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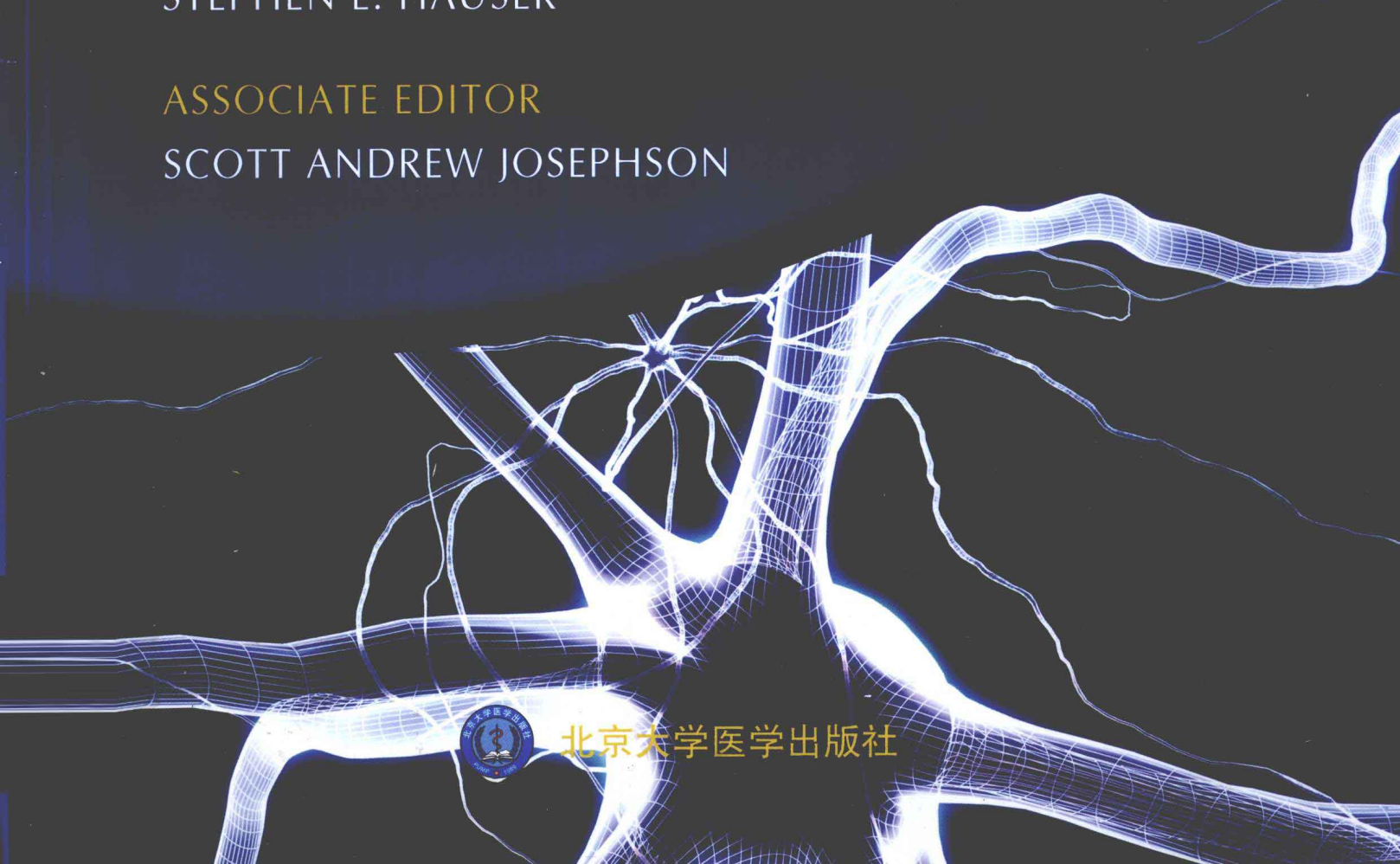
哈里森

临床神经病学

HARRISON'S Neurology in Clinical Medicine

EDITOR
STEPHEN L. HAUSER

ASSOCIATE EDITOR
SCOTT ANDREW JOSEPHSON



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HARRISON'S Neurology in Clinical Medicine

（第2版）

Editor

Stephen L. Hauser, MD

Robert A. Fishman Distinguished Professor and Chairman,
Department of Neurology, University of California, San Francisco

Associate Editor

Scott Andrew Josephson, MD

Assistant Clinical Professor of Neurology,
University of California, San Francisco

Mc Graw Hill Medical

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出版说明

《哈里森内科学》（Harrison's Principles of Internal Medicine）是一部内科学经典名著，也是美国及多个国家医学院校的首选内科学教科书。该书1945年由美国权威内科学家哈里森（Tinsley R. Harrison）首先提议并组织编写，第1版于1950年问世，并立即引起广泛的赞誉与好评。自此，随着医学科学的发展以及在市场的热销，该书每4年修订一次，历时半个多世纪，已出版至第17版，成为内科学发展的基石和风向标，享有“内科学著作之父”的美誉。

为了读者阅读和携带方便，更专注于内科学各亚科领域，《哈里森内科学》分册系列书问世了。该分册系列以《哈里森内科学》（第17版）中相关领域的内容为蓝本，并参考了《哈里森内科学》（第17版）出版以来的最新文献，强调基础与临床的整合，汇集了本领域内最新的进展，是内科学各亚科领域的权威教科书。

在医学领域，英文原版经典专著经过几十年甚至上百年的发展，在知识点的架构上形成了科学而完备的体系，不但语言规范、地道，而且更新及时，具有权威性和先进性。无论是临床医生、教师还是医学生，有这样一本经典专著放在案头，经常翻阅，不但可以获取医学知识，对提高专业外语水平也大有裨益。

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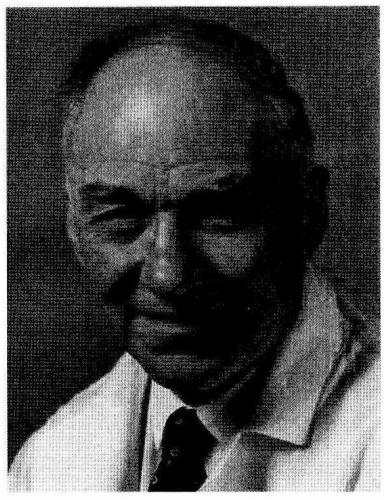

Raymond D. Adams, MD
1911–2008

For Ray Adams, editor of *Harrison's Principles of Internal Medicine* for more than three decades.

A mentor who taught by example,
a colleague who continues to inspire, and
a friend who is deeply missed.

Stephen L. Hauser, MD, for the Editors of *Harrison's*

CONTRIBUTORS

Numbers in brackets refer to the chapter(s) written or co-written by the contributor.

ANTHONY A. AMATO, MD
Associate Professor of Neurology, Harvard Medical School; Chief, Division of Neuromuscular Diseases, Department of Neurology, Brigham and Women's Hospital, Boston [43]

MICHAEL J. AMINOFF, MD, DSc
Professor of Neurology, School of Medicine, University of California, San Francisco [3, 10, 12]

ARTHUR K. ASBURY, MD
Van Meter Professor of Neurology Emeritus, University of Pennsylvania School of Medicine, Philadelphia [12, 41]

M. FLINT BEAL, MD
Anne Parrish Titzel Professor and Chair, Department of Neurology and Neuroscience, Weill Medical College of Cornell University; Neurologist-in-Chief, New York Presbyterian Hospital, New York [19, 29]

THOMAS D. BIRD, MD
Professor, Neurology and Medicine, University of Washington; Research Neurologist, Geriatric Research Education and Clinical Center, VA Puget Sound Health Care System, Seattle [23]

GERALD BLOOMFIELD, MD, MPH
Department of Internal Medicine, The Johns Hopkins University School of Medicine, Baltimore [Review and Self-Assessment]

CYNTHIA D. BROWN, MD
Department of Internal Medicine, The Johns Hopkins University School of Medicine, Baltimore [Review and Self-Assessment]

ROBERT H. BROWN, JR., MD, DPhil
Neurologist, Massachusetts General Hospital; Professor of Neurology, Harvard Medical School, Boston [27, 43]

MARK D. CARLSON, MD, MA
Chief Medical Officer and Senior Vice President, Clinical Affairs, St. Jude Medical, Sylmar; Adjunct Professor of Medicine, Case Western Reserve University, Cleveland [8]

VINAY CHAUDHRY, MD
Professor and Vice Chair, The Johns Hopkins University School of Medicine; Co-Director, EMG Laboratory, Johns Hopkins Hospital, Baltimore [40]

CHARLES A. CZEISLER, MD, PhD
Baldino Professor of Sleep Medicine, and Director, Division of Sleep Medicine, Harvard Medical School; Chief, Division of Sleep Medicine, Department of Medicine, Brigham and Women's Hospital, Boston [16]

MARINOS C. DALAKAS, MD
Professor of Neurology; Chief, Neuromuscular Diseases Section, NINDS, National Institute of Health, Bethesda [44]

JOSEP DALMAU, MD, PhD
Professor of Neurology, Division Neuro-Oncology, Department of Neurology, Philadelphia [39]

ROBERT B. DAROFF, MD
Gilbert W. Humphrey Professor of Neurology and Interim Chair, Department of Neurology, Case Western Reserve University School of Medicine and University Hospitals Case Medical Center, Cleveland [9]

MAHLON R. DELONG, MD
Timmie Professor of Neurology, Emory University School of Medicine, Atlanta [24]

WILLIAM P. DILLON, MD
Professor of Radiology, Neurology, and Neurosurgery; Vice-Chair, Department of Radiology; Chief, Neuroradiology, University of California, San Francisco [2, 46]

DANIEL B. DRACHMAN, MD
Professor of Neurology & Neuroscience; WW Smith Charitable Trust Professor of Neuroimmunology, The Johns Hopkins University School of Medicine, Baltimore [42]

JOEY D. ENGLISH, MD, PhD
Assistant Professor of Neurology, University of California, San Francisco [21]

JOHN W. ENGSTROM, MD
Professor of Neurology; Clinical Chief of Service; Neurology Residency Program Director, University of California, San Francisco [7, 28]

ANTHONY S. FAUCI, MD, DSc (Hon), DM&S (Hon), DHL (Hon), DPS (Hon), DLM (Hon), DMS (Hon)
Chief, Laboratory of Immunoregulation; Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda [37]

HOWARD L. FIELDS, MD, PhD
Professor of Neurology; Director, Wheeler Center for Neurobiology of Addiction, University of California, San Francisco [5]

ANDRE FURTADO, MD
Associate Specialist at the Department of Radiology, Neuroradiology Section, University of California, San Francisco [46]

PETER J. GOADSBY, MD, PhD, DSc
Professor of Clinical Neurology, Institute of Neurology, Queen Square London; Professor of Neurology, Department of Neurology, University of California, San Francisco [6]

DOUGLAS S. GOODIN, MD
Professor of Neurology, University of California, San Francisco [34]

STEPHEN L. HAUSER, MD
Robert A. Fishman Distinguished Professor and Chairman, Department of Neurology, University of California, San Francisco [1, 4, 19, 29, 30, 34, 41]

J. CLAUDE HEMPHILL, III, MD, MAS
Associate Professor of Clinical Neurology and Neurological Surgery, University of California, San Francisco; Director, Neurocritical Care Program, San Francisco General Hospital, San Francisco [22]

JONATHAN C. HORTON, MD, PhD
William F. Hoyt Professor of Neuro-Ophthalmology; Professor of Ophthalmology, Neurology, and Physiology, University of California, San Francisco [17]

STEVEN E. HYMAN, MD
Provost, Harvard University; Professor of Neurobiology, Harvard Medical School, Boston [48]

MARK A. ISRAEL, MD
Professor of Pediatrics and Genetics, Dartmouth Medical School; Director, Norris Cotton Cancer Center, Dartmouth-Hitchcock Medical Center, Lebanon [32]

J. LARRY JAMESON, MD, PhD
Professor of Medicine; Vice President for Medical Affairs and Lewis Landsberg Dean, Northwestern University Feinberg School of Medicine, Chicago [33]

S. CLAIBORNE JOHNSTON, MD, PhD
Professor, Neurology; Professor, Epidemiology and Biostatistics; Director, University of California, San Francisco Stroke Service, San Francisco [21]

SCOTT ANDREW JOSEPHSON, MD
Assistant Clinical Professor of Neurology, University of California, San Francisco [13, 45]

JORGE L. JUNCOS, MD
Associate Professor of Neurology, Emory University School of Medicine; Director of Neurology, Wesley Woods Hospital, Atlanta [24]

ERIC KANDEL, MD
University Professor; Fred Kavli Professor and Director, Kavli Institute for Brain Sciences; Senior Investigator, Howard Hughes Medical Institute, Columbia University, New York [48]

WALTER J. KOROSHETZ, MD
Deputy Director, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda [36]

ANIL K. LALWANI, MD
Mendik Foundation Professor and Chairman, Department of Otolaryngology; Professor, Department of Pediatrics; Professor, Department of Physiology and Neuroscience, New York University School of Medicine, New York [18]

H. CLIFFORD LANE, MD
Clinical Director; Director, Division of Clinical Research; Deputy Director, Clinical Research and Special Projects; Chief, Clinical and Molecular Retrovirology Section, Laboratory of Immunoregulation, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda [37]

PHILLIP A. LOW, MD
Robert D and Patricia E Kern Professor of Neurology, Mayo Clinic College of Medicine, Rochester [28]

DANIEL H. LOWENSTEIN, MD
Professor of Neurology; Director, University of California, San Francisco Epilepsy Center; Associate Dean for Clinical/Translational Research, San Francisco [1, 20]

JOSEPH B. MARTIN, MD, PhD, MA (Hon)
Dean Emeritus of the Faculty of Medicine, Edward R. and Anne G. Lefler Professor of Neurobiology, Harvard Medical School, Boston [1, 5]

NANCY K. MELLO, PhD
Professor of Psychology (Neuroscience), Harvard Medical School, Boston [52]

SHLOMO MELMED, MD
Senior Vice President, Academic Affairs; Associate Dean, Cedars Sinai Medical Center, David Geffen School of Medicine at UCLA, Los Angeles [33]

JERRY R. MENDELL, MD
Professor of Pediatrics, Neurology and Pathology, The Ohio State University; Director, Center for Gene Therapy, The Research Institute at Nationwide Children's Hospital, Columbus [43]

JACK H. MENDELSON,† MD
Professor of Psychiatry (Neuroscience), Harvard Medical School, Belmont [52]

M.-MARSEL MESULAM, MD
Director, Cognitive Neurology and Alzheimer's Disease Center; Dunbar Professor of Neurology and Psychiatry, Northwestern University Feinberg School of Medicine, Chicago [15]

BRUCE L. MILLER, MD
AW and Mary Margaret Clausen Distinguished Professor of Neurology, University of California, San Francisco School of Medicine, San Francisco [13, 23, 38]

C. WARREN OLANOW, MD
Henry P. and Georgette Goldschmidt Professor and Chairman of the Department of Neurology, Professor of Neuroscience, The Mount Sinai School of Medicine, New York [25]

STANLEY B. PRUSINER, MD
Director, Institute for Neurodegenerative Diseases; Professor, Department of Neurology; Professor, Department of Biochemistry and Biophysics, University of California, San Francisco [38]

NEIL H. RASKIN, MD
Professor of Neurology, University of California, San Francisco [6]

VICTOR I. REUS, MD
Professor, Department of Psychiatry, University of California, San Francisco School of Medicine; Attending Physician, Langley Porter Hospital and Clinics, San Francisco [49]

GARY S. RICHARDSON, MD
Assistant Professor of Psychiatry, Case Western Reserve University, Cleveland; Senior Research Scientist, Sleep Disorders and Research Center, Henry Ford Hospital, Detroit [16]

ELIZABETH ROBBINS, MD
Associate Clinical Professor, University of California, San Francisco [4]

GARY L. ROBERTSON, MD
Emeritus Professor of Medicine, Northwestern University Feinberg School of Medicine, Chicago [33]

KAREN L. ROOS, MD
John and Nancy Nelson Professor of Neurology, Indiana University School of Medicine, Indianapolis [35]

ALLAN H. ROPPER, MD
Executive Vice-Chair, Department of Neurology, Brigham and Women's Hospital, Harvard Medical School, Boston [14, 30, 31]

†Deceased.

ROGER N. ROSENBERG, MD
Zale Distinguished Chair and Professor of Neurology, Department of Neurology, University of Texas Southwestern Medical Center, Dallas [26]

MYRNA R. ROSENFELD, MD, PhD
Associate Professor of Neurology, Division Neuro-Oncology, Department of Neurology, University of Pennsylvania, Philadelphia [39]

STEPHEN M. SAGAR, MD
Professor of Neurology, Case Western Reserve School of Medicine; Director of Neuro-Oncology, Ireland Cancer Center, University Hospitals of Cleveland, Cleveland [32]

MARTIN A. SAMUELS, MD, *DSc (Hon)*
Chairman, Department of Neurology, Brigham and Women's Hospital; Professor of Neurology, Harvard Medical Center, Boston [45]

JOSHUA SCHIFFER, MD
Department of Internal Medicine, The Johns Hopkins University School of Medicine, Baltimore [Review and Self-Assessment]

MARC A. SCHUCKIT, MD
Distinguished Professor of Psychiatry, School of Medicine, University of California, San Diego; Director, Alcohol Research Center, VA San Diego Healthcare System, San Diego [50, 51]

WADE S. SMITH, MD, PhD
Professor of Neurology, Daryl R. Gress Endowed Chair of Neurocritical Care and Stroke; Director, University of California, San Francisco Neurovascular Service, San Francisco [21, 22]

ADAM SPIVAK, MD
Department of Internal Medicine, The Johns Hopkins University School of Medicine, Baltimore [Review and Self-Assessment]

STEPHEN E. STRAUS,† MD
Senior Investigator, Laboratory of Clinical Investigation, National Institute of Allergy and Infectious Diseases; Director, National Center for Complementary and Alternative Medicine, National Institutes of Health, Bethesda [47]

LEWIS SUDARSKY, MD
Associate Professor of Neurology, Harvard Medical School; Director of Movement Disorders, Brigham and Women's Hospital, Boston [11]

MORTON N. SWARTZ, MD
Professor of Medicine, Harvard Medical School; Chief, Jackson Firm Medical Service and Infectious Disease Unit, Massachusetts General Hospital, Boston [36]

KENNETH L. TYLER, MD
Reuler-Lewin Family Professor of Neurology and Professor of Medicine and Microbiology, University of Colorado Health Sciences Center; Chief, Neurology Service, Denver Veterans Affairs Medical Center, Denver [35]

CHARLES WIENER, MD
Professor of Medicine and Physiology; Vice Chair, Department of Medicine; Director, Osler Medical Training Program, The Johns Hopkins University School of Medicine, Baltimore [Review and Self-Assessment]

JOHN W. WINKELMAN, MD, PhD
Assistant Professor of Psychiatry, Harvard Medical School; Medical Director, Sleep Health Center, Brigham and Women's Hospital, Boston [16]

†Deceased.

PREFACE

The first edition of *Harrison's Neurology in Clinical Medicine* was an unqualified success. Readers responded enthusiastically to the convenient, attractive, expanded, and updated stand-alone volume, which was based upon the neurology and psychiatry sections from *Harrison's Principles of Internal Medicine.* Our original goal was to provide, in an easy-to-use format, full coverage of the most authoritative information available anywhere of clinically important topics in neurology and psychiatry, while retaining the focus on pathophysiology and therapy that has always been characteristic of *Harrison's.*

This new edition of Harrison's *Neurology in Clinical Medicine* has been extensively rewritten to highlight recent advances in the understanding, diagnosis, treatment and prevention of neurologic and psychiatric diseases. New chapters discuss the pathogenesis and treatment of headache, the clinical approach to imbalance, and the causes of confusion and delirium. Notable also are new chapters on essential tremor and movement disorders, peripheral neuropathy, and on neurologic problems in hospitalized patients. Many illustrative neuroimaging figures appear throughout the section, and a new atlas of neuroimaging findings has been added. Extensively updated coverage of the dementias, Parkinson's disease, and related neurodegenerative disorders highlight new findings from genetics, molecular imaging, cell biology, and clinical research that have transformed understanding of these common problems. Another new chapter, authored by Steve Hyman and Eric Kandel, reviews progress in deciphering the pathogenesis of common psychiatric disorders and discusses the remaining challenges to development of more effective treatments.

For many physicians, neurologic diseases represent particularly challenging problems. Acquisition of the requisite clinical skills is often viewed as time-consuming, difficult to master, and requiring a working knowledge of obscure anatomic facts and laundry lists of diagnostic possibilities. The patients themselves may be difficult, as neurologic disorders often alter an individual's capacity to recount the history of an illness or to even recognize that something is wrong. An additional obstacle is the development of independent neurology services, departments, and training programs at many medical centers, reducing the exposure of trainees in internal medicine to neurologic problems. All of these forces, acting within the fast-paced environment of modern medical practice, can lead to an overreliance on unfocused neuroimaging tests, suboptimal patient care, and unfortunate outcomes. Because neurologists represent less than 1% of all physicians, the vast majority of neurologic care must be delivered by nonspecialists who are often generalists and usually internists.

The old adage that neurologists "know everything but do nothing" has been rendered obsolete by advances in molecular medicine, imaging, bioengineering, and clinical research. Examples of new therapies include: thrombolytic therapy for acute ischemic stroke; endovascular recanalization for cerebrovascular disorders; intensive monitoring of brain pressure and cerebral blood flow for brain injury; effective therapies for immune-mediated neurologic disorders such as multiple sclerosis, immune neuropathies, myasthenia gravis, and myositis; new designer drugs for migraine; the first generation of rational therapies for neurodegenerative diseases; neural stimulators for Parkinson's disease; drugs for narcolepsy and other sleep disorders; and control of epilepsy by surgical resection of small seizure foci precisely localized by functional imaging and electrophysiology. The pipeline continues to grow, stimulated by a quickening tempo of discoveries generating opportunities for rational design of new diagnostics, interventions, and drugs.

The founding editors of *Harrison's Principles of Internal Medicine* acknowledged the importance of neurology but were uncertain as to its proper role in a textbook of internal medicine. An initial plan to exclude neurology from the first edition (1950) was reversed at the eleventh hour, and a neurology section was hastily prepared by Houston Merritt. By the second edition, the section was considerably enlarged by Raymond D. Adams, whose influence on the textbook was profound. The third neurology editor, Joseph B. Martin, brilliantly led the book during the 1980s and 1990s as neurology was transformed from a largely descriptive discipline to one of the most dynamic and rapidly evolving areas of medicine. With these changes, the growth of neurology coverage in *Harrison's* became so pronounced that Harrison suggested the book be retitled, "The Details of Neurology and Some Principles of Internal Medicine." His humorous comment, now legendary, underscores the

depth of coverage of neurologic medicine in *Harrison's* befitting its critical role in the practice of internal medicine.

The Editors are indebted to our authors, a group of internationally recognized authorities who have magnificently distilled a daunting body of information into the essential principles required to understand and manage commonly encountered neurological problems. We are also grateful to Dr. Andrew Scott Josephson who oversaw the updating process for the second edition of *Harrison's Neurology in Clinical Medicine*. Thanks also to Dr. Elizabeth Robbins, who has served for more than a decade as managing editor of the neurology section of *Harrison's*; she has overseen the complex logistics required to produce a multiauthored textbook, and has promoted exceptional standards for clarity, language and style. Finally, we wish to acknowledge and express our great appreciation to our colleagues at McGraw-Hill. This new volume was championed by James Shanahan and impeccably managed by Kim Davis.

We live in an electronic, wireless age. Information is downloaded rather than pulled from the shelf. Some have questioned the value of traditional books in this new era. We believe that as the volume of information, and the ways to access this information, continues to grow, the need to grasp the essential concepts of medical practice becomes even more challenging. One of our young colleagues recently remarked that he uses the Internet to find facts, but that he reads *Harrison's* to learn medicine. Our aim has always been to provide the reader with an integrated, organic summary of the science and the practice of medicine rather than a mere compendium of chapters, and we are delighted and humbled by the continuing and quite remarkable growth in popularity of *Harrison's* at a time when many "classics" in medicine seem less relevant than in years past.

It is our sincere hope that you will enjoy using *Harrison's Neurology in Clinical Medicine, Second Edition* as an authoritative source for the most up-to-date information in clinical neurology.

NOTE TO READERS ON ELECTRONIC ACCESS TO THE FAMILY OF *HARRISON'S* PUBLICATIONS THE NEUROLOGIC METHOD

The *Harrison's* collection of publications has expanded as information delivery technology has evolved. *Harrison's Online (HOL)* is now one of the standard informational resources used in medical centers throughout the United States. In addition to the full content of the parent text, *HOL* offers frequent updates from and links to the emerging scientific and clinical literature; an expanded collection of reference citations; audio recordings and Podcasts of lectures by authorities in the various specialties of medicine; and other helpful supplementary materials such as a complete database of pharmacologic therapeutics, self-assessment questions for examination and board review; and an expanded collection of clinical photographs. Video clips of cardiac and endoscopic imaging are also available on *HOL*. Future iterations of *HOL* will include expanded use of such supplementary multimedia materials to illustrate further key concepts and clinical approaches discussed in the parent text.

In 2006, in recognition of the increasing time pressures placed on clinicians and the increasing use of electronic medical records systems, *Harrison's Practice of Medicine (HP)* made its debut. *HP* is a comprehensive database of specific clinical topics built from the ground up to provide authoritative guidance quickly at the point of care. *HP* is highly structured so that physicians and other health professionals can access the most salient features of any one of more than 700 diseases and clinical presentations within minutes. This innovative new application is updated regularly and includes fully integrated, detailed information on brand name and generic drugs. In addition, hyperlinks throughout *HP* enable quick access to the primary literature via PubMed. *HP* is available via the Internet and on PDA.

Stephen L. Hauser, MD

NOTICE

Medicine is an ever-changing science. As new research and clinical experience broaden our knowledge, changes in treatment and drug therapy are required. The authors and the publisher of this work have checked with sources believed to be reliable in their efforts to provide information that is complete and generally in accord with the standards accepted at the time of publication. However, in view of the possibility of human error or changes in medical sciences, neither the authors nor the publisher nor any other party who has been involved in the preparation or publication of this work warrants that the information contained herein is in every respect accurate or complete, and they disclaim all responsibility for any errors or omissions or for the results obtained from use of the information contained in this work. Readers are encouraged to confirm the information contained herein with other sources. For example and in particular, readers are advised to check the product information sheet included in the package of each drug they plan to administer to be certain that the information contained in this work is accurate and that changes have not been made in the recommended dose or in the contraindications for administration. This recommendation is of particular importance in connection with new or infrequently used drugs.

Review and self-assessment questions and answers were taken from Wiener C, Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, Loscalzo J (editors) Bloomfield G, Brown CD, Schiffer J, Spivak A (contributing editors). *Harrison's Principles of Internal Medicine Self-Assessment and Board Review*, 17th ed. New York, McGraw-Hill, 2008, ISBN 978-0-07-149619-3.

The global icons call greater attention to key epidemiologic and clinical differences in the practice of medicine throughout the world.

The genetic icons identify a clinical issue with an explicit genetic relationship.

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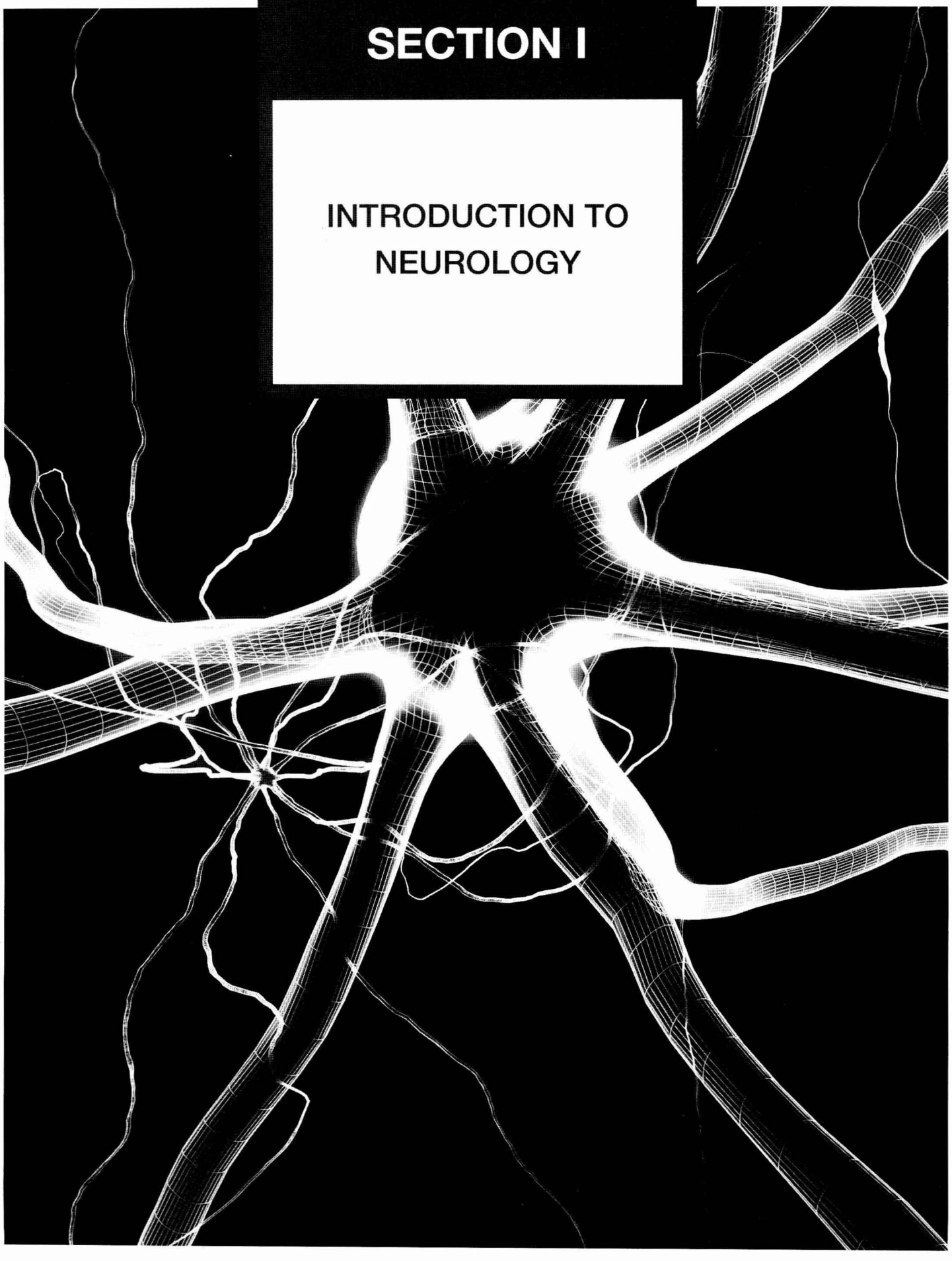
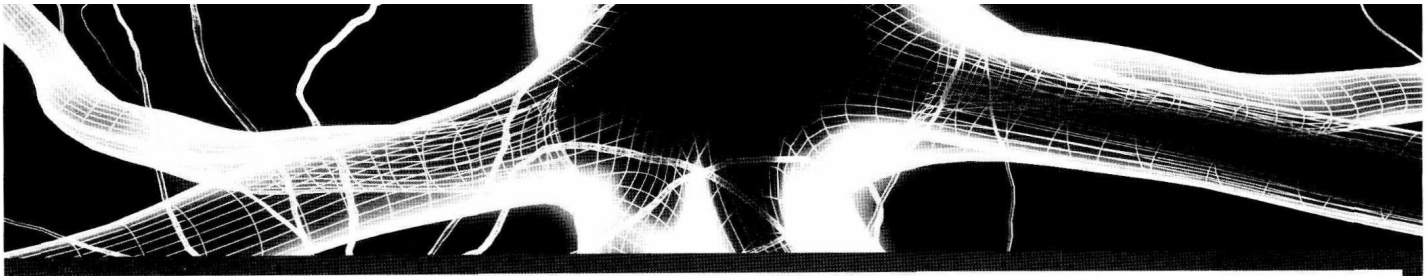
SECTION I

INTRODUCTION TO NEUROLOGY





CHAPTER 1

APPROACH TO THE PATIENT WITH NEUROLOGIC DISEASE

Daniel H. Lowenstein ■ Joseph B. Martin ■ Stephen L. Hauser

Neurologic diseases are common and costly. According to one estimate, 180 million Americans suffer from a nervous system disorder, resulting in an annual cost of over $700 billion. The aggregate cost is even greater than that for cardiovascular disease (**Table 1-1**). Globally, these disorders are responsible for 28% of all years lived with a disability. Most patients with neurologic symptoms seek care from internists and other generalists rather than from neurologists. Because therapies now exist for many neurologic disorders, a skillful approach to diagnosis is essential. Errors commonly result from an overreliance on costly neuroimaging procedures and laboratory tests, which, although useful, do not substitute for an adequate history and examination. The proper approach to the patient with a neurologic illness begins with the patient and focuses the clinical problem first in anatomic and then in pathophysiologic terms; only then should a specific diagnosis be entertained. This method ensures that technology is judiciously applied, a correct diagnosis is established in an efficient manner, and treatment is promptly initiated.

THE NEUROLOGIC METHOD

Locate the Lesion(s)

The first priority is to identify the region of the nervous system that is likely to be responsible for the symptoms. Can the disorder be mapped to one specific location, is it multifocal, or is a diffuse process present? Are the symptoms restricted to the nervous system, or do they arise in the context of a systemic illness? Is the problem in the central nervous system (CNS), the peripheral nervous system (PNS), or both? If in the CNS, is the cerebral cortex, basal ganglia, brainstem, cerebellum, or spinal cord responsible? Are the pain-sensitive meninges involved? If in the PNS, could the disorder be located in peripheral nerves and, if so, are motor or sensory nerves primarily affected, or is a lesion in the neuromuscular junction or muscle more likely?

The first clues to defining the anatomic area of involvement appear in the history, and the examination is then directed to confirm or rule out these impressions and to clarify uncertainties. A more detailed examination of a particular region of the CNS or PNS is often indicated. For example, the examination of a patient who presents with a history of ascending paresthesias and weakness should be directed toward deciding, among other things, if the location of the lesion is in the spinal cord or peripheral nerves. Focal back pain, a spinal cord sensory level, and incontinence suggest a spinal cord origin, whereas a stocking-glove pattern of sensory loss suggests peripheral nerve disease; areflexia usually indicates peripheral neuropathy but may also be present with spinal shock in acute spinal cord disorders.

Deciding "where the lesion is" accomplishes the task of limiting the possible etiologies to a manageable, finite number. In addition, this strategy safeguards against making serious errors. Symptoms of recurrent vertigo, diplopia, and nystagmus should not trigger "multiple

TABLE 1-1

PREVALENCE OF NEUROLOGIC AND PSYCHIATRIC DISEASES WORLDWIDE

DISORDER	PATIENTS, MILLIONS
Nutritional disorders and neuropathies	352
Migraine	326
Trauma	170
Depression	154
Alcoholism	91
Cerebrovascular diseases	61
Epilepsy	50
Schizophrenia	25
Dementia	24
Neurologic infections	18
Drug abuse	15

Source: World Health Organization estimates, 2002–2005.

sclerosis" as an answer (etiology) but "brainstem" or "pons" (location); then a diagnosis of brainstem arteriovenous malformation will not be missed for lack of consideration. Similarly, the combination of optic neuritis and spastic ataxic paraparesis should initially suggest optic nerve and spinal cord disease; multiple sclerosis (MS), CNS syphilis, and vitamin B_{12} deficiency are treatable disorders that can produce this syndrome. Once the question, "Where is the lesion?" is answered, then the question, "What is the lesion?" can be addressed.

Define the Pathophysiology

Clues to the pathophysiology of the disease process may also be present in the history. Primary neuronal (gray matter) disorders may present as early cognitive disturbances, movement disorders, or seizures, whereas white matter involvement produces predominantly "long tract" disorders of motor, sensory, visual, and cerebellar pathways. Progressive and symmetric symptoms often have a metabolic or degenerative origin; in such cases lesions are usually not sharply circumscribed. Thus, a patient with paraparesis and a clear spinal cord sensory level is unlikely to have vitamin B_{12} deficiency as the explanation. A Lhermitte symptom (electric shock–like sensations evoked by neck flexion) is due to ectopic impulse generation in white matter pathways and occurs with demyelination in the cervical spinal cord; among many possible causes, this symptom may indicate MS in a young adult or compressive cervical spondylosis in an older person. Symptoms that worsen after exposure to heat or exercise may indicate conduction block in demyelinated axons, as occurs in MS. A patient with recurrent episodes of diplopia and dysarthria associated with exercise or fatigue may have a disorder of neuromuscular transmission such as myasthenia gravis. Slowly advancing visual scotoma with luminous edges, termed *fortification spectra*, indicates spreading cortical depression, typically with migraine.

THE NEUROLOGIC HISTORY

Attention to the description of the symptoms experienced by the patient and substantiated by family members and others often permits an accurate localization and determination of the probable cause of the complaints, even before the neurologic examination is performed. The history also helps to bring a focus to the neurologic examination that follows. Each complaint should be pursued as far as possible to elucidate the location of the lesion, the likely underlying pathophysiology, and potential etiologies. For example, a patient complains of weakness of the right arm. What are the associated features? Does the patient have difficulty with brushing hair or reaching upward (proximal) or buttoning buttons or opening a twist-top bottle (distal)? Negative associations may also be crucial. A patient with a right hemiparesis without a language deficit likely has a lesion (internal capsule, brainstem, or spinal cord) different from that of a patient with a right hemiparesis and aphasia (left hemisphere). Other pertinent features of the history include the following:

1. *Temporal course of the illness.* It is important to determine the precise time of appearance and rate of progression of the symptoms experienced by the patient. The rapid onset of a neurologic complaint, occurring within seconds or minutes, usually indicates a vascular event, a seizure, or migraine. The onset of sensory symptoms located in one extremity that spread over a few seconds to adjacent portions of that extremity and then to the other regions of the body suggests a seizure. A more gradual onset and less well localized symptoms point to the possibility of a transient ischemic attack (TIA). A similar but slower temporal march of symptoms accompanied by headache, nausea, or visual disturbance suggests migraine. The presence of "positive" sensory symptoms (e.g., tingling or sensations that are difficult to describe) or involuntary motor movements suggests a seizure; in contrast, transient loss of function (negative symptoms) suggests a TIA. A stuttering onset where symptoms appear, stabilize, and then progress over hours or days also suggests cerebrovascular disease; an additional history of transient remission or regression indicates that the process is more likely due to ischemia rather than hemorrhage. A gradual evolution of symptoms over hours or days suggests a toxic, metabolic, infectious, or inflammatory process. Progressing symptoms associated with the systemic manifestations of fever, stiff