5, 7).

With luxol fast blue stains, myelin of the peripheral nervous system generally stains deep blue whereas that of the central nervous system is a light greenish blue.



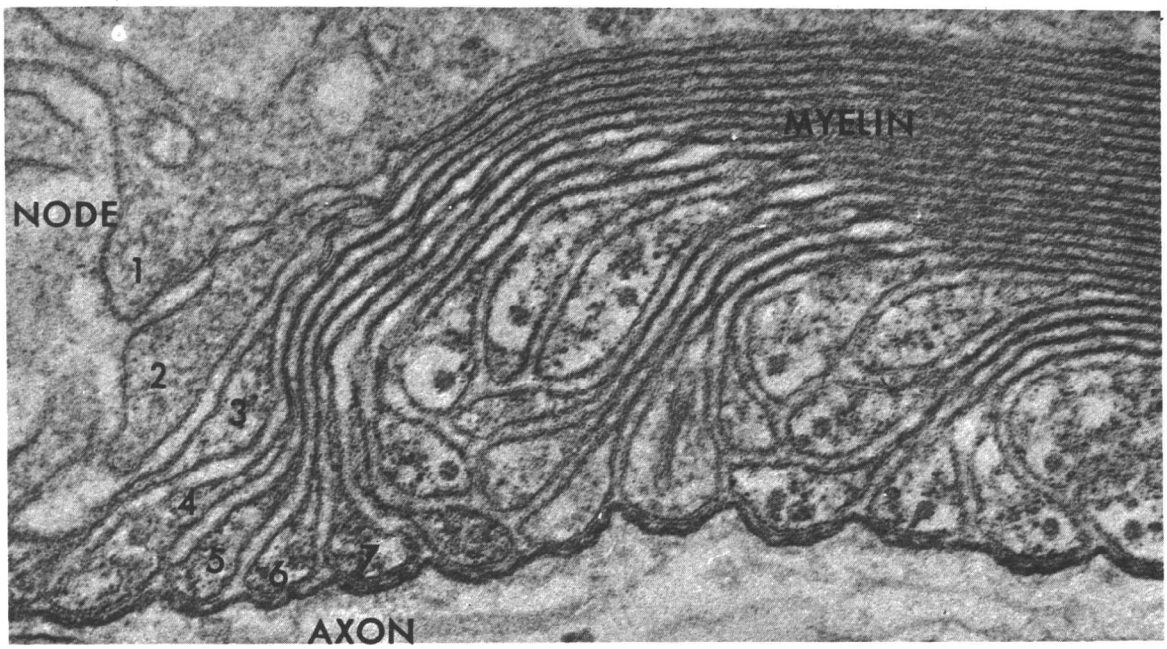
NORMAL PERIPHERAL NERVE

Figure 5. This electron micrograph of a tissue section is oriented in the long axis of the axon at the node of Ranvier. The most superficial spiral Schwann cell wrap, layer number 1, extends nearest the nodal gap. Deeper Schwann cell wraps terminate progressively further from the node. In all layers, cytoplasm can be recognized near the node. It is also evident in the most superficial and the deepest wrap in all regions. Most wraps are recognized in internodal regions as myelin membranes. The axon is limited by a cell membrane. The basement membrane is a continuous sheath over the Schwann cells which bridges the nodal gap. The perineurial Schwann cell is surrounded by a basement membrane. × 30,000. A.F.I.P. Atlas No. 67-2-245.



SCHMIDT-LANTERMAN INCISURE

Figure 6. This electron micrograph of a tissue section through the Schmidt-Lanterman incisure of the myelin sheath is oriented in the long axis of the nerve. The Schwann cell layers do not terminate at Schmidt-Lanterman incisures as they do at nodes of Ranvier (fig. 7). Some incisures traverse the entire myelin sheath in a straight line; others form a zigzag pattern. On the opposite side of the axon, a mirror-image structure was seen in the tissue section. × 95,000. A.F.I.P. Atlas No. 67-2–247.



SCHWANN CELL SHEATH

Figure 7. The Schwann cell sheath is seen in a myelinated nerve adjacent to a node of Ranvier. The electron micrograph shows a tissue section oriented in the long axis of the nerve. Each Schwann cell layer terminates in a cytoplasmic loop in the nodal region. × 100,000. A.F.I.P. Atlas No. 67-2–246.

Nerve: A gross structure such as a cranial or peripheral nerve or an autonomic nervous system nerve. The neurons, their axons, and the endoneurial, perineurial, and epineurial sheaths are parts of a nerve.

Nerve cell: Neuron.

Nerve fascicle: A subunit of a nerve (gross structure) which is encased by perineurium (fig. 4).

Nerve fiber: One or a group of axons plus their Schwann cell sheaths.

Neurilemma: The extracellular basement membrane and collagen network that ensheaths Schwann cells (Causey).

Perineurium: A tubular structure composed of concentric alternating layers of perineurial cells (Schwann cells) and collagen bundles. The perineurium surrounds a group of axons, their encasing Schwann cells, and the endoneurium to form a nerve fascicle. Nerve fascicles are bound together by the epineurium to form a nerve (fig. 4).

Perineurial cell: The cells that form the encircling neuroectodermal sheath of the perineurium. Perineurial cells have a basement membrane. The cells are indistinguishable morphologically from Schwann cells, but are not generally accepted as Schwann cells because they do not intimately sheath axons. The perineurial cells are not fibrocytes but may function as facultative fibroblasts and produce collagen. (See page 29 for reasons why perineurial cells can be considered as Schwann cells.)

Peripheral nervous system: That part of the nervous system where neurons and their processes (axons) are encased by Schwann cells (fig. 8). In the central nervous system