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HARRISON'S

NEUROLOGY IN CLINICAL MEDICINE

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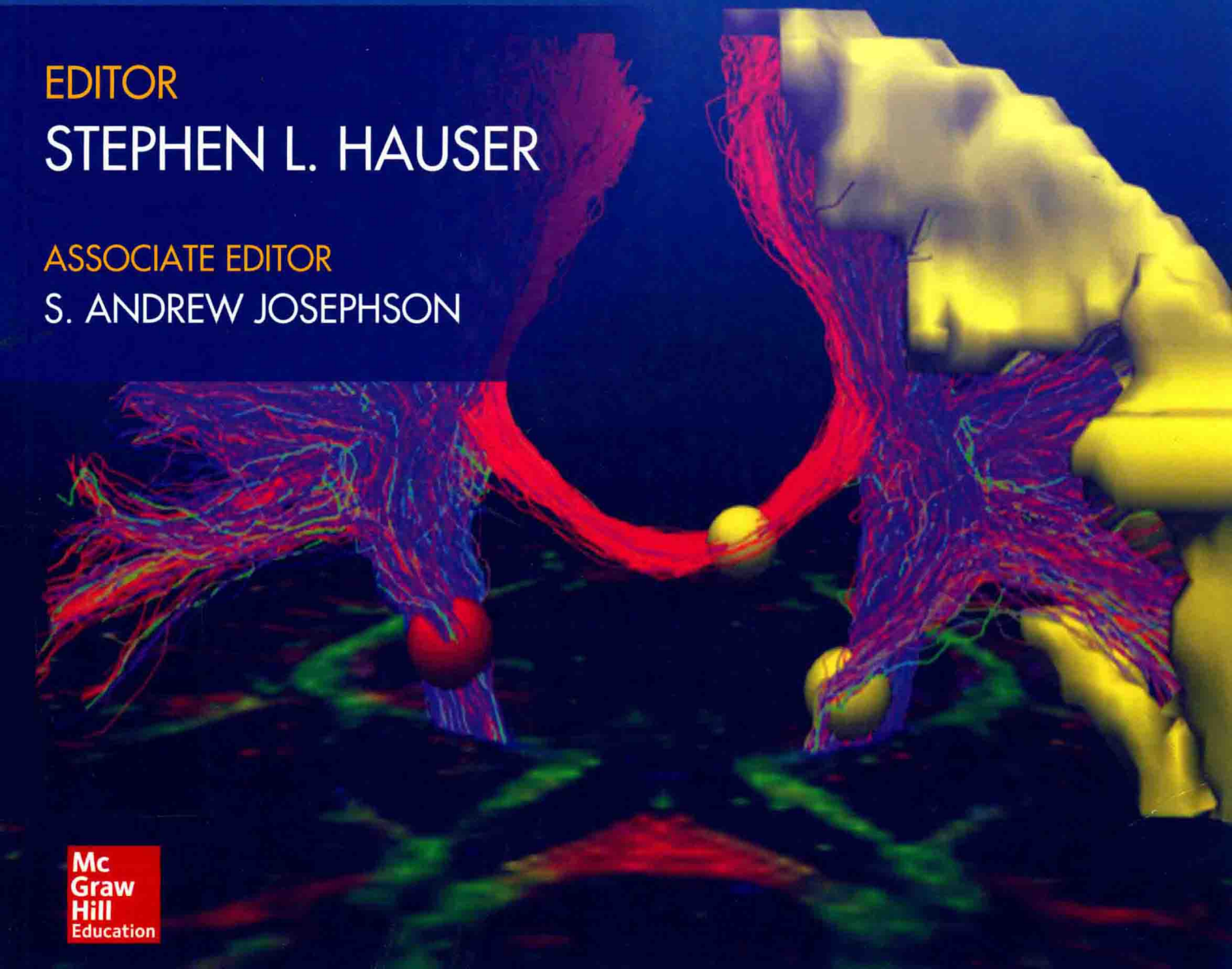

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NEUROLOGY IN CLINICAL MEDICINE

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NEUROLOGY IN CLINICAL MEDICINE

Derived from Harrison's Principles of Internal Medicine, 18th Edition

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PREFACE

The first two editions of *Harrison's Neurology in Clinical Medicine* were unqualified successes. 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 third edition of *Harrison's Neurology in Clinical Medicine* has been extensively updated to highlight recent advances in the understanding, diagnosis, treatment, and prevention of neurologic and psychiatric diseases. New chapters discuss the pathogenesis and treatment of syncope, dizziness and vertigo, smell and taste disorders, Parkinson's disease, tumors of the nervous system, peripheral neuropathy, and neuropsychiatric problems among war veterans, among other topics. Extensively updated coverage of the dementias highlights new findings from genetics, molecular imaging, cell biology, and clinical research that are transforming our understanding of these common problems. Neuroimmunology is another dynamic and rapidly changing field of neurology, and the new edition of *Harrison's* provides extensive coverage of progress in this area, including a practical guide to navigating the large number of treatment options now available for multiple sclerosis. Another new chapter reviews advances in deciphering the pathogenesis of common psychiatric disorders and discusses challenges to the development of more effective treatments. Many illustrative neuroimaging figures appear throughout the section, and an updated and expanded atlas of neuroimaging findings is also included. We are extremely pleased that readers of the new edition of *Harrison's* will for the first time be able to access a remarkable series of high-definition video presentations including wonderful guides to screening and detailed neurological examinations, as well as video libraries illustrating gait disorders, focal cerebral disorders, and neuro-ophthalmologic disturbances.

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; 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 neurologic problems. Thanks also to Dr. Elizabeth Robbins who has served for more than 15 years 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. We are of course cognizant of the flexibility in information delivery that today's readers seek, and so we have also made the third edition of *Harrison's Neurology in Clinical Medicine* available in a number of eBook formats for all major devices, including the iPad (available via the iBookstore).

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

Stephen L. Hauser, MD

SECTION I

INTRODUCTION TO NEUROLOGY

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 CM, Brown CD, Hemnes AR (eds). *Harrison's Self-Assessment and Board Review,* 18th ed. New York, McGraw-Hill, 2012, ISBN 978-0-07-177195-5.

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.

CONTENTS

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 recent estimates by the World Health Organization, neurologic disorders affect over 1 billion people worldwide (Table 1-1), constitute 6.3% of the global burden of disease, and cause 12% of global deaths. 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, while 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.

TABLE 1-1

PREVALENCE OF NEUROLOGIC AND PSYCHIATRIC DISEASES WORLDWIDE

DISORDER	PATIENTS, MILLIONS
Nutritional disorders and neuropathies	352
Migraine	326
Trauma	170
Cerebrovascular diseases	61
Epilepsy	50
Dementia	24
Neurologic infections	18

Source: World Health Organization estimates, 2002–2005.

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 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 neck, and altered level of consciousness imply an infectious process. Relapsing and remitting symptoms involving different levels of the nervous system suggest MS or other inflammatory processes. Slowly progressive symptoms without remissions are characteristic of neurodegenerative disorders, chronic infections, gradual intoxications, and neoplasms.
2. *Patients' descriptions of the complaint.* The same words often mean different things to different patients. "Dizziness" may imply impending syncope, a sense of disequilibrium, or true spinning vertigo. "Numbness" may mean a complete loss of feeling, a positive sensation such as tingling, or even weakness. "Blurred vision" may be used to describe unilateral visual loss, as in transient monocular blindness, or diplopia. The interpretation of the true meaning of the words used by patients to describe symptoms