Clinical Neurology & Neuroanatomy

A Localization-Based Approach

Aaron L. Berkowitz

2nd Edition

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Second Edition

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This book is dedicated to:

My mentors Dr. Martin A. Samuels, Dr. Allan H. Ropper, and Dr. Steven K. Feske, who through their extraordinary mentorship and teaching trained me not only in the science of Neurology, but in the art of Medicine.

The students and residents at Harvard Medical School and the Partners Neurology residency program (Boston); the residents and faculty at Hôpital Universitaire de Mirebalais, Hôpital St. Nicolas de St. Marc, and Hôpital St. Boniface (Haiti); and the students and residents at Queen Elizabeth Central Hospital and Kamuzu Central Hospital (Malawi), who through their brilliant questions and insatiable desire to learn taught me how to teach neurology.

The patients with and through whom I learned the practice of neurology and medicine, and whose courage in the face of suffering inspires us to learn more about their diseases, teach what we learn to others, and serve them and their families to the best of our abilities.

My wife Nina, whose boundless support, encouragement, and companionship have been both a sustaining force and a source of great joy.

My father (in memoriam), who instilled in me a passion for science, medicine, and service.

Contents

Foreword

So much of neurology exists only "in use". This is the neurology that is practiced in the clinics, wards, and offices of seasoned clinicians and cannot be found in large encyclopedic textbooks of neurology or smaller monographs intended for medical students. The accumulated experience of the neurologist can be distilled to a number of action items and thought processes that are challenging to articulate.

Dr. Aaron Berkowitz has written a book that occupies just this position. He has taken the transactional daily work of neurology and produced a wonderfully readable, concise, but by no means superficial book that fits well in the current pedagogic environment. One might ask whether any book on neurology is needed now that disembodied information is so easily available on the web and algorithms for various signs, symptoms, and diseases abound. But between information that is as often misleading as it is useful, and the storehouse of wisdom accumulated over a long career, sits a great body of neurological knowledge. It is this assembled knowledge that allows us to efficiently move through the workday and can be taught to students and residents during their rotations. Berkowitz's book is more than a compendium or teaching guide and is far superior to existing books of its size and scope because of the thoughtfulness with which the knowledge about diseases and neurological conditions has been assembled. He gets right down to business, addressing almost every major point that is encountered on the wards and in the clinic.

A book such as this one is more suitable for neurology than for any other branch of medicine. We still depend on the interface between our own refined clinical skills and our decisions regarding diagnosis and treatment. The pearls contained here about the meaning of particulars of the history and examination cannot be found elsewhere. The book makes a seamless transit from these data to practical wisdom about their application. The material is clear and avoids the ambiguity that clutters most other books. In doing so, it also incorporates the latest thinking from clinical trials and together, these features provide one of the best modern outlooks on the pragmatic practice of neurology.

It takes a certain outlook on pedagogy and practice to produce such a book. Dr. Berkowitz has more than succeeded, and I find myself looking at a number of the chapters over and over to reorient myself to solid teaching and practice.

Allan H. Ropper, MD
Professor of Neurology
Harvard Medical School
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Preface to the First Edition

There are many extraordinary neurology and neuroanatomy textbooks. Innumerable clinical pearls can be gleaned from dedicated time spent with these texts as a student, trainee, and practitioner. Yet when I was a student and then a trainee, I found that there was no single text that provided a comprehensive introduction to clinical neuroanatomy, its application to neurology, and the diagnosis and management of both common and rare neurologic diseases in one concise volume. I had wished that there was a book that could be read cover-to-cover as a student rotating through neurology, or when I was a soon-to-be neurology resident at the end of my medical internship, or as a quick reference to efficiently review topics as a neurology resident—a book in which one or more chapters could be read in a single sitting. As I began to teach neuroanatomy and neurology to students, residents, and non-neurologists, I learned that they too wished for such a book. In *Clinical Neurology & Neuroanatomy: A Localization-Based Approach*, I decided to attempt to write that book.

Some of the many essential textbooks that nearly all neurologists return to throughout training and practice include Brazis' *Localization in Clinical Neurology*, Patten's *Neurologic Differential Diagnosis*, and Blumenfeld's *Neuroanatomy through Clinical Cases* for neurologic localization and clinical neuroanatomy; Adams and Victor's *Principles of Neurology* and Bradley's *Neurology in Clinical Practice* for clinical neurology. *Clinical Neurology & Neuroanatomy: A Localization-Based Approach* is, by design, a fraction of the size of any one of these books, and is meant to provide a concise but comprehensive framework to facilitate engagement with those texts. My goal is to distill clinical neuroanatomy, clinical neurology, and their interrelations to their fundamental principles so as to explain them clearly and simply. In so doing, I hope to convey the core material essential to the practice of neurology in an efficient and easily digestible format with the depth and detail required of neurology residents and neurologists reviewing for recertification examinations, but also with sufficient clarity and brevity for medical students on neurology rotations and non-neurologists in settings where there are few or no neurologists.

In Part 1 of this book, clinically relevant neuroanatomy is presented in clinical context in order to provide a framework for neurologic localization and differential diagnosis. The diseases mentioned in localization-based discussions of differential diagnoses in Part 1 are then discussed in clinical detail with respect to their diagnosis and management in Part 2. For example, in Chapter 5, the anatomy of the spinal cord and its relation to clinical syndromes involving the spinal cord are discussed. The differential diagnosis of myelopathy is presented, but the evaluation and management of many of the diseases mentioned that can cause myelopathy are discussed in Part 2 (e.g., vascular diseases of the spinal cord are discussed in Ch. 19, infections of the spine in Ch. 20, inflammatory conditions of the spinal cord in Ch. 21). Part 1 of this book can therefore be consulted for a neuroanatomical localization-based approach to symptom evaluation, and Part 2 for the clinical features, diagnosis, and management of neurologic diseases. Certain diseases are more logically discussed directly in the context of their underlying anatomy, and where this is the case, these diseases are discussed in Part 1 (e.g., trigeminal neuralgia and Bell's palsy in Ch. 13 on the trigeminal and facial nerves; benign paroxysmal positional vertigo in Ch. 12 on the vestibular system and the approach to vertigo).

Neurology is learned by taking care of patients: thinking through localization and differential diagnosis, evaluation, and management of individual patients, and discussing these patients' cases with one's clinical teachers and colleagues. This book is of course no replacement for that experience. However, my hope is that this book will serve as a guide to and through that process.

Aaron L. Berkowitz, MD, PhD

Preface to the Second Edition

In the five years since the first edition of this book, there has been an explosion in new knowledge that directly impacts our care of patients with neurologic disease. New treatments have emerged for epilepsy, multiple sclerosis, and migraine. New diseases have been characterized (antibody-mediated syndromes), new criteria for diagnosis of existing diseases have been established (multiple sclerosis), and new categorizations of existing diseases have been created (brain tumors). New clinical trial data has transformed the treatment of acute stroke. New treatments for systemic cancer (immunotherapy and CAR T-cell therapy) have generated a new spectrum of cancer treatment-associated neurologic conditions. All of these exciting updates are included in this second edition, and still this book will likely have aspects that are out-of-date as soon as it goes to press. What other field of medicine has come so far in so short a time, and yet still has so far to go? This constant evolution is one of many aspects that makes neurology such a dynamic, engaging, and meaningful field to study and practice.

When I set out to revise this book to include all of the above developments, some colleagues said, "Well, at least you won't have to revise the neuroanatomy that doesn't change." While neuroanatomy may not change, it is vast and we are constantly learning more through study and practice. I've had the great fortune to work with students and residents whose questions have helped me learn more, deepen my understanding, and find new ways to teach. I've also been fortunate to receive feedback from readers and colleagues on topics to add, concepts to clarify, and clinical correlations to emphasize. Thanks to the incredible artistry of Craig Durant and his colleagues at Dragonfly Media. This second edition includes many new drawings of the neuroanatomical pathways as well as narrated animations available on the AccessMedicine website.

In working on this second edition, I have been fortunate to receive feedback from subspecialist experts, who helped to make sure I didn't miss any developments and that my understanding of the latest updates in their fields were correct, precise, and practical. I extend my utmost gratitude to Dr. Jong Woo Lee (Epilepsy, Brigham and Women's Hospital), Dr. Tracey Milligan (Epilepsy, New York Medical College), Dr. Justin Sattin (Vascular Neurology, University of Wisconsin), Dr. Eli Zimmerman (Vascular Neurology, Vanderbilt University), Dr. Casey Albin (Neuro-Critical Care, Emory), Dr. Arun Venkatesan (Neuro-Infectious Disease, Johns Hopkins), Dr. Pria Anand (Neuro-Infectious Disease, Boston University), Dr. Shamik Bhattacharyya (Multiple Sclerosis and Autoimmune Neurology, BWH), Dr. Emmanuelle Waubant (Multiple Sclerosis, UCSF), Dr. Andrew Stern (Cognitive/Behavioral Neurology, BWH), Dr. Emily Ferenczi (Movement Disorders, BWH), Dr. Joshua Budhu (Neuro-Oncology, BWH/MGH), Dr. Maya Graham (Neuro-Oncology, Memorial Sloan-Kettering), Dr. Rebecca Burch (Headache, BWH), Dr. Christopher Doughty (Neuromuscular, BWH), Dr. Tabby Kennedy (Neuroradiology, University of Wisconsin).

Acknowledgments

I am very fortunate to have trained in neurology under two of the field's great luminaries, Dr. Allan H. Ropper and Dr. Martin A. Samuels. They are not only two virtuosic neurologists, they are extraordinary teachers, inspiring and dedicated mentors, and serve as role models of the Complete Physician toward which to strive.

Dr. Steve Feske has also been an extremely important guru in my development as a neurologist. I have learned so much from discussing cases with him, and admire his balance of clinical wisdom and rigorous analysis of the evidence (or lack thereof) when approaching the most complex cases with extreme clarity. I often find myself "trying to ask my inner Feske" when faced with vexing clinical dilemmas.

I would also like to thank the faculty of the Partners Neurology Residency Program who trained me, with special gratitude to Dr. Tracey Milligan, Dr. Nagagopal Venna, Dr. Steve M. Greenberg, Dr. Albert Hung, Dr. Sashank Prasad, Dr. Anthony Amato, Dr. Tracey Cho, Dr. Joshua Klein, and Dr. Sherry Chou for their clinical teaching and mentorship.

I have learned so much from the residents and students with whom I have been privileged to work in Boston, in Haiti, and in Malawi. Their questions and their pursuit of answers to questions I could not answer have enriched my own knowledge, and in turn, have helped me to develop as a teacher of neurology and neuroanatomy.

In Haiti, where there is one neurologist for 10 million citizens, I have had the honor of teaching neurology to family practitioners and internists for the last several years. Dr. Patrick Jouissance, my long-time colleague in Haiti, once said to me after a week of neurology training for his family medicine residents, "We need a clear and concise neurology textbook- please write one for us!" I hope he and his residents will find that this book fulfills their request.

In writing the first edition of this book, I was fortunate that my expert subspecialty colleagues from Brigham and Women's Hospital (BWH) and Massachusetts General Hospital (MGH) took time out of their busy schedules to review individual chapters in their areas of expertise, and this book has benefited greatly from their thoughtful reviews and insightful suggestions. I extend enormous thanks to Dr. Anthony Amato (Neuromuscular Diseases, BWH), Dr. Shamik Bhattacharyya (Multiple Sclerosis and Autoimmune Neurology, BWH), Dr. Tracey Cho (Neuro-infectious Diseases, MGH), Dr. Thomas Cochrane (Neuromuscular Diseases, BWH), Dr. Barbara Dworetzky (Epilepsy, BWH), Dr. Claudio DeGusmao (Pediatric and Transitional Neurology, BWH), Dr. Steven Feske (Vascular neurology and Neurocritical care, BWH), Dr. Steven M. Greenberg (Vascular neurology, MGH), Dr. Albert Hung (Movement Disorders, BWH/MGH), Dr. Tamara Kaplan (Fellow in Multiple Sclerosis and Demyelinating Diseases, BWH), Dr. Joshua Klein (Neuroradiology and Neurology, BWH), Dr. Jong Woo Lee (Epilepsy, BWH), Dr. Jennifer Lyons (Neuro-infectious Diseases, BWH), Dr. Scott McGinnis (Behavioral and Cognitive Neurology, BWH), Dr. William Mullally (Headache, BWH), Dr. Lakshmi Nayak (Neuro-oncology, BWH), Dr. Page Pennell (Epilepsy, BWH), Dr. Sashank Prasad (Neuro-ophthalmology, BWH), and Dr. James Stankiewicz (Multiple Sclerosis and Demyelinating Diseases, BWH).

I am also grateful to the residents and medical students who took the book for a "test drive" and provided thoughtful feedback: Dr. Emer McGrath, Dr. Pooja Raibagkar, Dr. Francois Roosevelt, Dr. Michael Erkkinen, and Cathy Hao.

The first edition of this book would not have been possible without the phenomenal stewardship of Andrew Moyer and the efforts of his team at McGraw Hill. Andrew guided this book from idea to production and he and his team developed creative ways to enhance the pedagogy of the text and figures through their layout and presentation. I am grateful to Tim Hiscock, Peter Boyle, and their team at McGraw Hill for shepherding this book through its second edition. Tasneem Kauser and her team at KnowledgeWorks Global Ltd. effectively and efficiently transformed the countless text and image files with which I provided them into the book you are holding and were a pleasure to work with.

Finally, to the patients who have taught me all of the neurology I know, I hope that this book will honor your courage in facing neurologic disease and your generosity in allowing us to learn from you.

PART I NEUROANATOMY & NEUROANATOMIC LOCALIZATION

Diagnostic Reasoning in Neurology & the Neurologic History & Examination

CHAPTER 1

CHAPTER CONTENTS

Differential diagnosis in neurology is based on two main components determined from the clinical history and physical examination:

- The **localization** of the neuroanatomic origin(s) of the patient's symptoms and signs
- The **time course** over which these symptoms and signs have arisen and evolved

These give rise to what I call the "fundamental equation" of differential diagnosis in neurology:

Differential Diagnosis = Localization × Time course

Localization relies on the clinical history and neurologic examination to determine *where* in the nervous system the problem is. To some extent, knowing *where* the problem is already begins to circumscribe *what* the problem is, since each level of the nervous system has a particular differential diagnosis for the types of disease processes that can affect it. The time course over which neurologic symptoms arise and evolve provides crucial information in determining *what* the problem is, since different disease processes emerge and evolve over different time frames.

LOCALIZATION IN NEUROLOGIC DIAGNOSIS: DETERMINING *WHERE* THE PROBLEM IS

Localization is the process of determining *where* in the nervous system the patient's disease process is occurring: Is the problem in the central nervous system (CNS), the peripheral nervous system (PNS), or both? Within the CNS, is there a lesion in the brain, brainstem, cerebellum, or spinal cord? More precisely, *where* is the lesion within those structures? For example, which *level* of the brainstem or spinal cord? Which hemisphere(s), lobe(s), and gyrus/gyri of the brain? Within the PNS, is the lesion at the level of the spinal roots, dorsal root ganglia, peripheral nerves, neuromuscular junction, or

muscles? If there is a root, nerve, or muscle problem, which root(s), nerve(s), and/or muscle(s) is/are involved?

Nervous system diseases may affect particular **structures** (e.g., the basal ganglia, the cerebellum, the peripheral nerves), a particular **tissue type** (e.g., white matter vs gray matter of the brain; myelin of peripheral nerves vs their axons), or one or more particular **systems** (e.g., the motor system, the limbic system).

Localization requires a detailed understanding of neuroanatomy. Part 1 of this book presents clinical neuroanatomy alongside the clinical approach to symptoms and signs related to the anatomy under discussion. Diseases that are mentioned in Part 1 of this book are discussed in more detail with respect to their clinical features, diagnosis, and treatment in Part 2.

Localization begins with the clinical history, which should elucidate the nature of the patient's presenting symptom(s) and allow for an initial idea of potential localization(s). For example, is a chief concern of "difficulty walking" due to weakness, impaired coordination, altered sensation, pain, decreased vision, higher-order motor dysfunction, or a non-neurologic (e.g., orthopedic) condition? The neurologic examination provides further clues as to the neuroanatomic localization of the patient's symptoms (see "Introduction to the Neurologic Examination").

TIME COURSE IN NEUROLOGIC DIAGNOSIS: DETERMINING *WHAT* THE PROBLEM IS (FIG. 1–1)

The time course of symptom onset and evolution may be described as **sudden/hyperacute** (seconds to minutes), **acute** (hours to days), **subacute** (weeks to months), or **chronic** (months to years). The following is a general "first pass" in neurologic differential diagnosis based on the timing of symptom onset and pace of symptom evolution (with a few exceptions noted below):

- **Hyperacute (seconds to minutes)**:
  - **Vascular** (e.g., ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage)
  - **Seizure**
  - **Migraine**
  - **Metabolic** (e.g., hyperglycemia or hypoglycemia)
  - **Medications/Toxins**
  - **Trauma**

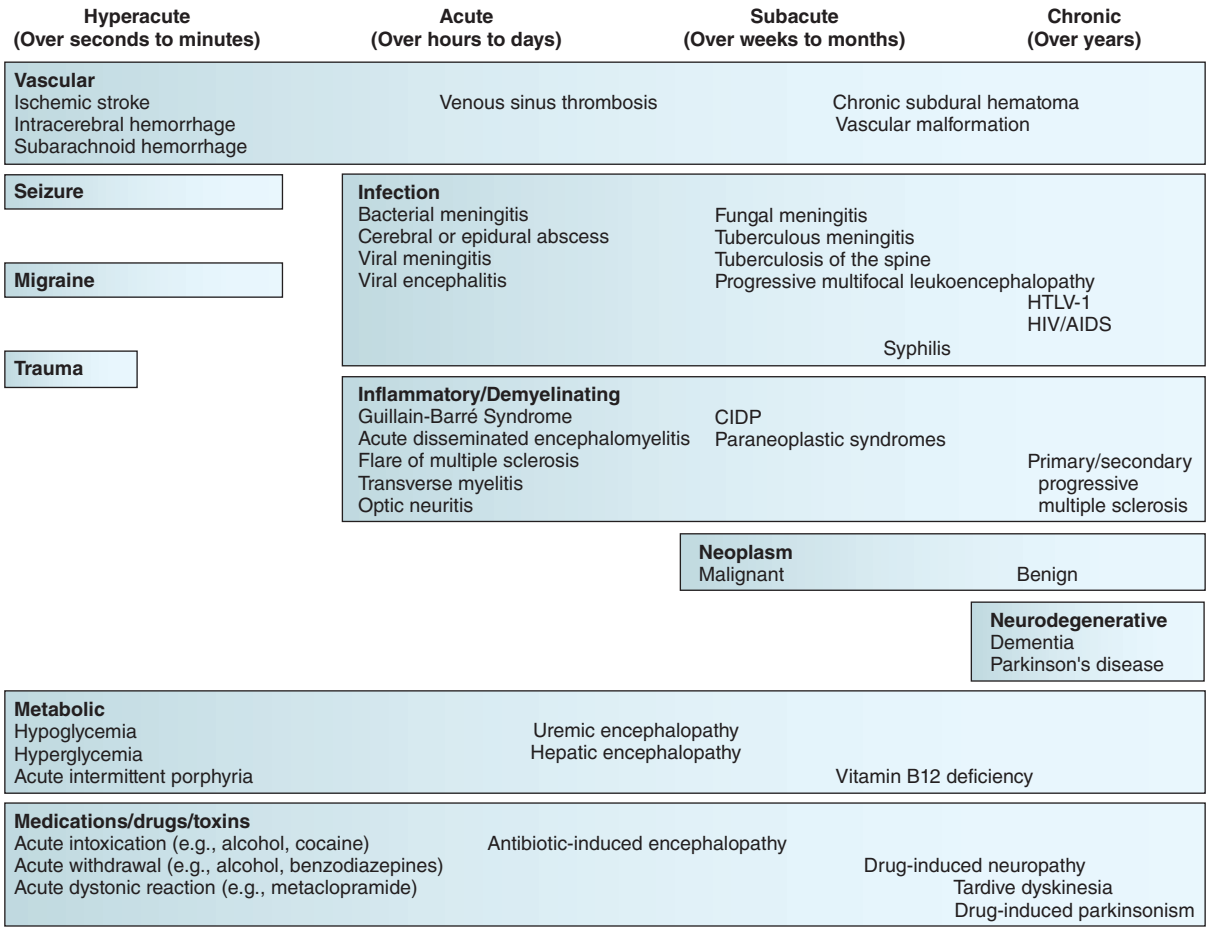

FIGURE 1–1 **Schematic showing differential diagnosis of neurologic disease by time course.**

- **Acute (hours to days)**:
  - **Infectious** (bacterial and viral infections of the nervous system; e.g., meningitis, encephalitis, abscess)
  - **Immune-mediated** (e.g., Guillain-Barré syndrome, flare of multiple sclerosis)
  - **Metabolic** (e.g., uremia, hepatic encephalopathy, hyponatremia or hypernatremia)
  - **Medications/Toxins**
- **Subacute (weeks to months)**
  - **Neoplastic**
  - **Immune-mediated** (e.g., paraneoplastic/antibody-mediated syndromes)
  - **Infectious** (fungal, tuberculous, and parasitic infections, neurologic complications of HIV)
  - **Metabolic** (e.g., vitamin B12 deficiency)
  - **Medications/Toxins**
- **Chronic (months to years)**
  - **Degenerative diseases** (e.g., Alzheimer's disease, Parkinson's disease)
  - **Genetic** (e.g., Charcot-Marie-Tooth, hereditary spastic paraplegia, Huntington disease)
  - **Metabolic**
  - **Medications/Toxins**

Note that if one keeps in mind that metabolic abnormalities, medications, and toxins can cause neurologic dysfunction over nearly any time course (depending on the metabolic abnormality, medication, or toxin), the rest of this schema distills to:

- **Hyperacute**: vascular, seizure, migraine, trauma
- **Acute to subacute**: infectious, immune-mediated
- **Subacute to chronic**: neoplastic, immune-mediated, infectious
- **Chronic**: degenerative, genetic

There are a few important exceptions to this general schema:

- Nonacute disease processes may present acutely. For example, although focal deficits from tumors usually emerge and evolve subacutely, a brain tumor may be asymptomatic until it causes a seizure. Another example is relapsing-remitting multiple sclerosis, a chronic disease characterized by acute flares.
- Although most vascular problems present hyperacutely, chronic subdural hematoma is an example of a vascular condition that presents subacutely/chronically (see Ch. 19).
- Fungal infections, tuberculosis, and neurologic complications of HIV can present subacutely compared to bacterial and viral infections, which present more acutely (see Ch. 20).

With the exception of seizure and migraine, which are exclusively cerebral phenomena, the other categories apply across most levels of the neuraxis. For example, sudden-onset findings localizing to a particular part of the brain suggest a vascular cause, and this is also true of the spinal cord (e.g., spinal infarct, spinal epidural hemorrhage) and even of a sudden-onset peripheral nerve palsy (e.g., nerve infarction as can be seen in vasculitis). Acute inflammatory disease of the brain (e.g., acute flare of multiple sclerosis), spine (e.g., transverse myelitis), or peripheral nerves (e.g., Guillain-Barré syndrome) all emerge and evolve over hours to days.

ASSOCIATED SYMPTOMS & SIGNS IN NEUROLOGIC DIAGNOSIS

In addition to the time course of symptom onset and evolution, the history must elicit associated concurrent or preceding symptoms to contextualize the patient's primary symptom. For example, if the presenting symptom is weakness, is this weakness accompanied by sensory changes and/or pain? Is the presenting symptom restricted to the limb most prominently noted by the patient or is it also present elsewhere? If the symptom is headache, is there associated nausea/vomiting or are there visual changes? Such questions establish the full range of the patient's symptoms beyond the "chief concern" most salient to the patient, aiding in localization of the cause of the patient's symptoms.

Of course, as in all areas of medicine, each symptom must also be fully characterized with respect to its quality, severity, exacerbating and alleviating factors, and any accompanying symptoms. The patient's presenting symptom(s) must also be contextualized with respect to the past medical history, family history, social history, and medications.

The clinical history should allow for an initial hypothesis to be generated about *where* in the nervous system the problem may be as well as *what* it may be, and the neurologic examination provides further information to support or refute this hypothesis.

INTRODUCTION TO THE NEUROLOGIC EXAMINATION

The neurologic examination is a critical tool in localization, confirming or refuting hypotheses generated during the history, or sometimes giving rise to new ones entirely. For example, is the patient's presenting problem of "difficulty moving one hand" due to weakness, slowed movement, numbness, pain, incoordination, or inability to execute a complex movement plan? Each of these possibilities can be tested in the course of the neurologic examination.

With each element of the neurologic examination, it is important to consider which systems and structures within the nervous system are being evaluated and how their dysfunction could manifest. When working toward mastery of the neurologic examination and its interpretation, it is helpful to try to imagine the pathways involved while examining them. For example, when testing the pupillary light reflex, think: "afferent via optic nerve to pretectal nuclei of the midbrain, efferent via Edinger-Westphal nuclei to the oculomotor nerves" (see Ch. 10). When testing a muscle, think about the name of the muscle and its nerve and nerve root supply (see Chs. 16–17).

The neurologic examination is divided into seven components:

1. **Mental status**
2. **Cranial nerves**
3. **Motor**
4. **Sensory**
5. **Reflexes**
6. **Coordination**
7. **Gait**

Each of these components of the neurologic examination has countless individual examination maneuvers, and only the basic elements are briefly introduced here. Many more detailed aspects of the examination of each system are described in Chapters 3–17 alongside a more in-depth discussion of the neuroanatomic localization and clinical significance of abnormal examination findings.

Examination of Mental Status

The examination of the patient's mental status evaluates two aspects of the mental state:

- The **level of consciousness**
- The integrity of individual **cognitive functions** (e.g., attention, memory, language, calculation, abstract reasoning, praxis)

Examination of the Level of Consciousness: Assessment of the Reticular Activating System, Thalami, & Cerebral Hemispheres

The neuroanatomic substrates of consciousness include the reticular activating system and other ascending projections from the brainstem, which project to the bilateral thalami and to the bilateral cerebral hemispheres.

The level of consciousness refers to the patient's state of arousal: Is the patient awake? If the patient is awake, is she or he alert? If the patient is alert, is she or he attentive? If the patient is not awake, can she or he be awakened by voice or is vigorous stimulation required to awaken the patient? Once awakened, is wakefulness maintained or does the patient fall back to sleep? These types of descriptions are more precise for clinical communication than stating that a patient is **delirious** (fluctuating acute confusion), **lethargic** or **somnolent** (falls asleep without repeated stimulation), **stuporous** (requires vigorous and/or painful physical stimulation to be awakened), **obtunded** (somewhere between somnolent and stuporous), or **comatose** (not able to be aroused by any stimulus of any sort and no response to the environment). These terms may mean different things to different clinicians, and so the precise descriptions noted above are generally preferable when describing a patient's mental state.

Examination of the Integrity of Cognitive Functions: Assessment of the Cerebral Hemispheres

The neuroanatomic substrates of cognition reside in the cerebral hemispheres. Individual cortical regions, networks of these regions and subcortical structures, and their interconnections are specialized for different cognitive functions (see Ch. 7).

Generally, the examiner develops a good sense of the patient's mental status during the history: Is the patient's flow of ideas logical and clear? Is the patient's speech fluent? Does the recounting of recent and past events demonstrate that the patient's memory is intact? Does the patient respond appropriately to questions? Difficulties with any of these may give initial inklings of cognitive deficits that can be further evaluated on the mental status examination.

If the patient is not awake, or not arousable for long enough to engage in the examination, cognition cannot be tested. If the patient is awake and alert, the first cognitive modality to test is **attention**. If the patient's attention is impaired, the other cognitive domains cannot be effectively evaluated. For example, if you are sending or reading a text message during a lecture, despite hearing what the lecturer says, you may not remember it later: without paying attention, you cannot store the information in memory. Similarly, if you are not paying attention to what someone is saying to you, you may not understand what is said, and your response may not make sense, so your language comprehension in that moment may be suboptimal. Therefore, cognitive modalities beyond attention can only be reliably tested if attention is intact.

***Examination of Attention: A Function of the Frontal and Parietal Lobes*—**Attention cannot occur without perception. For example, if a patient is blind, the patient cannot pay attention to a visual stimulus. The ability to select what to pay attention to and the ability to maintain attention are subserved by the frontal and parietal lobes. Attention can be tested by assessing the patient's ability to recite a string of numbers forward and backward (digit span), asking the patient to recite the days of the week (or the months of the year) backward, asking the patient to spell the word "world" backward (or another word of similar length), or asking the patient to subtract seven serially from 100 (100, 93, 86, and so on). These tasks require maintaining attention and concentration on the task at hand, and any lapse in attention will cause the patient to get lost, or make other errors (e.g., start going forward rather than backward). Note that the spelling task requires language ability and the subtraction task requires calculation, so forward and backward repetition of a string of numbers of increasing length provided by the examiner or recitation of the days of the week (or months of the year) backward may be simpler and less confounded ways of testing attention.

Inattention is a core feature of the altered mental state in delirium (see Ch. 22), and inattention to one-half of the world (**neglect**) can be seen with parietal lesions (most commonly right parietal lesions producing left-sided neglect; see Ch. 7).

***Examination of Memory: A Function of the Temporal Lobes*—**Short-term memory can be tested by asking patients about the recent past (e.g., what they had for breakfast that

morning, current events), and long-term memory can be tested by asking about the remote past (e.g., where they were born, went to school), although accuracy of the responses may be hard for the examiner to verify if the patient is being examined alone. Note that even patients with the most profound deficits in memory due to neurologic conditions should never forget their own names. Forgetting one's own name is almost always an indication of a psychiatric condition.

Short-term memory can also be tested by asking the patient to remember three or more words and then asking the patient to recall these words 5 minutes later after the rest of the examination. The words used should be in different categories so they cannot be easily "joined" by the patient (e.g., "blue" and "shirt" could be stored and recalled as one element "blue shirt"); the words "red," "window," and "honesty" are commonly used for this test. If the patient cannot recall one or more of the words spontaneously after 5 minutes, category clues can be given (for "red," "window," and "honesty": a color, a part of a building, and a character trait). If these cues do not elicit a memory of the words, the patient can then be given a list of choices to see if the patient can recognize the words from a list.

Memory loss is called **amnesia**. **Retrograde amnesia** refers to the inability to recall events from the past, and **anterograde amnesia** refers to the inability to form new memories. Amnesia generally occurs due to dysfunction of one or both temporal lobes, particularly medial temporal lobe structures such as the hippocampus. Deficits in memory are a core feature of Alzheimer's disease and transient global amnesia (see Ch. 22).

Examination of Language: A Function of the Frontal and Temporal Lobes (Most Commonly in the Left Hemisphere)— Language has several components: production (spoken and written), comprehension (hearing and reading), and repetition. The various combinations of deficits in aspects of spoken language are called **aphasias**, and are described in Chapter 7. In right-handed patients (and in most left-handed patients), language is predominantly a function of the left hemisphere: Broca's area for language production is in the left inferior frontal gyrus, and Wernicke's area for language comprehension is in the left posterior superior temporal gyrus (see Ch. 7). Language can be affected by any lesion in one or both of these regions including stroke (see Ch. 19), tumor (see Ch. 24), or neurodegenerative diseases such as primary progressive aphasia (see Ch. 22). Aphasia should be distinguished from **dysarthria**, which refers to a difficulty articulating speech but with preserved language content and structure.

Many other aspects of cognitive function can be tested depending on the clinical context, including visuospatial ability, abstract reasoning, calculation, and ability to perform complex learned motor tasks (**praxis**), some of which are discussed in more detail in later chapters.

The Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA) are examples of bedside tests that evaluate a number of cognitive functions in different domains. These tests are useful in characterizing a patient's cognitive deficits as well as in making comparisons over time. More extensive neuropsychological testing batteries can also be performed.

Examination of the Cranial Nerves

The cranial nerve examination evaluates the neurologic functions of the structures of the head and neck. Although this portion of the examination is called the "cranial nerve" examination, it also tests the brainstem (the site of the cranial nerve nuclei), and, in many cases, the cerebral hemispheres (which are the ultimate recipients of incoming sensory information from the cranial nerves [e.g., vision, hearing, taste, smell, facial sensation], and which provide descending control of the motor functions of the motor cranial nerves to the muscles of the head and neck). The brainstem and cranial nerves, their functions and pathways, and the conditions that affect them are discussed in Chapters 9–14.

Cranial Nerve 1: Olfactory Nerve

Cranial nerve 1 (CN 1) is the olfactory nerve, which conveys the sense of smell from the nose to the olfactory cortex (inferior frontal and medial temporal lobes). This is the only sensory modality that sends information directly to the cortex without a stop in the thalamus en route (although the olfactory cortex does send projections to the thalamus). Thus, testing smell is a test not only of CN 1, but also its corresponding sensory cortex (see Ch. 14).

Cranial Nerve 2: Optic Nerve

Cranial nerve 2 (CN 2) is the optic nerve, which transmits visual information from the retinae to the occipital cortex (see Ch. 6). CN 2 also transmits light information to the midbrain as the afferent limb of the pupillary light reflex. The pupillary light reflex tests CN 2 (afferent), CN 3 (efferent), and the midbrain nuclei and pathways that connect them (see Ch. 10). Examining visual acuity and visual fields tests the eyes, optic nerves, the visual cortex in the occipital lobes, and the pathways that connect them (see Ch. 6). CN 2 is the only cranial nerve—and the only nerve for that matter—that can be directly visualized on the physical examination: The optic nerve head can be seen by fundoscopy. CN 2 is also the only cranial nerve that is part of the CNS; all others are peripheral nerves.

Cranial Nerve 3 (Oculomotor Nerve), Cranial Nerve 4 (Trochlear Nerve), & Cranial Nerve 6 (Abducens Nerve)

Cranial nerves 3 (the oculomotor nerve), 4 (the trochlear nerve), and 6 (the abducens nerve) control the movements of the eyes. CN 3 also controls elevation of the eyelid and constriction of the pupil. Therefore, tests of eye movements examine these three nerves and their interconnections in the brainstem. Examining the ability to follow instructions to look in a specific direction

(**saccades**) and to follow the examiner's finger (**smooth pursuit**) tests not only cranial nerves 3, 4, and 6 and their brainstem pathways, but also the cerebellum and cortical eye fields (see Ch. 11).

Cranial Nerve 5: Trigeminal Nerve

Cranial nerve 5 is the trigeminal nerve, which transmits facial sensation to the sensory cortex by way of the brainstem and ventral posterior medial nucleus of the thalamus, and also controls the muscles of mastication (chewing). Testing facial sensation (i.e., light touch, temperature, and pain) and evaluation of the strength of jaw opening and closure are tests of the trigeminal nerve, its brainstem nuclei, and the sensory and motor centers with which they communicate in the cerebral hemispheres (VPM of the thalamus and postcentral gyrus for facial sensation; precentral gyrus for motor supply to the jaw musculature). The trigeminal nerve carries the afferent limb of the corneal reflex (eye closure with stimulation of the cornea); the efferent limb travels in CN 7. CN 5 provides both the afferent and efferent limbs of the jaw jerk reflex (see Ch. 13).

Cranial Nerve 7: Facial Nerve

Cranial nerve 7 is the facial nerve, the main function of which is to control the movements of facial musculature (it has a number of other functions discussed in Ch. 13). Asking the patient to raise the eyebrows and close the eyes tightly tests the upper facial muscles, and asking the patient to smile tests the lower facial muscles. Differences in patterns of facial weakness with respect to the upper and lower face can help localize the site of dysfunction to the facial nerve itself or the motor cortex and descending pathways that control it (see Ch. 13).

Cranial Nerve 8: Vestibulocochlear Nerve

Cranial nerve 8 is the vestibulocochlear nerve, responsible for transmitting auditory and vestibular information to the brain. The auditory portion is tested by assessing patients' hearing in both ears (which tests the integrity of the pathway from the inner ear, through the nerve, through the brainstem and thalamus up to the auditory cortex in the superior temporal lobe). The vestibular portion and its brainstem connections with the eye movement nuclei (CNs 3, 4, and 6) can be assessed by various maneuvers that examine the interaction of head movements and eye movements (see Ch. 12).

Cranial Nerve 9 (Glossopharyngeal Nerve) & Cranial Nerve 10 (Vagus Nerve)

Cranial nerve 9 (the glossopharyngeal nerve) and cranial nerve 10 (the vagus nerve) have a number of roles including innervation of the muscles of the larynx and pharynx, and afferent and efferent visceral autonomic functions (see Ch. 14). Dysfunction may cause difficulty with articulation of speech (**dysarthria**), decreased speech volume (**hypophonia**), and/or difficulty swallowing (**dysphagia**). Aside from assessing for dysarthria and hypophonia, CNs 9 and 10 can only be evaluated on examination by assessing palate elevation (primarily a function of CN 10) and the gag reflex (afferent limb is supplied primarily by CN 9; efferent limb primarily by CN 10; see Ch. 14).

Cranial Nerve 11: Spinal Accessory Nerve

Cranial nerve 11 is the spinal accessory nerve, which controls the trapezius (shoulder elevation) and the sternocleidomastoid (turning the head) (see Ch. 14). CNs 1 and 11 are the only cranial nerves that do not make any contact with the brainstem. CN 11 is comprised of spinal roots, but exits the skull with other cranial nerves through the jugular foramen.

Cranial Nerve 12: Hypoglossal Nerve

Cranial nerve 12 is the hypoglossal nerve, which controls the muscles of the tongue. It is assessed by asking the patient to protrude and move the tongue. Like CN 7 and the motor component of CN 5, its motor control comes from the motor cortex (precentral gyrus), so weakness of the tongue on one side can localize anywhere along the pathway from the contralateral motor cortex to its connections with the CN 12 nucleus in the medulla to the hypoglossal nerve itself (see Ch. 14).

Examination of the Motor System

The motor system spans the entire nervous system: brain, brainstem, spinal cord, (ventral) nerve roots, peripheral nerves, neuromuscular junction, and muscle (see Ch. 4). In addition to testing the strength of all muscles during the motor examination and looking for weakness or differences between the left and right sides, the motor examination assesses for muscle bulk (**atrophy** refers to loss of muscle bulk), muscle **tone** (increased tone refers to resistance when passively moving a joint; decreased tone or flaccidity refers to decreased resistance), speed of movements (**bradykinesia** refers to a slowing of movements), or any abnormal movements (e.g., fasciculations of muscle, tremor). The ways in which these features of the examination can aid in localizing motor problems along the neuraxis are discussed in Chapter 4.

Strength is graded on a 0–5 scale:

- 5: Full strength
- 4: Able to apply force against resistance but less than full strength
- 3: Able to move against gravity but not against resistance
- 2: Able to move from side to side but not against gravity
- 1: Most minimal detectable movement (a "flicker" of movement)
- 0: Unable to move at all

+ and – may be added to these designations. For example, 5– suggests strength that is nearly but not quite full.

Weakness is referred to as **paresis**, and complete paralysis is called **plegia**. For example, weakness of both legs is called

paraparesis, paralysis of both legs is called **paraplegia**, weakness on one side of the body is referred to as **hemiparesis**, and paralysis of one limb is called **monoplegia**.

Examination of the Sensory System

The sensory system begins in the skin (for pain, temperature, light touch, and vibration sensation), and tendons/muscles (for **proprioception**—perception of where the body is in space). Peripheral nerves transmit this information to the spinal cord via dorsal root ganglia and dorsal roots. Sensory information then travels in various pathways to and through the brainstem, the thalamus, and ultimately the somatosensory cortex in the anterior parietal lobe (postcentral gyrus). The distribution of sensory loss on the body and the affected sensory modalities are the key points that help localize lesions of the sensory pathways (see Ch. 4). Pain sensation is generally assessed with a pin (to assess the spinothalamic tracts; see Ch. 4). Vibration sensation is assessed by holding a 128 Hz tuning fork to a joint (e.g., interphalangeal joint of big toe) and assessing if the patient can feel it and, if so, for how long (to assess the dorsal columns; see Ch. 4). Proprioception can be assessed by moving a joint up or down and asking the patient to identify the direction of movement with their eyes closed (this also assesses the dorsal columns, but is considered less sensitive than testing vibration [see Ch. 4]). Proprioception can also be assessed by having the patient stand with the feet together and eyes closed: If proprioception is impaired, without vision to compensate when the eyes are closed, the patient will be unable to maintain balance (**Romberg sign**).

Examination of the Reflexes (Fig. 1–2)

Reflexes test the nerves and roots that provide sensory input to the spinal cord and receive motor output from the spinal cord, as well as the interconnections between the motor and sensory pathways in the spinal cord. Reflexes can be diminished (**hyporeflexia**) or absent (**areflexia**) with lesions in the PNS (roots, nerves) and increased (**hyperreflexia**) with lesions in the CNS (brain, brainstem, spinal cord), discussed further in Chapter 4. The most commonly tested reflexes are the biceps (C5-C6, musculocutaneous nerve), brachioradialis (C6, radial nerve), and triceps (C7-C8, radial nerve) in the upper extremities; and the patella (L3-L4, femoral nerve) and ankle/Achilles (S1-S2, tibial nerve) in the lower extremities. The associated nerve roots can be remembered by the mnemonic 1-2 – 3-4 – 5-6 – 7-8, counting from the ankle (S1,2), upward to the patella (L3,4), to the biceps (C5,6) and brachioradialis (C6), and, finally, to the triceps (C7,8).

If a patient's reflexes are not able to be elicited in the usual manner, reinforcement maneuvers may be attempted. For the upper extremities, the patient can be asked to bite down while the reflexes are being tested. For the lower extremities, the patient can be asked to curl the fingers of one hand into the fingers of the other and pull at the moment the reflex hammer strikes (**Jendrassik maneuver**). Elicitation of reflexes only by reinforcement is a sign of hyporeflexia.

Reflexes are described as normal, increased (hyperreflexia), decreased (hyporeflexia), or absent (areflexia). 0 is used to designate areflexia, 1+ signifies hyporeflexia (diminished or requiring reinforcement), 2+ signifies normal reflexes, 3+ denotes hyperreflexia, and 4+ denotes hyperreflexia with

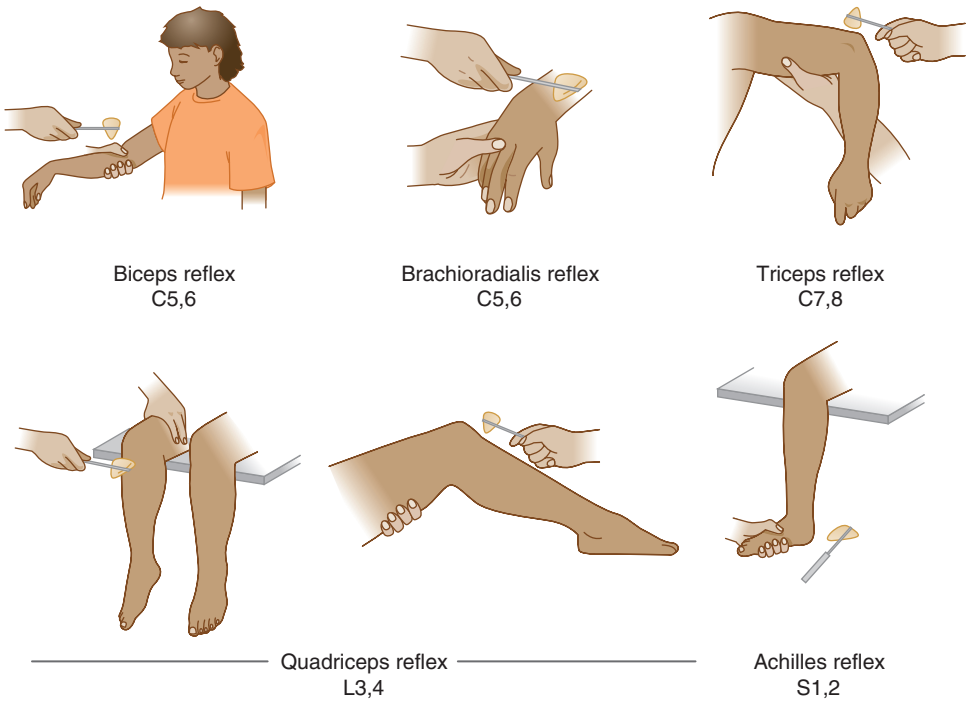

FIGURE 1–2 Schematic showing deep tendon reflexes. Reproduced with permission from Aminoff M, Greenberg D, Simon R: *Clinical Neurology*, 9th ed. New York, NY: McGraw Hill; 2015.

TABLE 1–1 Neuroanatomic Structures & Pathways Evaluated in the Neurologic Examination.

	Structures/Pathways Evaluated	Chapter(s) Where Discussed
MENTAL STATUS		
Arousal	Reticular activating system, bilateral thalami, and cerebral hemispheres	Chapter 7
Attention	Frontal and parietal lobes	Chapter 7
Memory	Temporal lobes	Chapter 7
Language	Frontal and temporal lobes (usually left)	Chapter 7
Praxis	Frontal and parietal lobes	Chapter 7
Abstract reasoning	Frontal lobes	Chapter 7
Visuospatial processing	Occipital and parietal lobes	Chapter 6
CRANIAL NERVES		
Smell	CN 1 and olfactory cortex	Chapter 14
Pupillary light reflex	CNs 2 and 3; midbrain nuclei and pathways	Chapter 10
Visual acuity and fields	Eyes, CN 2, thalamus (lateral geniculate nucleus [LGN]), optic radiations, occipital cortex	Chapter 6
Eye movements	CNs 3, 4, and 6, brainstem pathways, frontal and parietal eye fields, cerebellum for saccades and smooth pursuit	Chapter 11
Facial sensation	CN 5, brainstem pathways, thalamus (ventral posterior medial nucleus [VPM]), somatosensory cortex	Chapter 13
Facial movements	CN 7, motor pathway from precentral gyrus to CN 7 nucleus in pons	Chapter 13
Hearing	Inner ear, CN 8, brainstem auditory pathways, thalamus (medial geniculate nucleus [MGN]), auditory cortex in superior temporal gyrus	Chapter 12
Vestibular system	Inner ear, CN 8, brainstem pathways and their connections with nuclei of CNs 3, 4, 6, and cerebellum	Chapter 12
Palate elevation and gag reflex	CNs 9 and 10, their pathways in the medulla, and motor control from the precentral gyrus	Chapter 14
Sternocleidomastoid and trapezius strength	CN 11 and motor control from the precentral gyrus	Chapter 14
Tongue movements	CN 12 and motor control from the precentral gyrus	Chapter 14
MOTOR		
Strength	Corticospinal tract (precentral gyrus through subcortical white matter, brainstem, and spinal cord), ventral roots, peripheral nerves, neuromuscular junction, and muscle	Chapters 4, 15–17, 29, 30
Higher-order motor control	Basal ganglia	Chapter 7
SENSORY	Peripheral nerves, dorsal root ganglia, dorsal roots, spinal cord and brainstem pathways, thalamus (ventral posterior lateral nucleus [VPL]), postcentral gyrus	Chapter 4
REFLEXES	Peripheral nerves, nerve roots, and spinal cord	Chapter 4
COORDINATION	Cerebellum and its sensory input	Chapter 8
GAIT	Motor, sensation, coordination pathways	Chapter 1

CN: Cranial nerve

clonus. Clonus is rhythmic oscillating movement at a joint, most commonly elicited by briskly dorsiflexing the ankle and holding the foot dorsiflexed. Clonus should be described in terms of the number of beats of clonus, and it should be noted whether clonus stops spontaneously or is sustained. Clonus is discussed further in Chapter 4.

Another sign of hyperreflexia that may be observed is **spread** of reflexes: eliciting one reflex leads to simultaneous activation of adjacent reflexes. For example, eliciting the biceps reflex causes simultaneous finger flexion or eliciting the patellar reflex leads to simultaneous ankle plantarflexion.

Pathologic Reflexes

The pathologic reflex tested for most commonly is the **Babinski sign**. To elicit this sign, the examiner strokes the sole of the foot

slowly from the heel along the lateral aspect of the sole, and then continues medially along the base of the toes: The normal (non-pathologic) response is flexion of the toes. In contrast, the Babinski sign is characterized by an extensor response: extension of the big toe (a "thumbs-up" of the big toe; this may be accompanied by fanning of all toes and/or the triple flexion response of dorsiflexion, knee flexion, and hip flexion). The Babinski sign is associated with a lesion of the CNS (brain, brainstem, or spinal cord), specifically the corticospinal tract (see Ch. 4). The Babinski sign occurs normally in infants but is always abnormal in childhood and adulthood.

Other signs that can demonstrate a pathologic extensor response in the big toe like the Babinski sign include: **Chaddock sign** (stroke lateral aspect of dorsum of foot from lateral malleolus toward fifth toe), **Oppenheim sign** (stroke the tibia downward from the knee toward the foot), **Gordon sign** (squeeze the calf), and **Bing sign** (pinching one of the toes; pricking the dorsum of the fourth or fifth toe with pin in original description). If any of these maneuvers causes an extensor response of the big toe (which may be accompanied by the triple flexion response), this signifies corticospinal tract dysfunction.

Hoffman's sign is an upper-extremity analogue to Babinski's sign, elicited by flicking the middle finger and observing for flexion of the fingers and thumb (see Ch. 4).

A number of reflexes called **frontal release signs** can be seen in patients with dementia, but may also be seen in normal elderly adults (and like Babinski's sign, are normal in infants) (see Ch. 22).

Examination of Coordination

Coordination is usually tested by having the patient move the index finger back and forth between the examiner's finger and the patient's nose, sliding the heel down the shin, and performing rhythmic rapid alternating movements. When the patient is performing the finger–nose task, it is important that the target (i.e., the examiner's finger) be sufficiently far from the patient so that the patient must extend the arm fully to reach it, otherwise subtle ataxia at the extremes of motion may be missed. Note that coordination testing may be confounded if the patient has weakness, as actions attempted by weak muscles can appear uncoordinated.

Ataxia refers to uncoordinated movements, **dysmetria** refers to inaccuracy of movements (overshooting or undershooting a target), and **dysdiadochokinesia** refers to uncoordinated rapid alternating movements. All of these abnormalities in coordination are associated most commonly with disorders of the cerebellum, but note that the cerebellum needs proprioceptive input to perform its coordinating function. Therefore, ataxia can also be caused by impaired proprioception (e.g., due to nerve, dorsal root, dorsal root ganglia, or spinal cord disease), which is called **sensory ataxia** (see Ch. 8).

Examination of Gait

Gait relies on optimal function of all levels of the nervous system. The pattern of gait can suggest various types of lesions in the central or peripheral nervous system, and in some instances, particular diseases. Examples include:

- **Steppage gait:** The foot is lifted high off the ground and is slapped down. This occurs when there is dorsiflexion weakness causing foot drop (see Ch. 17).
- **Trendelenburg gait:** The pelvis drops toward the opposite side when the weight is balanced on the leg on the affected side during walking. This occurs when there is gluteal muscle weakness.
- **Parkinsonian gait:** Stooped, small-stepped, shuffling gait, with difficulty turning (see Ch. 23).
- **Magnetic gait:** The feet are lifted only briefly off the ground before being returned briskly to the ground (as if a magnet were pulling them down). This can be seen in normal pressure hydrocephalus (see Ch. 22) and with proprioceptive dysfunction (see Ch. 4).
- **Ataxic gait:** A wide-based and unsteady gait. This is seen in cerebellar dysfunction (as can be seen in alcohol intoxication) and severe proprioceptive dysfunction.
- **Spastic gait:** The leg is extended, the foot plantarflexed, and the entire leg **circumducted** (swung out to the side) with each step. If both legs are spastic, this pattern can lead to a **scissor** gait. This is a pattern seen with CNS dysfunction of the motor system (brain, brainstem, and/or spinal cord).

A summary of the localizing value of the various components of the examination is presented in Table 1–1 with references to chapters where these individual components are discussed further.

The General Examination in Neurologic Diagnosis

The general physical examination is also of great importance in patients with neurologic symptoms and signs to evaluate for any signs of systemic disease that may be producing neurologic manifestations. The following are a few of many possible examples. In patients with stroke, a detailed cardiovascular examination should evaluate for carotid bruit (a sign of possible carotid stenosis), cardiac arrhythmia, and cardiac murmur (which could suggest valvular disease including endocarditis). Orthostatic vital signs may be abnormal in patients with autonomic neuropathies (see Ch. 27) and multiple systems atrophy (see Ch. 23). Pallor could suggest anemia, which may be due to vitamin B12 deficiency, a cause of myelopathy and neuropathy. Signs of chronic illness could suggest underlying malignancy, inflammatory disease, or chronic infection (e.g., HIV), all of which can have neurologic manifestations. Characteristic skin findings may be seen in dermatomyositis (see Ch. 30) and in neurocutaneous syndromes such as tuberous sclerosis and neurofibromatosis (see Ch. 24).