11th edition

CLINICAL NEUROLOGY

David A. Greenberg • Michael J. Aminoff • Roger P. Simon

McGraw Hill LANGE®

a LANGE medical book

Clinical Neurology

ELEVENTH EDITION

David A. Greenberg, MD, PhD
Professor Emeritus
Buck Institute for Research on Aging
Novato, California

Michael J. Aminoff, MD, DSc, FRCP
Distinguished Professor
Department of Neurology
School of Medicine
University of California, San Francisco
San Francisco, California

Roger P. Simon, MD
Professor of Medicine (Neurology) and Neurobiology
Morehouse School of Medicine
Clinical Professor of Neurology
Emory University
Atlanta, Georgia

New York Chicago San Francisco Lisbon London Madrid Mexico City
Milan New Delhi San Juan Seoul Singapore Sydney Toronto

ISBN: 978-1-26-045836-7
MHID: 1-26-045836-9

The material in this eBook also appears in the print version of this title: ISBN: 978-1-26-045835-0, MHID: 1-26-045835-0.

eBook conversion by codeMantra
Version 1.0

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 changes in medical sciences, neither the editors 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.

To our families.

This page intentionally left blank

Contents

This page intentionally left blank

Preface

With this 11th edition, *Clinical Neurology* enters its fourth decade of publication. Its goal remains to provide students, residents, and practitioners with an introduction to neurology that is clear, informative, and current. To this end, the approach is problem-oriented, and the text has been updated to reflect new aspects of pathophysiology, diagnosis, and treatment.

Recent advances covered in this edition include new developments in neurogenetics, pathogenesis of neurodegenerative disorders, and treatment of neurologic infections, migraine, cluster headache, amyotrophic lateral sclerosis, spinal muscular atrophy, multiple sclerosis, epilepsy, and stroke.

We are indebted to Andrew Moyer, Christie Naglieri, Sheryl Krato, and the staff at McGraw-Hill, to Martha Johnson for copyediting, to Parag Mittal at Cenveo Publisher Services, and to the following colleagues who provided materials or suggestions for this edition: Peter Anderson, Jose Biller, Allitia Dibernardo, William P. Dillon, Alisa Gean, Maeve Burns Greenberg, Jason Handwerker, Rock Heyman, Annie Hiniker, Chris Jungreis, Catherine Lomen-Hoerth, Kanar Karim, Robert Laureno, Nancy Newman, Howard Rowley, Shahriar Salamat, Seth Wright, and Howard Yonas.

David A. Greenberg
Michael J. Aminoff
Roger P. Simon

This page intentionally left blank

Neurologic History & Examination

1

HISTORY

Taking a history from a patient with a neurologic complaint is fundamentally the same as taking any history.

Age

Age can be a clue to the cause of a neurologic problem. For example, migraine, epilepsy, multiple sclerosis, and Huntington disease usually have their onset by middle age, whereas Alzheimer disease, Parkinson disease, brain tumors, and stroke predominantly affect older individuals.

Chief Complaint

The chief complaint should be defined as clearly as possible, because it will guide evaluation toward—or away from—the correct diagnosis. The goal is for the patient to describe the nature of the problem in a word or phrase.

Common neurologic complaints include confusion, dizziness, weakness, shaking, numbness, blurred vision, and spells. Each of these terms means different things to different people, so it is critical to clarify what the patient is trying to convey.

A. Confusion

Confusion may be reported by the patient or by family members. Symptoms can include memory impairment, getting lost, difficulty understanding or producing spoken or written language, problems with numbers, faulty judgment, personality change, or combinations thereof. Symptoms of confusion may be difficult to characterize, so specific examples should be sought.

B. Dizziness

Dizziness can mean **vertigo** (the illusion of movement of oneself or the environment), **imbalance** (unsteadiness due to extrapyramidal, vestibular, cerebellar, or sensory deficits), or **presyncope** (light-headedness resulting from cerebral hypoperfusion).

C. Weakness

Weakness is the term neurologists use to mean loss of power resulting from disorders affecting motor pathways in the central or peripheral nervous system or skeletal muscle. However, patients sometimes use this term when they mean generalized fatigue, lethargy, or even sensory disturbances.

D. Shaking

Shaking may represent abnormal movements such as **tremor**, **chorea**, **athetosis**, **myoclonus**, or **fasciculation**, but the patient is unlikely to use these terms. Correct classification depends on observing the movements in question or, if they are not present when the history is taken, asking the patient to demonstrate them.

E. Numbness

Numbness can refer to any of a variety of sensory disturbances, including **hypesthesia** (decreased sensitivity), **hyperesthesia** (increased sensitivity), or **paresthesia** ("pins and needles" sensation). Patients occasionally also use this term to signify weakness.

F. Blurred Vision

Blurred vision may represent **diplopia** (double vision), ocular oscillations, reduced visual acuity, or visual field cuts.

G. Spells

Spells imply episodic and often recurrent symptoms such as in **epilepsy** or **syncope** (fainting).

History of Present Illness

The history of present illness should provide a detailed description of the chief complaint, including the following features.

A. Quality and Severity of Symptoms

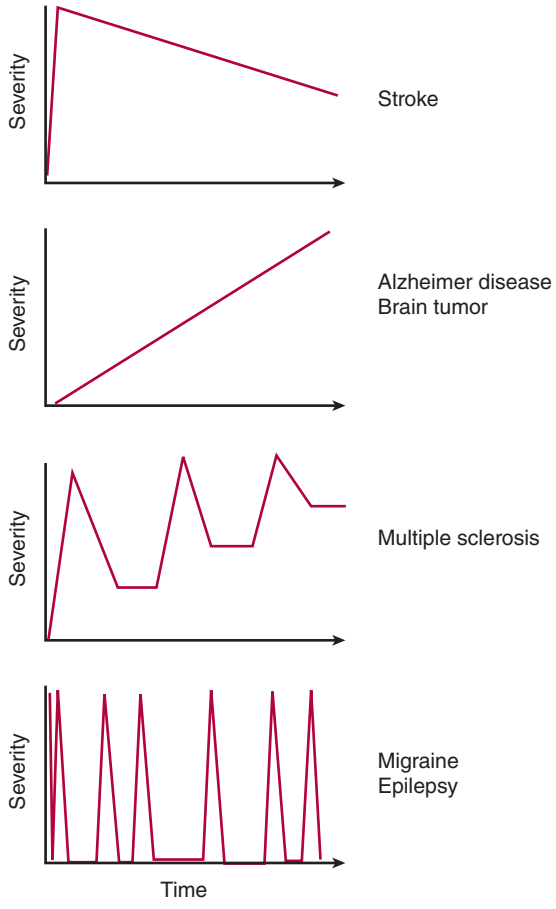
Some symptoms, such as pain, may have distinctive features. Neuropathic pain—which results from direct injury to nerves—may be described as especially unpleasant (**dysesthesia**) and may be accompanied by increased sensitivity to pain (**hyperalgesia**) or touch (**hyperesthesia**), or by the perception of a normally innocuous stimulus as painful (**allodynia**). The severity of symptoms should also be ascertained. Although thresholds for seeking medical attention vary among patients, it is often useful to ask a patient to rank the present complaint in relation to past problems.

B. Location of Symptoms

Patients should be encouraged to localize their symptoms as precisely as possible because location is often critical to neurologic diagnosis. The distribution of weakness, decreased sensation, or pain helps point to a specific site in the nervous system (anatomic diagnosis).

C. Time Course

It is important to determine when the problem began, whether it came on abruptly or insidiously, and if its subsequent course has been characterized by improvement, worsening, or exacerbation and remission (**Figure 1-1**).



▲ **Figure 1-1.** Temporal patterns of neurologic disease and examples of each.

For episodic disorders, such as headache or seizures, the time course of individual episodes should also be determined.

D. Precipitating, Exacerbating, and Alleviating Factors

Some symptoms may appear to be spontaneous, but in other cases, patients are aware of factors that precipitate or worsen symptoms, and which they can avoid, or factors that prevent symptoms or provide relief.

E. Associated Symptoms

Associated symptoms can assist with anatomic or etiologic diagnosis. For example, neck pain accompanying leg weakness suggests cervical myelopathy (spinal cord disorder), and fever in the setting of headache suggests meningitis.

Past Medical History

The past medical history may provide clues to the cause of a neurologic complaint.

A. Illnesses

Preexisting illnesses that can predispose to neurologic disease include hypertension, diabetes, heart disease, cancer, and immune disorders.

B. Operations

Open heart surgery may be complicated by stroke or a confusional state. Entrapment neuropathies (disorders of a peripheral nerve due to local pressure) affecting the upper or lower extremity may occur perioperatively.

C. Obstetric History

Pregnancy can worsen epilepsy, partly due to altered metabolism of anticonvulsant drugs, and may increase or decrease the frequency of migraine attacks. Pregnancy is a predisposing condition for entrapment neuropathies, especially **carpal tunnel syndrome** (median neuropathy) and **meralgia paresthetica** (lateral femoral cutaneous neuropathy). Traumatic neuropathies affecting the obturator, femoral, or peroneal nerve may result from pressure exerted by the fetal head or obstetric forceps during delivery. **Eclampsia** is a life-threatening syndrome in which generalized tonic-clonic seizures complicate the course of preeclampsia (hypertension with proteinuria) during pregnancy.

D. Medications

A wide range of medications can cause adverse neurologic effects, including confusional states or coma, headache, ataxia, neuromuscular disorders, neuropathy, and seizures.

E. Immunizations

Vaccination can prevent neurologic diseases such as poliomyelitis, diphtheria, tetanus, shingles, rabies, meningococcal or *Haemophilus influenzae* meningitis, and Japanese encephalitis. Rare complications include postvaccination autoimmune encephalitis, myelitis, or neuritis (inflammation of the brain, spinal cord, or peripheral nerves). Vaccination does not increase the risk for autism or other neurodevelopmental disorders.

F. Diet

Deficiency of vitamin B_1 (thiamin) is responsible for the **Wernicke–Korsakoff syndrome** and polyneuropathy in alcoholics. Vitamin B_3 (niacin) deficiency causes pellagra, which is characterized by dementia. Vitamin B_{12} (cobalamin) deficiency may produce **combined systems disease** (degeneration of corticospinal tracts and posterior columns in the spinal cord) and dementia. Inadequate intake of vitamin E (tocopherol) can lead to spinal cord degeneration. Hypervitaminosis A can produce intracranial hypertension (**pseudotumor cerebri**) with headache, visual deficits, and seizures, whereas excessive intake of vitamin B_6 (pyridoxine) is a cause of polyneuropathy. Excessive consumption of fats is a risk factor for stroke. Ingestion of improperly preserved foods containing botulinum toxin causes **botulism**, which presents with descending paralysis.

G. Tobacco, Alcohol, and Other Recreational Drug Use

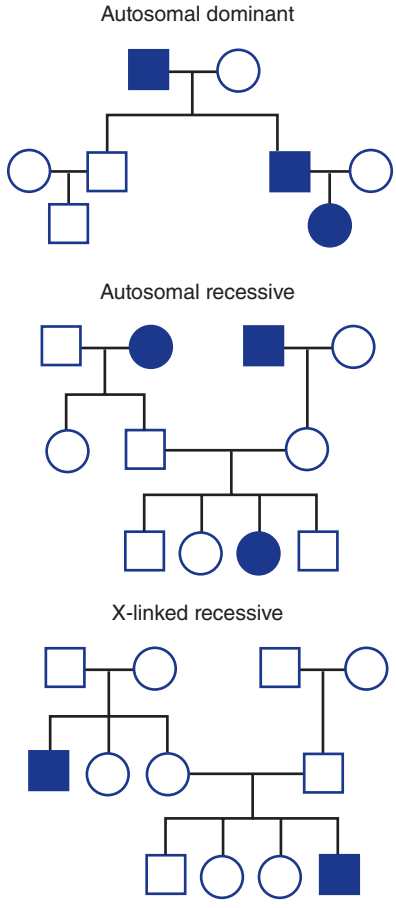
Tobacco use is associated with lung and other cancers, which may metastasize to the central nervous system or produce paraneoplastic neurologic syndromes. Alcohol abuse can produce withdrawal seizures, polyneuropathy, and nutritional disorders of the nervous system. Intravenous drug use is associated with HIV disease, brain embolus from endocarditis, and vasculitis. Several illicit drugs can cause seizures, a confusional state, or coma.

Family History

This should include past or current diseases in the spouse and first- (parents, siblings, children) and second- (grandparents, grandchildren) degree relatives. Several neurologic diseases exhibit Mendelian inheritance, such as Huntington disease (autosomal dominant), Wilson disease (autosomal recessive), and Duchenne muscular dystrophy (X-linked recessive), and the mode of inheritance may be discernible from the pedigree (**Figure 1-2**).

Social History

Information about the patient's education and occupation helps determine whether cognitive performance is appropriate to the patient's background. The sexual history may



▲ **Figure 1-2.** Simple Mendelian patterns of inheritance. Squares represent males, circles represent females, and filled symbols represent affected individuals.

indicate risk for sexually transmitted diseases that affect the nervous system, such as syphilis or HIV disease. The travel history can document exposure to infections endemic to particular geographic areas.

Review of Systems

Complaints elicited in the review of systems may point to a systemic cause or correlate of a neurologic problem.

1. **General**—Weight loss may suggest an underlying neoplasm and fever indicate an infection. Snoring or chronic daytime sleepiness may be associated with obstructive sleep apnea, which is a risk factor for stroke.
2. **Immune**—Systemic vasculitis may be associated with stroke or neuropathy. Acquired immune deficiency syndrome (AIDS) may lead to dementia, myelopathy, neuropathy, myopathy, or infections (eg, toxoplasmosis) or tumors (eg, lymphoma) affecting the nervous system.
3. **Hematologic**—Polycythemia may predispose to ischemic stroke, whereas thrombocytopenia and coagulopathy are associated with intracranial hemorrhage.
4. **Endocrine**—Diabetes increases the risk for stroke and neuropathy. Hypothyroidism may lead to coma, dementia, or ataxia.
5. **Skin**—Characteristic skin lesions are seen in certain disorders that affect the nervous system, such as neurofibromatosis and postherpetic neuralgia.
6. **Eyes, ears, nose, and throat**—Visual deficits can be the presenting symptom in multiple sclerosis and intracranial hypertension. Olfactory impairment may be an early feature of Parkinson disease or Alzheimer disease.
7. **Cardiovascular—**Ischemic or valvular heart disease and hypertension are major risk factors for stroke. Syncope may be the result of autonomic insufficiency.
8. **Respiratory**—Myasthenia gravis and Guillain-Barré syndrome can cause acute respiratory failure. Cough, hemoptysis, or night sweats may be manifestations of tuberculosis or lung neoplasm, which can disseminate to the nervous system.
9. **Gastrointestinal**—Hematemesis, jaundice, and diarrhea suggest hepatic encephalopathy as the cause of a confusional state. Constipation may be an early symptom of Parkinson disease.
10. **Genitourinary**—Urinary retention, incontinence, and impotence may be manifestations of peripheral neuropathy, myelopathy, or autonomic failure associated with certain movement disorders (eg, multisystem atrophy).
11. **Musculoskeletal**—Muscle pain and tenderness accompany the myopathy of polymyositis.
12. **Neurologic**—Neurologic symptoms seemingly unrelated to the chief complaint can aid in the diagnosis of disorders that affect multiple sites in the nervous system, such as vitamin B_{12} deficiency, syphilis, or AIDS.
13. **Psychiatric**—Psychosis, depression, or mania may be a manifestation of several neurologic disorders.

Summary

Upon completion of the history, the examiner should have a clear understanding of the chief complaint, including its location and time course, as well as familiarity with elements of the past medical history, family and social history, and review of systems that may be related to the complaint. This information helps guide the general physical and neurologic examinations, which should focus on areas suggested by the history. For example, in an elderly patient who presents with the sudden onset of hemiparesis and hemisensory loss, which is likely to be due to stroke,

the general physical examination should stress the cardiovascular system, because a variety of cardiovascular disorders predispose to stroke. On the other hand, if a patient complains of pain and numbness in the hand, much of the examination should be devoted to evaluating sensation, strength, and reflexes in the affected upper extremity.

GENERAL PHYSICAL EXAMINATION

The general physical examination should focus on systemic signs often associated with neurologic problems.

Vital Signs

A. Blood Pressure

Elevated blood pressure may indicate chronic **hypertension**, which is a risk factor for stroke and is also seen acutely in the setting of hypertensive encephalopathy, ischemic stroke, or intracerebral or subarachnoid hemorrhage. Blood pressure that drops by ≥20 mm Hg (systolic) or ≥10 mm Hg (diastolic) when a patient switches from recumbent to upright signifies **orthostatic hypotension**. If the drop in blood pressure is accompanied by a compensatory increase in pulse rate, sympathetic autonomic reflexes are intact, and the likely cause is hypovolemia. However, the absence of a compensatory response is consistent with central (eg, multisystem atrophy) or peripheral (eg, polyneuropathy) disorders of sympathetic function or an effect of sympatholytic (eg, antihypertensive) drugs.

B. Pulse

A rapid or irregular pulse—especially the irregularly irregular pulse of **atrial fibrillation**—may point to a cardiac arrhythmia as the cause of stroke or syncope.

C. Respiratory Rate

The respiratory rate may provide a clue to the cause of a metabolic disturbance associated with coma or a confusional state. Rapid respiration (tachypnea) can be seen in hepatic encephalopathy, pulmonary disorders, sepsis, or salicylate intoxication; depressed respiration is observed with pulmonary disorders and sedative drug intoxication. Tachypnea may also occur in neuromuscular disease affecting the diaphragm. Abnormal respiratory patterns may be observed in coma: Cheyne-Stokes breathing (alternating deep breaths, or hyperpnea, and apnea) can occur in metabolic disorders or with hemispheric lesions, whereas apneustic, cluster, or ataxic breathing implies a brainstem disorder.

D. Temperature

Fever (hyperthermia) occurs with infection of the meninges (meningitis), brain (encephalitis), or spinal cord (myelitis). Hypothermia can be seen in ethanol or sedative drug intoxication, hypoglycemia, hepatic encephalopathy, Wernicke encephalopathy, and hypothyroidism.

Skin

Jaundice (icterus) suggests liver disease as the cause of a confusional state or movement disorder. Coarse dry skin, dry brittle hair, and subcutaneous edema are characteristic of hypothyroidism. Petechiae are seen in meningococcal meningitis, and petechiae or ecchymoses may suggest a coagulopathy as the cause of subdural, intracerebral, or paraspinal hemorrhage. Bacterial endocarditis, a cause of stroke, can produce a variety of cutaneous lesions, including splinter (subungual) hemorrhages, Osler nodes (painful swellings on the distal fingers), and Janeway lesions (painless hemorrhages on the palms and soles). Hot, dry skin accompanies anticholinergic drug intoxication.

Head, Eyes, Ears, & Neck

A. Head

Examination of the head may reveal signs of trauma, such as scalp lacerations or contusions. Basal skull fracture may produce postauricular hematoma (**Battle sign**), periorbital hematoma (**raccoon eyes**), hemotympanum, or cerebrospinal fluid (CSF) otorrhea or rhinorrhea (**Figure 1-3**). Percussion of the skull over a subdural hematoma may cause pain. A bruit heard over the skull is associated with arteriovenous malformations.

B. Eyes

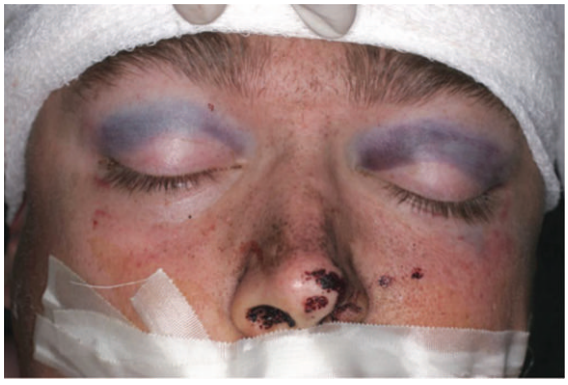
Icteric sclerae are seen in liver disease. Pigmented (**Kayser–Fleischer**) corneal rings—best seen by slit-lamp examination—are produced by copper deposits in Wilson disease. Retinal hemorrhages (Roth spots) occur in bacterial endocarditis, which may cause stroke. Exophthalmos is observed with hyperthyroidism, orbital or retroorbital masses, and cavernous sinus thrombosis.

C. Ears

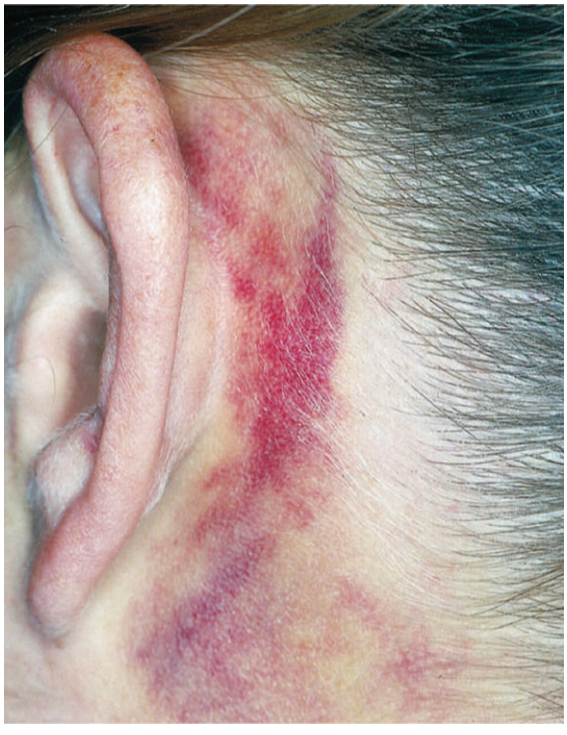
Otoscopic examination shows bulging, opacity, and erythema of the tympanic membrane in otitis media, which may spread to produce bacterial meningitis.

D. Neck

Meningeal signs (**Figure 1-4**), such as neck stiffness on passive flexion, thigh flexion upon flexion of the neck (**Brudzinski sign**), and resistance to passive extension of the knee with the hip flexed (**Kernig sign**), are seen in meningitis and subarachnoid hemorrhage. Restricted lateral movement (flexion or rotation) of the neck may accompany cervical spondylosis. Auscultation of the neck may reveal a carotid bruit, which can be a risk factor for stroke.

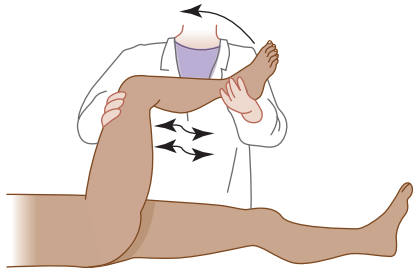


A

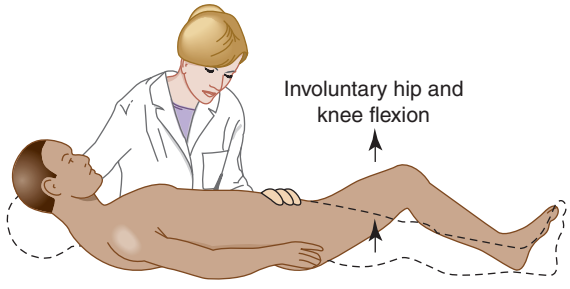


B

▲ **Figure 1-3.** Signs of head trauma include periorbital (raccoon eyes, **A**) (Reproduced with permission from Knoop K, Stack L, Storrow A, Thurman RJ. *Atlas of Emergency Medicine*. 4th ed. New York, NY: McGraw Hill; 2016. Photo contributor Kevin J. Knoop) or postauricular (Battle sign, **B**) hematoma, each of which suggests basal skull fracture. (Reproduced with permission from Knoop K, Stack L, Storrow A, Thurman RJ. *Atlas of Emergency Medicine*. 4th ed. New York, NY: McGraw Hill; 2016. Photo contributor: Frank Birinyi.)



A Kernig sign



B Brudzinski sign

▲ **Figure 1-4.** Signs of meningeal irritation. Kernig sign (**A**) is resistance to passive extension at the knee with the hip flexed. Brudzinski sign (**B**) is flexion at the hip and knee in response to passive flexion of the neck. (Reproduced with permission from LeBlond RF, DeGowin RL, Brown DD. *DeGowin's Diagnostic Examination*. 9th ed. New York, NY: McGraw Hill; 2009.)

▶ Chest & Cardiovascular

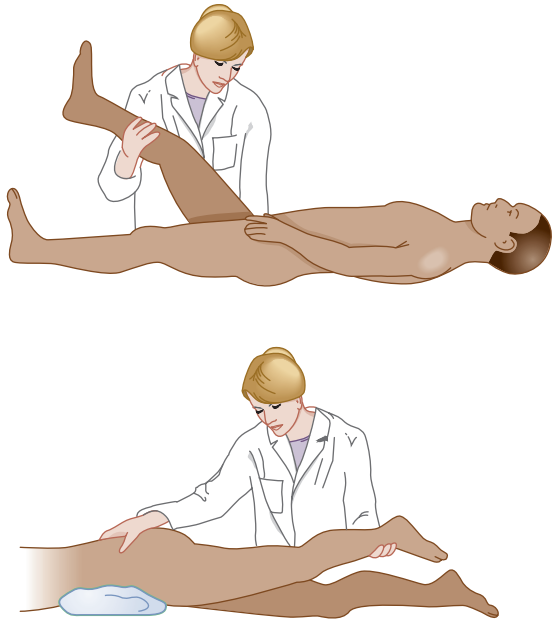
Signs of respiratory muscle weakness—such as intercostal muscle retraction and the use of accessory muscles—may occur in neuromuscular disorders. Heart murmurs may be associated with valvular heart disease and infective endocarditis, which predispose to stroke.

▶ Abdomen

Abdominal examination may suggest liver disease and is always important in patients with the new onset of back pain, because intra-abdominal processes such as pancreatic carcinoma or aortic aneurysm may present with pain that radiates to the back.

▶ Extremities & Back

Raising the extended leg with the patient supine (straight leg raising, or **Lasègue sign**) stretches the L4-S2 roots and sciatic nerve, whereas raising the extended leg with the patient prone (reverse straight leg raising) stretches the



▲ **Figure 1-5.** Signs of lumbosacral nerve root irritation. The straight leg raising or Lasègue sign (top) is pain in an L4-S2 root or sciatic nerve distribution in response to raising the extended leg with the patient supine. The reverse straight leg raising sign (bottom) is pain in an L2-L4 root or femoral nerve distribution in response to raising the extended leg with the patient prone. (Reproduced with permission from LeBlond RF, DeGowin RL, Brown DD. *DeGowin's Diagnostic Examination.* 9th ed. New York, NY: McGraw Hill; 2009.)

L2-L4 roots and femoral nerve and may reproduce radicular pain with lesions affecting these structures (**Figure 1-5**). Localized pain with percussion of the spine may be a sign of vertebral or epidural infection. Auscultation of the spine may reveal a bruit due to spinal vascular malformation.

Rectal & Pelvic

Rectal examination can provide evidence of gastrointestinal bleeding, which is a common precipitant of hepatic encephalopathy. Rectal or pelvic examination may disclose a mass lesion responsible for pain referred to the back.

NEUROLOGIC EXAMINATION

The neurologic examination should be tailored to the patient's specific complaint. All parts of the examination—mental status, cranial nerves, motor function, sensory function, coordination, reflexes, and stance and gait—should be covered, but the points of emphasis will differ. The history should have raised questions that the examination can now address. For example, if the complaint is weakness, the examiner seeks to determine its distribution and severity and whether it is accompanied by deficits in other areas, such as sensation and reflexes. The goal is to obtain the information necessary to generate an anatomic diagnosis.

Mental Status

The mental status examination addresses two key questions: (1) Is **level of consciousness** (wakefulness or alertness) normal or abnormal? (2) If the level of consciousness is adequate to permit more detailed examination, is **cognitive function** normal, and if not, what is the nature and extent of the abnormality?

A. Level of Consciousness

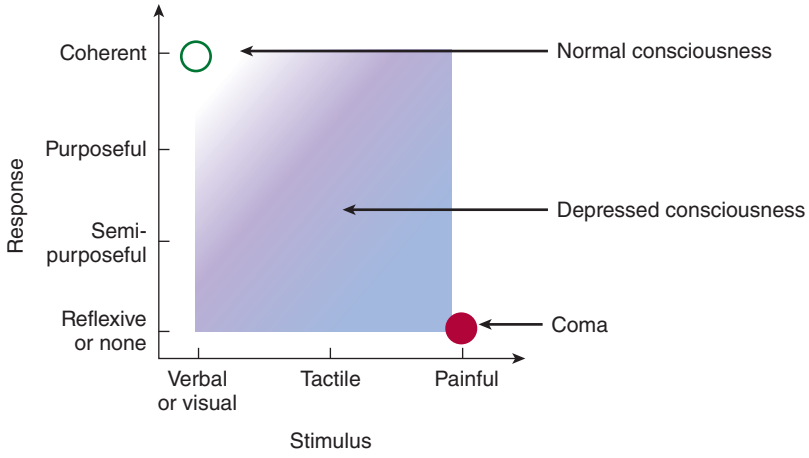
Consciousness is awareness of the internal and external world, and the level of consciousness is described in terms of the patient's apparent state of wakefulness and response to stimuli. A patient with a normal level of consciousness is **awake** (or can be easily awakened), **alert** (responds appropriately to visual or verbal cues), and **oriented** (knows who and where he or she is and the approximate date and time).

Abnormal (depressed) consciousness represents a continuum ranging from mild sleepiness to unarousable unresponsiveness (**coma**). Depressed consciousness short of coma is sometimes referred to as a confusional state, delirium, or stupor, but should be characterized more precisely in terms of the stimulus–response patterns observed. Progressively more severe impairment of consciousness requires stimuli of increasing intensity to elicit increasingly primitive (nonpurposeful or reflexive) responses (**Figure 1-6**).

B. Cognitive Function

Cognitive function involves many spheres of activity, some thought to be localized and others dispersed throughout the cerebral hemispheres. The strategy in examining cognitive function is to assess a range of specific functions and, if abnormalities are found, to evaluate whether these can be attributed to a specific brain region or require more widespread involvement of the brain. For example, discrete disorders of language (**aphasia**) and memory (**amnesia**) can often be assigned to a circumscribed area of the brain, whereas more global deterioration of cognitive function, as seen in **dementia**, implies diffuse or multifocal disease.

1. **Bifrontal or diffuse functions—Attention** is the ability to focus on a particular sensory stimulus to the exclusion of others; **concentration** is sustained attention. Attention can be tested by asking the patient to immediately repeat a series of digits (a normal person can repeat five to seven digits correctly), and concentration can be tested by having the patient count backward from 100 by 7s.



▲ **Figure 1-6.** Assessment of level of consciousness in relation to the patient's response to stimulation. A normally conscious patient responds coherently to visual or verbal stimulation, whereas a patient with impaired consciousness requires increasingly intense stimulation and exhibits increasingly primitive responses.

Abstract thought processes like **insight** and **judgment** can be assessed by asking the patient to list similarities and differences between objects (eg, an apple and an orange), interpret proverbs (overly concrete interpretations suggest impaired abstraction ability), or describe what he or she would do in a hypothetical situation requiring judgment (eg, finding an addressed envelope on the street).

Fund of knowledge can be tested by asking for information that a normal person of the patient's age and cultural background would possess (eg, the name of the President, sports stars, or other celebrities, or major events in the news). This is not intended to test intelligence, but to determine whether the patient has been incorporating new information in the recent past.

Affect is the external expression of internal **mood** and may be manifested by talkativeness or lack thereof, facial expression, and posture.

Conversation with the patient may reveal abnormalities of thought content, such as **delusions** or **hallucinations**, which are usually associated with psychiatric disease, but can also exist in confusional states (eg, alcohol withdrawal).

2. **Memory**—Memory is the ability to register, store, and retrieve information and can be impaired by either diffuse cortical or bilateral temporal lobe disease. Memory is assessed by testing **immediate recall**, **recent memory**, and **remote memory**, which correspond roughly to registration, storage, and retrieval.

   Tests of **immediate recall** are similar to tests of attention (see earlier discussion) and include having the patient immediately repeat a list of numbers or objects. To test **recent memory**, the patient can be asked to repeat a list of items 3-5 minutes later. **Remote memory** is tested by asking the patient about facts he or she can be expected to have learned in past years, such as personal or family data or major historic events.

   Confusional states typically impair immediate recall, whereas memory disorders (**amnesia**) are characteristically associated with predominant involvement of recent memory, with remote memory preserved until late stages. Personal and emotionally charged memories tend to be preferentially spared, whereas the opposite may be true in **psychogenic amnesia**. Inability of an awake and alert patient to remember his or her own name strongly suggests a psychiatric disorder.

3. **Language**—The key elements of language are comprehension, repetition, fluency, naming, reading, and writing, and all should be tested when a language disorder (**aphasia**) is suspected. There are a variety of aphasia syndromes, each characterized by a particular pattern of language impairment (**Table 1-1**) and often correlating with a specific site of pathology (**Figure 1-7**).

   Expressive (also called **nonfluent**, **motor**, or **Broca**) **aphasia** is characterized by paucity of spontaneous speech and by the agrammatical and telegraphic nature of the little speech that is produced. Language expression is tested by listening for these abnormalities as the patient speaks spontaneously and answers questions. Patients with this syndrome are also unable to write normally or to repeat (tested with a content-poor phrase such as "no ifs, ands, or buts"), but their language comprehension is intact. Thus, if the patient is asked to do something that does not require language expression

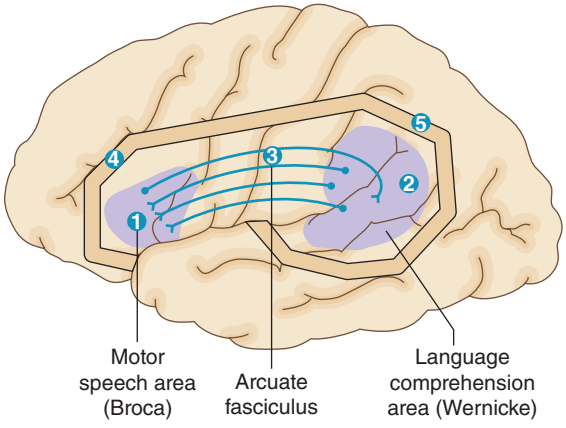
Table 1-1. Aphasia Syndromes.

Type	Fluency	Comprehension	Repetition
Expressive (Broca)	–	+	–
Receptive (Wernicke)	+	–	–
Global	–	–	–
Conduction	+	+	–
Transcortical expressive	–	+	+
Transcortical receptive	+	–	+
Transcortical global	–	–	+
Anomic (naming)	+	+	+

+, preserved; –, impaired.

(eg, "close your eyes"), he or she can do it. The patient is typically aware of the disorder and frustrated by it.

In **receptive** (also called **fluent**, **sensory**, or **Wernicke**) **aphasia**, language expression is preserved, but comprehension and repetition are impaired. A large volume of language is produced, but it lacks meaning and may include paraphasic errors (use of words that sound similar to the correct word) and neologisms (made-up words). Comprehension of written language is similarly poor, and repetition is defective. The patient cannot follow oral or written commands, but can imitate the examiner's action when prompted by a gesture to do so. These patients are usually unaware of and therefore not disturbed by their aphasia.



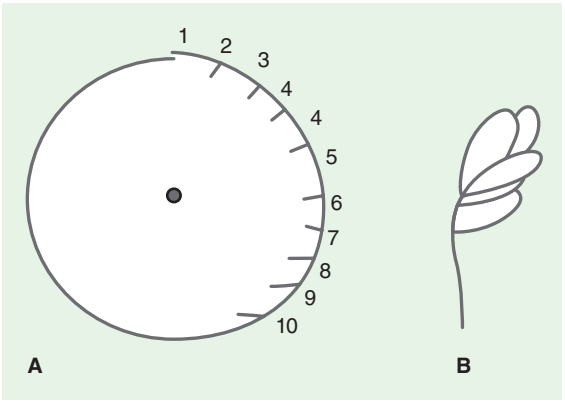
▲ **Figure 1-7.** Brain areas implicated in stroke-related aphasia include the language comprehension (Wernicke) area, the motor speech (Broca) area, and the arcuate fasciculus. Ischemic lesions at the numbered sites produce (1) expressive aphasia, (2) receptive aphasia, (3) conduction aphasia, (4) transcortical expressive aphasia, (5) transcortical receptive aphasia, and (1, 2, and 3) global aphasia. In neurodegenerative disorders such as frontotemporal dementia, however, cortical atrophy in (2) correlates better with impaired repetition than with impaired comprehension. See also Table 1-1. (Modified with permission from Waxman SG. *Clinical Neuroanatomy*. 26th ed. New York, NY: McGraw Hill; 2010.)

Global aphasia combines features of expressive and receptive aphasia—patients can neither express, comprehend, nor repeat spoken or written language.

Other forms of aphasia include **conduction aphasia**, in which repetition is impaired whereas expression and comprehension are intact; **transcortical aphasia**, in which expressive, receptive, or global aphasia occurs with intact repetition; and **anomic aphasia**, a selective disorder of naming.

Language is distinct from **speech**, the final motor step in oral expression of language. A speech disorder (**dysarthria**) may be difficult to distinguish from aphasia, but always spares oral and written language comprehension and written expression.

4. **Sensory integration**—Sensory integration disorders result from parietal lobe lesions and cause misperception of or inattention to sensory stimuli on the side of the body opposite the lesion, even though primary sensory modalities (eg, touch) are intact. Patients with parietal lesions may exhibit various signs. **Astereognosis** is the inability to identify by touch an object placed in the hand, such as a coin, key, or safety pin. **Agraphesthesia** is the inability to identify by touch a number written on the hand. Failure of **two-point discrimination** is the inability to differentiate between a single stimulus and two simultaneously applied, adjacent but separated, stimuli that can be distinguished by a normal person (or on the opposite side). For example, the points of two pens can be applied together on a fingertip and gradually separated until they are perceived as separate objects; the distance at which this occurs is recorded. **Allesthesia** is misplaced (typically more proximal) localization of a tactile stimulus. **Extinction** is the failure to perceive a visual or tactile stimulus when it is applied bilaterally, even though it can be perceived when applied unilaterally. **Neglect** is failure to attend to space or use the limbs on one side of the body. **Anosognosia** is unawareness of a neurologic deficit. **Constructional apraxia** is the inability to draw accurate representations of external space, such as filling in the numbers on a clock face or copying geometric figures (**Figure 1-8**).
5. **Motor integration**—Praxis is the application of motor learning, and **apraxia** is the inability to perform previously learned tasks despite intact motor and sensory function.



▲ **Figure 1-8.** Unilateral (left-sided) neglect in a patient with a right parietal lesion. The patient was asked to fill in the numbers on the face of a clock (**A**) and to draw a flower (**B**). (Reproduced with permission from Waxman SG. *Clinical Neuroanatomy.* 26th ed. New York, NY: McGraw Hill; 2010.)

Tests for apraxia include asking the patient to simulate the use of a key, comb, or fork. Unilateral apraxias are commonly caused by contralateral premotor frontal cortex lesions. Bilateral apraxias, such as gait apraxia, may be seen with bifrontal or diffuse cerebral lesions.

Cranial Nerves

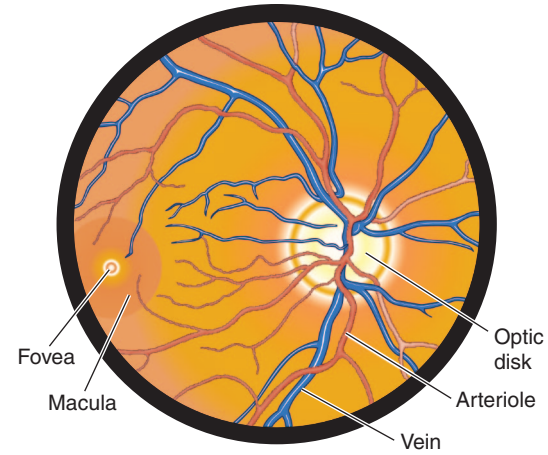
A. Olfactory (I) Nerve

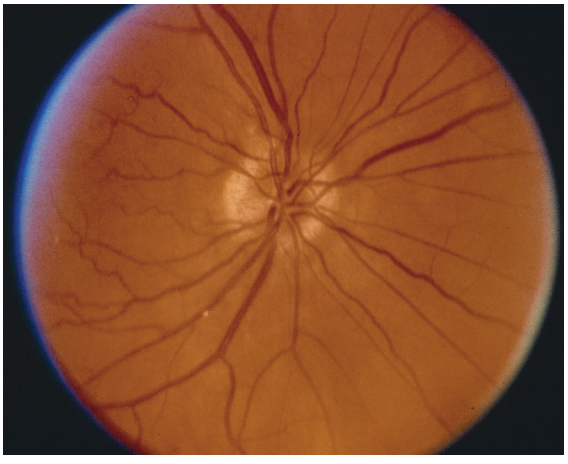
The olfactory nerve mediates the sense of smell (olfaction) and is tested by asking the patient to identify common scents, such as coffee, vanilla, peppermint, or cloves. Normal function can be assumed if the patient detects the smell, even if unable to identify it. Each nostril is tested separately. Irritants such as alcohol should not be used because they may be detected as noxious stimuli independent of olfaction.

B. Optic (II) Nerve

The optic nerve transmits visual information from the retina, through the optic chiasm (where fibers from the nasal, or medial, sides of both retinas, conveying information from the temporal, or lateral, halves of both visual fields, cross), and then via the optic tracts to the lateral geniculate nuclei of the thalami. Optic nerve function is assessed separately for each eye and involves inspecting the back of the eye (optic fundus) by direct ophthalmoscopy, measuring visual acuity, and mapping the visual field as follows:

1. **Ophthalmoscopy** should be conducted in a dark room to dilate the pupils, which makes it easier to see the fundus.

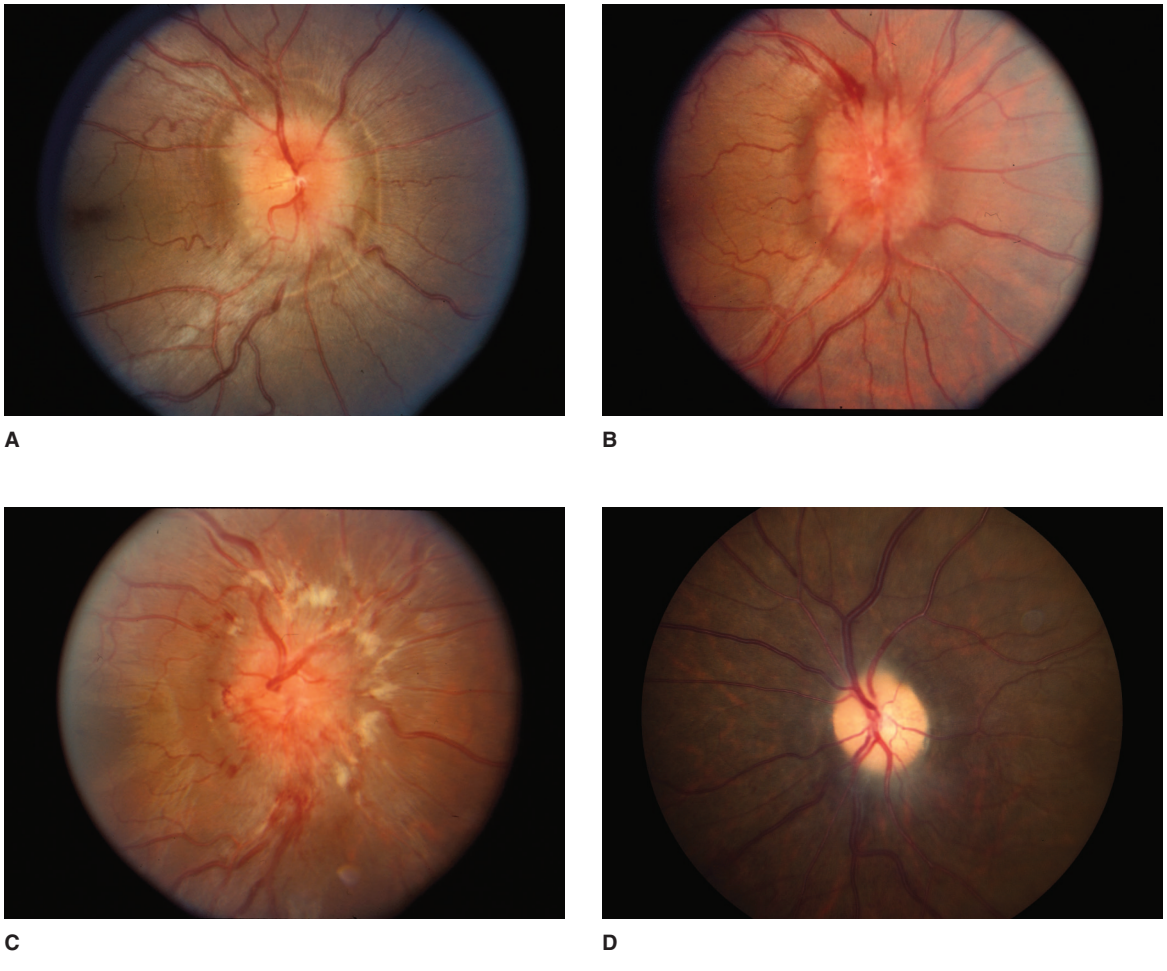




▲ **Figure 1-9.** Normal optic fundus. The diagram (**A**) shows landmarks corresponding to the photograph (**B**). (Reproduced with permission from Vaughan D, Asbury T, Riordan-Eva P. *General Ophthalmology*. 15th ed. Stamford, CT: Appleton & Lange; 1999. Photo contributor: Diane Beeston.)

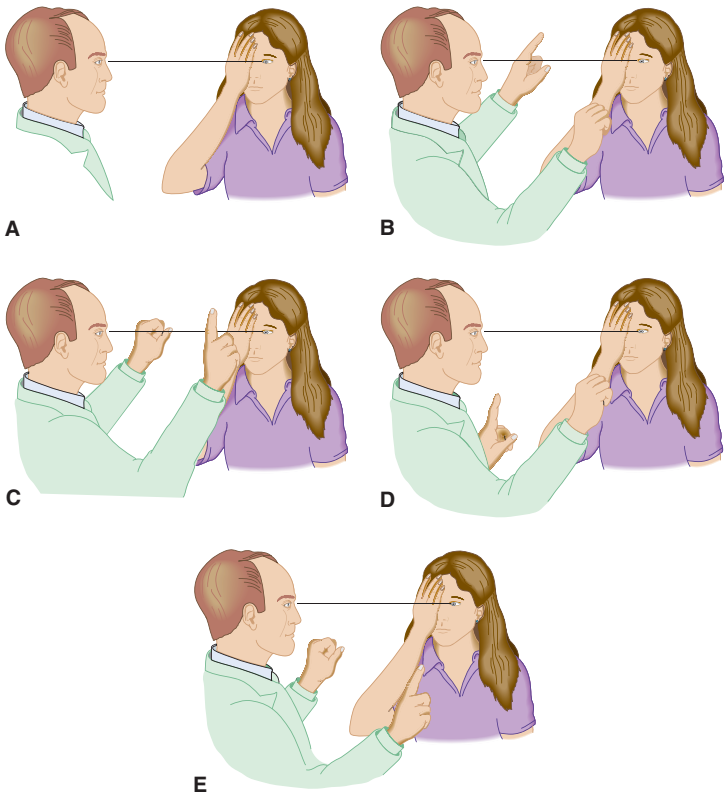
Mydriatic (sympathomimetic or anticholinergic) eye drops are sometimes used to enhance dilation, but this should not be done until visual acuity and pupillary reflexes are tested, nor in patients with untreated closed angle glaucoma or an intracranial mass lesion that might lead to transtentorial herniation. In the latter case, the ability to test pupillary reflexes is essential to detect clinical progression. The normal **optic disk** (**Figure 1-9**) is a yellowish, oval structure situated nasally at the posterior pole of the eye. The margins of

the disk and the blood vessels that cross it should be sharply demarcated, and the veins should show spontaneous pulsations. The **macula**, an area paler than the rest of the retina, is located about two disk diameters temporal to the temporal margin of the optic disk and can be visualized by having the patient look at the light from the ophthalmoscope. In neurologic patients, the most important abnormality to identify is swelling of the optic disk resulting from increased intracranial pressure (**papilledema**). In early papilledema (**Figure 1-10**), the retinal veins appear engorged, and spontaneous venous pulsations are absent. The disk may be hyperemic with linear hemorrhages at its borders. The disk margins become blurred, initially at the nasal edge. In fully developed papilledema, the optic disk is elevated above the plane of the retina, and blood vessels crossing the disk border are obscured. Papilledema is almost always bilateral, does not typically impair vision except for enlargement of the blind spot, and is not painful. Another abnormality—**optic disk pallor**—is produced by atrophy of the optic nerve. It can be seen in patients with multiple sclerosis or other disorders of the optic nerve and is associated with defects in visual acuity, visual fields, or pupillary reactivity.



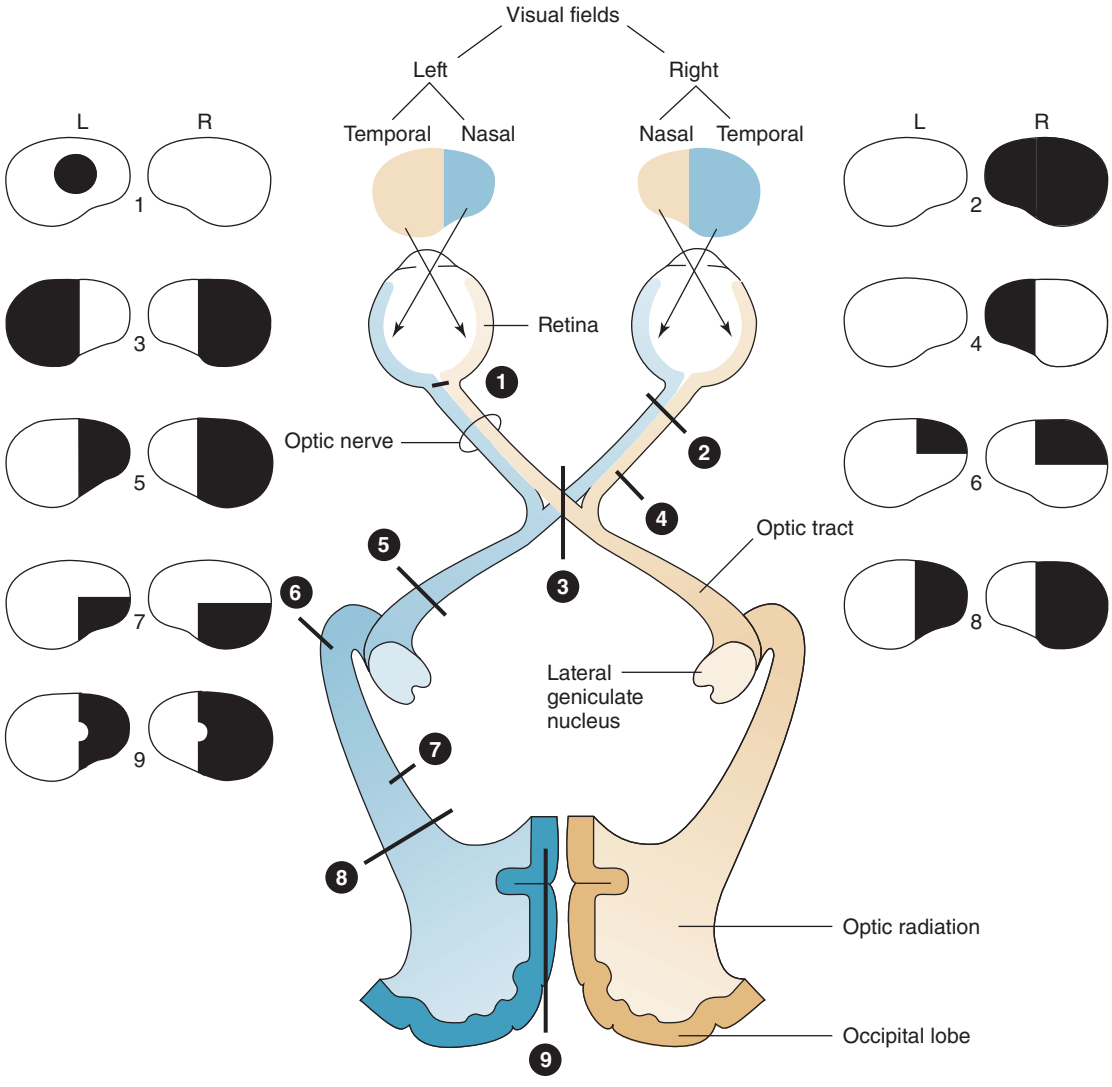
▲ **Figure 1-10.** Optic fundus in papilledema. (**A**) In early papilledema, the superior and inferior margins of the optic disk are blurred by the thickened layer of nerve fibers entering the disk. (**B**) Moderate papilledema with disk swelling. (**C**) In fully developed papilledema, the optic disk is swollen, elevated, and congested, and the retinal veins are markedly dilated; swollen nerve fibers (white patches) and hemorrhages can be seen. (**D**) In chronic atrophic papilledema, the optic disk is pale and slightly elevated, and its margins are blurred. (Used with permission from Nancy Newman.)

2. **Visual acuity** should be tested with refractive errors corrected, so patients who wear glasses should be examined with them on. Acuity is tested in each eye separately, using a Snellen eye chart approximately 6 m (20 ft) away for distant vision or a Rosenbaum pocket eye chart approximately 36 cm (14 in) away for near vision. The smallest line of print that can be read is noted, and acuity is expressed as a fraction, in which the numerator is the distance at which the line of print can be read by the patient, and the denominator is the distance at which it can be read by someone with normal vision. Thus, 20/20 indicates normal acuity, with the denominator increasing as vision worsens. More severe impairment can be graded according to the distance at which the patient can count fingers, discern hand movement, or perceive light. Red–green color vision is often disproportionately impaired with optic nerve lesions and can be tested using colored pens or hatpins or with color vision plates.
3. **Visual fields** are tested for each eye separately, most often using the **confrontation** technique (**Figure 1-11**). The examiner stands at about arm's length from the patient, the patient's eye that is not being tested and the examiner's eye opposite it are closed or covered, and the patient is instructed to fix on the examiner's open eye, superimposing the monocular fields of patient and examiner. Using the index finger of either hand to locate the peripheral limits of the patient's field, the examiner then moves the finger slowly inward in all directions until the patient detects it. The size of the patient's **central scotoma (blind spot)**, located in the temporal half of the visual field, can also be measured in relation to the examiner's. The object of confrontation testing is to determine whether the patient's visual field is coextensive with—or more restricted than—the examiner's. Another approach is to use the head of a hatpin as the visual target. Subtle field defects may be detected by asking the patient to compare the brightness of colored objects presented at different sites in the field or by measuring the fields using a hatpin with a red head as the target. Gross abnormalities can be detected in less than fully alert patients by determining whether



▲ **Figure 1-11.** Confrontation testing of the visual field. (**A**) The left eye of the patient and the right eye of the examiner are aligned. (**B**) Testing the superior nasal quadrant. (**C**) Testing the superior temporal quadrant. (**D**) Testing the inferior nasal quadrant. (**E**) Testing the inferior temporal quadrant. The procedure is repeated for the patient's other eye.

they blink when the examiner's finger is brought toward the patient's eye from various directions. In some situations (eg, following the course of a progressive or resolving defect), the visual fields should be mapped more precisely, using perimetry techniques such as tangent screen or automated perimetry testing. Common visual field abnormalities and their anatomic correlates are shown in **Figure 1-12**.

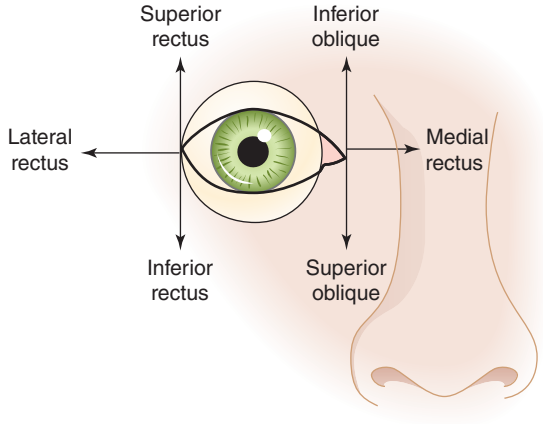


▲ **Figure 1-12.** Common visual field defects (black) and their anatomic bases. 1. **Central scotoma** caused by inflammation of the optic disk (optic neuritis) or optic nerve (retrobulbar neuritis). 2. **Total blindness of the right eye** from a complete lesion of the right optic nerve. 3. **Bitemporal hemianopia** caused by pressure exerted on the optic chiasm by a pituitary tumor. 4. **Right nasal hemianopia** caused by a perichiasmal lesion (eg, calcified internal carotid artery). 5. **Right homonymous hemianopia** from a lesion of the left optic tract. 6. **Right homonymous superior quadrantanopia** caused by partial involvement of the optic radiation by a lesion in the left temporal lobe (Meyer loop). 7. Right homonymous inferior quadrantanopia caused by partial involvement of the optic radiation by a lesion in the left parietal lobe. 8. **Right homonymous hemianopia** from a complete lesion of the left optic radiation. (A similar defect may also result from lesion 9.) 9. **Right homonymous hemianopia (with macular sparing)** resulting from posterior cerebral artery occlusion.

C. Oculomotor (III), Trochlear (IV), and Abducens (VI) Nerves

These three nerves control the action of the intraocular (pupillary sphincter) and extraocular muscles.

1. **Pupils**—The diameter and shape of the pupils in ambient light and their responses to light and accommodation should be ascertained. Normal pupils average ~3 mm in diameter in a well-lit room, but can vary from ~6 mm in children to <2 mm in the elderly, and can differ in size from side to side by ~1 mm (**physiologic anisocoria**). Pupils should be round and regular in shape. Normal pupils constrict briskly in response to direct illumination, and somewhat less so to illumination of the pupil on the opposite side (consensual response), and dilate again rapidly when the source of illumination is removed. When the eyes converge to focus on a nearer object such as the tip of one's nose (**accommodation**), normal pupils constrict. Pupillary constriction (**miosis**) is mediated through parasympathetic fibers that originate in the midbrain and travel with the oculomotor nerve to the eye. Interruption of this pathway, such as by a hemispheric mass lesion producing coma and compressing the oculomotor nerve as it exits the brainstem, produces a dilated (~7 mm) unreactive pupil. Pupillary dilation is controlled by a three-neuron sympathetic relay, from the hypothalamus, through the brainstem to the T1 level of the spinal cord, to the superior cervical ganglion, and to the eye. Lesions of this pathway result in constricted (≤1 mm) unreactive pupils. Other common pupillary abnormalities are listed in **Table 1-2**.
2. **Eyelids and orbits**—The eyelids (**palpebrae**) should be examined with the patient's eyes open. The distance between the upper and lower lids (interpalpebral fissure) is usually ~10 mm and approximately equal in the two eyes. The upper lid normally covers 1-2 mm of the iris, but this is increased by drooping of the lid (**ptosis**) due to lesions of the levator palpebrae muscle or its oculomotor (III) or sympathetic nerve supply. Ptosis occurs together with miosis (and sometimes defective sweating, or **anhidrosis**, of the forehead) in **Horner syndrome**. Abnormal protrusion of the eye from the orbit (**exophthalmos** or **proptosis**) is best detected by standing behind the seated patient and looking down at his or her eyes.
3. **Eye movements**—Movement of the eyes is accomplished by the action of six muscles attached to each globe, which act to move the eye into the six cardinal positions of gaze (**Figure 1-13**). Equal and opposed actions of these muscles in the resting state place the eye in mid- or primary position (looking directly forward). When the function of an extraocular muscle is disrupted, the eye is unable to move in the direction of action of the affected muscle (**ophthalmoplegia**) and may deviate in the opposite direction because of the unopposed action of other extraocular muscles. When the eyes are thus misaligned, visual images of perceived



▲ **Figure 1-13.** Six cardinal positions of gaze for testing eye movement. The eye is abducted by the lateral rectus and adducted by the medial rectus. The abducted eye is elevated by the superior rectus and depressed by the inferior rectus; the adducted eye is elevated by the inferior oblique and depressed by the superior oblique. All extraocular muscles are innervated by the oculomotor (III) nerve except the superior oblique, which is innervated by the trochlear (IV) nerve, and the lateral rectus, which is innervated by the abducens (VI) nerve.

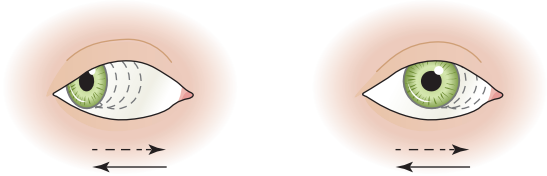
Table 1-2. Common Pupillary Abnormalities.

Name	Appearance	Reactivity (light)	Reactivity (accommodation)	Site of Lesion
Adie (tonic) pupil	Unilateral large pupil	Sluggish	Normal	Ciliary ganglion
Argyll Robertson pupil	Bilateral small, irregular pupils	Absent	Normal	Midbrain
Horner syndrome	Unilateral small pupil and ptosis	Normal	Normal	Sympathetic innervation of eye
Marcus Gunn pupil	Normal	Consensual > direct	Normal	Optic nerve

objects fall at a different place on each retina, creating the illusion of double vision or **diplopia**. The extraocular muscles are innervated by the oculomotor (III), trochlear (IV), and abducens (VI) nerves, and defects in eye movement may result from either muscle or nerve lesions. The oculomotor (III) nerve innervates all the extraocular muscles except the superior oblique, which is innervated by the trochlear (IV) nerve, and the lateral rectus, which is innervated by the abducens (VI) nerve. Because of their differential innervation, the pattern of ocular muscle involvement in pathologic conditions can help to distinguish a disorder of the ocular muscles per se from a disorder that affects a cranial nerve.

Eye movement is tested by having the patient look at a flashlight held in each of the cardinal positions of gaze and observing whether the eyes move fully and in a yoked (**conjugate**) fashion in each direction. With normal conjugate gaze, light from the flashlight falls at the same spot on both corneas. Limitations of eye movement and any disconjugacy should be noted. If the patient complains of diplopia, the weak muscle responsible should be identified by having the patient gaze in the direction in which the separation of images is greatest. Each eye is then covered in turn, and the patient is asked to report which of the two (near or far) images disappears. The image displaced farther in the direction of gaze is always referable to the weak eye. Alternatively, one eye is covered with translucent red glass, plastic, or cellophane, which allows the eye responsible for each image to be identified. For example, with weakness of the left lateral rectus muscle, diplopia is maximal on leftward gaze, and the leftmost of the two images seen disappears when the left eye is covered.

4. **Ocular oscillations—Nystagmus**, or rhythmic oscillation of the eyes, can occur at the extremes of voluntary gaze in normal subjects. In other settings, however, it may be due to anticonvulsant or sedative drugs, or reflect disease affecting the extraocular muscles or their innervation, or vestibular or cerebellar pathways. The most common form, **jerk nystagmus**, consists of a slow phase of movement followed by a fast phase in the opposite direction (**Figure 1-14**). To detect nystagmus, the eyes are observed in the primary position and in each of the cardinal positions of gaze. If nystagmus is observed, it should be described in terms of the position of gaze in which it occurs, its direction, its amplitude (fine or coarse), precipitating factors such as changes in head position, and associated symptoms, such as vertigo. The direction of jerk nystagmus (eg, leftward-beating nystagmus) is, by convention, the direction of the fast phase. Jerk nystagmus usually increases in amplitude with gaze in the direction of the fast phase (Alexander law). A less common form of nystagmus is **pendular nystagmus**, which usually begins in infancy and is of equal velocity in both directions.



A End-position nystagmus **B** Nystagmus in primary position

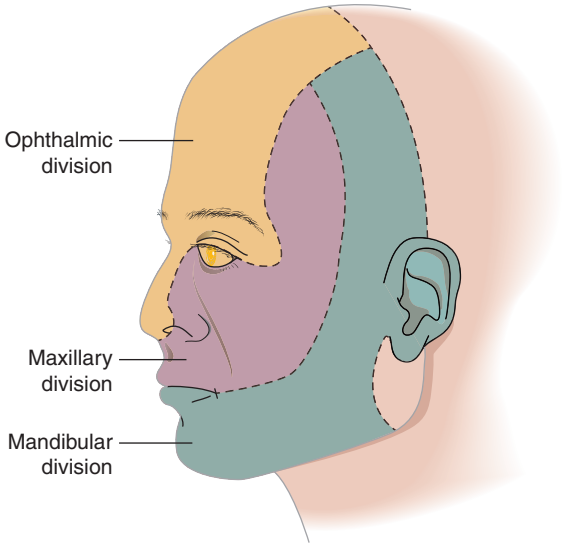
▲ **Figure 1-14.** Nystagmus. A slow drift of the eyes away from the position of fixation (broken arrows) is corrected by a fast movement back (solid arrows). The direction of the nystagmus is named from the fast component. Nystagmus in the primary position of gaze is more often pathologic than is nystagmus in the end position. (Reproduced with permission from LeBlond RF, DeGowin RL, Brown DD. *DeGowin's Diagnostic Examination.* 9th ed. New York, NY: McGraw Hill; 2009.)

D. Trigeminal (V) Nerve

The trigeminal nerve conveys sensory fibers from the face and motor fibers to the muscles of mastication. Facial touch and temperature sensation are tested, respectively, by touching and by placing the cool surface of a tuning fork on both sides of the face in the distribution of each division of the trigeminal nerve—**ophthalmic** (**V1**, forehead), **maxillary** (**V2**, cheek), and **mandibular** (**V3**, jaw) (**Figure 1-15**). The patient is asked if the sensation is the same on both sides and, if not, on which side the stimulus is felt less well, or as less cool. To test the **corneal reflex**, a wisp of cotton is swept lightly across the cornea overlying the iris (not the surrounding white sclera) on the lateral surface of the eye (out of the subject's view). The normal response, which is mediated by a reflex arc that depends on trigeminal (V1) nerve sensory function and facial (VII) nerve motor function, is bilateral blinking of the eyes. With impaired trigeminal function, neither eye blinks, whereas unilateral blinking implies a facial nerve lesion on the unblinking side. Trigeminal motor function is tested by observing the symmetry of opening and closing of the mouth; on opening, the jaw may deviate toward the weak side, causing the face to look askew. More subtle weakness can be detected by asking the patient to clench the teeth and attempting to force the jaw open. Normal jaw strength cannot be overcome by the examiner.

E. Facial (VII) Nerve

The facial nerve supplies the facial muscles and mediates taste sensation from about the anterior two-thirds of the tongue (**Figure 1-16**). To test facial strength, the patient's face should be observed for symmetry or asymmetry of the palpebral fissures and nasolabial folds at rest. The patient is asked to wrinkle the forehead,

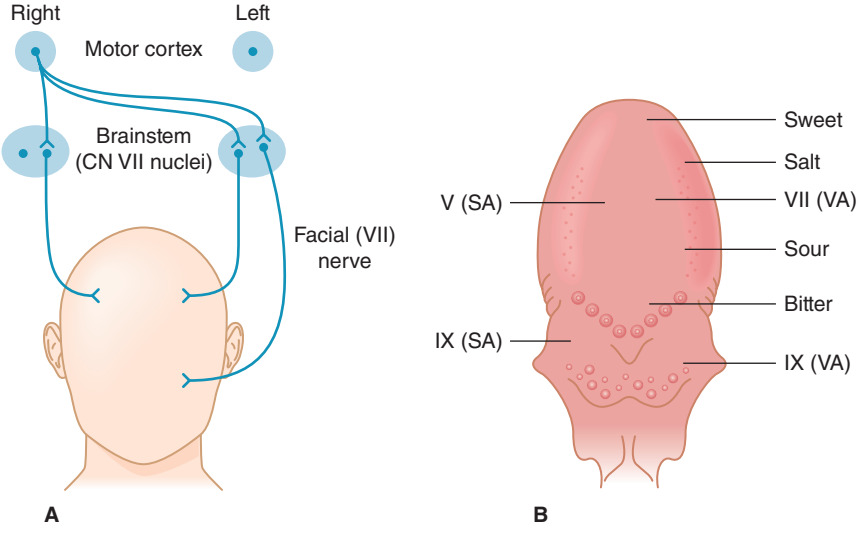


▲ **Figure 1-15.** Trigeminal (V) nerve sensory divisions: ophthalmic (V1), maxillary (V2), and mandibular (V3). (Reproduced with permission from Waxman SG. *Clinical Neuroanatomy*. 26th ed. New York, NY: McGraw Hill; 2010.)

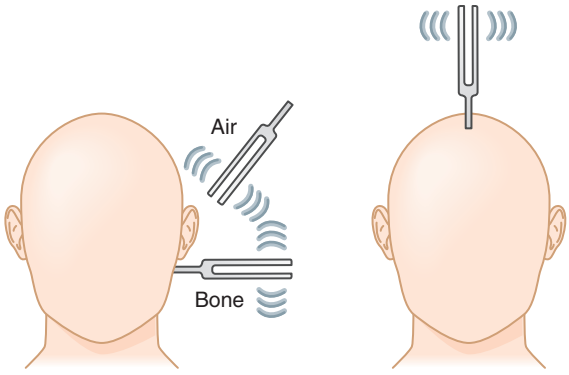
squeeze the eyes tightly shut (looking for asymmetry in the extent to which the eyelashes protrude), and smile or show the teeth. Again the examiner looks for symmetry or asymmetry. With a peripheral (facial nerve) lesion, an entire side of the face is weak, and the eye cannot be fully closed. With a central (eg, hemispheric) lesion, the forehead is spared, and some ability to close the eye is retained. This discrepancy is thought to result from dual cortical motor input to the upper face. Bilateral facial weakness cannot be detected by comparing the two sides. Instead, the patient is asked to squeeze both eyes tightly shut, press the lips tightly together, or puff out the cheeks. If strength is normal, the examiner should not be able to pry open the eyelids, force apart the lips, or force air out of the mouth by compressing the cheeks. Facial weakness may be associated with dysarthria that is most pronounced for *m* sounds. If the patient is normally able to whistle, this ability may be lost with facial weakness. To test taste sensation, cotton-tipped applicators are dipped in sweet, sour, salty, or bitter solutions and placed on the protruded tongue, and the patient is asked to identify the taste.

F. Vestibulocochlear (VIII) Nerve

The vestibulocochlear nerve has two divisions—auditory and vestibular—which are involved in hearing and equilibrium, respectively. Examination should include otoscopic inspection of the auditory canals and tympanic membranes, assessment of auditory acuity in each ear, and Weber and Rinne tests performed with a 512-Hz tuning fork. Auditory acuity can be tested crudely by rubbing



▲ **Figure 1-16.** Facial (VII) nerve. (**A**) Central and peripheral motor innervation of the face. The motor cortex projects to both sides of the forehead, but only to the contralateral lower face (eyes and below). (**B**) Somatic afferent (SA, touch; labels at left) and visceral afferent (VA, taste; labels at right) innervation of the tongue by the trigeminal (V), facial (VII), and glossopharyngeal (IX) nerves. (Reproduced with permission from Waxman SG. *Clinical Neuroanatomy*. 26th ed. New York, NY: McGraw Hill; 2010.)



Hearing loss	Rinne test (Conduction)	Weber test (Localization)
None	Air > bone	Midline
Sensorineural	Air > bone	Normal ear
Conductive	Bone > air	Affected ear

▲ **Figure 1-17.** Tests to distinguish sensorineural from conductive hearing loss.

thumb and forefinger together approximately 2 in. from each ear.

If the patient complains of hearing loss or cannot hear the finger rub, the nature of the hearing deficit should be explored. To perform the **Rinne test** (**Figure 1-17**), the base of a lightly vibrating 512-Hz tuning fork is placed on the mastoid process of the temporal bone until the sound can no longer be heard; the tuning fork is then moved near the opening of the external auditory canal. In patients with normal hearing or sensorineural hearing loss, air in the auditory canal conducts sound better than bone, and the tone can still be heard. With conductive hearing loss, the patient hears the bone-conducted tone, with the tuning fork on the mastoid process, longer than he or she hears the air-conducted tone. In the **Weber test** (see Figure 1-17), the handle of the vibrating 512-Hz tuning fork is placed in the middle of the forehead. With conductive hearing loss, the tone will sound louder in the affected ear; with sensorineural hearing loss, the tone will be louder in the normal ear.

In patients who complain of positional vertigo, the **Nylen–Bárány or Dix–Hallpike maneuver** (**Figure 1-18**) can be used to try to reproduce the symptom. The patient is seated on a table with the head and eyes directed forward and is then quickly lowered to a supine position with the head over the table edge, ~30° below horizontal. The test is repeated with the patient's head and eyes turned 45° to the right and again with the head and eyes turned 45° to the left. The eyes are observed for nystagmus, and the patient is asked to note the onset, severity, and cessation of vertigo, if it occurs.

G. Glossopharyngeal (IX) and Vagus (X) Nerves

The glossopharyngeal and vagus nerves innervate muscles of the pharynx and larynx involved in swallowing and phonation. The glossopharyngeal nerve also conveys touch from the posterior one-third of the tongue, tonsils, tympanic membrane, and Eustachian tube, as well as taste from the posterior one-third of the tongue. The vagus nerve contains sensory fibers from the larynx, pharynx, external auditory canal, tympanic membrane, and posterior fossa meninges.

Motor function of these nerves is tested by asking the patient to say "ah" with the mouth open and looking for full and symmetric elevation of the palate. With unilateral weakness, the palate fails to elevate on the affected side; with bilateral weakness, neither side elevates. Patients with palatal weakness may also exhibit dysarthria, which affects especially *k* sounds. Sensory function can be tested by the gag reflex: the back of the tongue is touched on each side in turn using a tongue depressor or cotton-tipped applicator, and differences in the magnitude of gag responses are noted.

H. Spinal Accessory (XI) Nerve

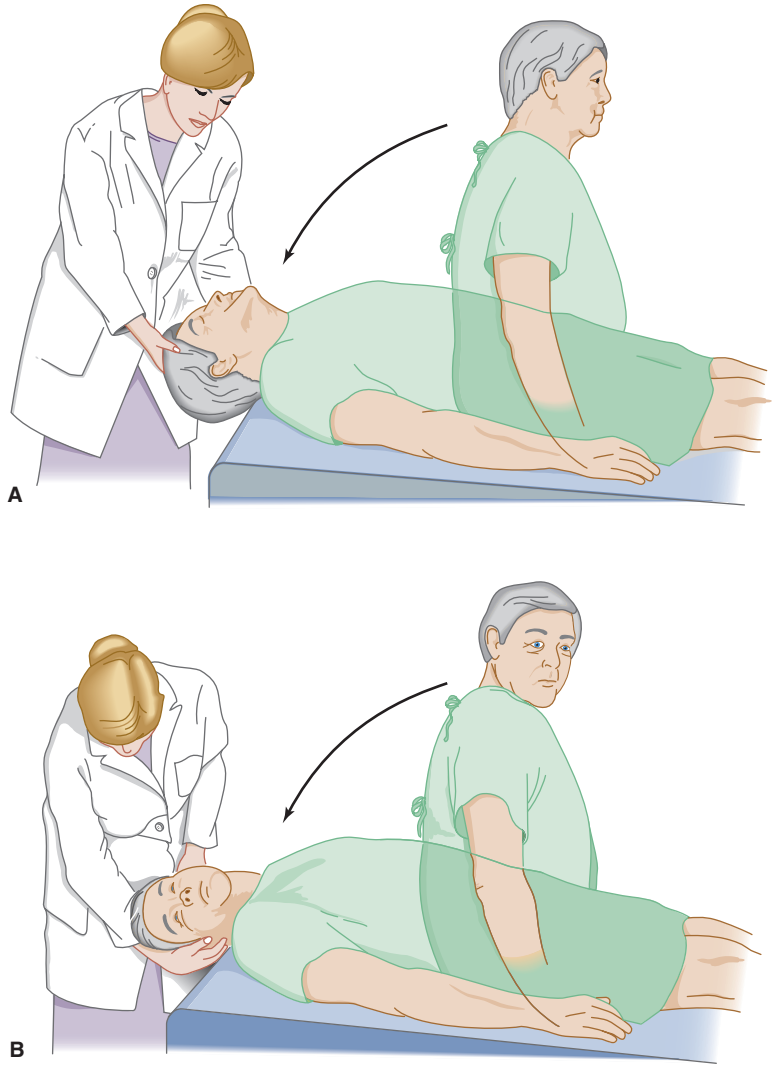
The spinal accessory nerve innervates the sternocleidomastoid and trapezius muscles. The sternocleidomastoid is tested by asking the patient to rotate the head against resistance provided by the examiner's hand, which is placed on the patient's jaw. Sternocleidomastoid weakness results in decreased ability to rotate the head *away* from the weak side. The trapezius is tested by having the patient shrug the shoulders against resistance and noting any asymmetry.

I. Hypoglossal (XII) Nerve

The hypoglossal nerve innervates the tongue muscles. It can be tested by having the patient push the tongue against the inside of the cheek while the examiner presses on the outside of the cheek. With unilateral tongue weakness, the ability to press against the *opposite* cheek is reduced. There may be also deviation of the protruded tongue toward the weak side, although facial weakness may result in false-positive tests. Tongue weakness also produces dysarthria with prominent slurring of labial (*l*) sounds. Denervation of the tongue may be associated with wasting (**atrophy**) and twitching (**fasciculation**).

▶ Motor Function

Motor function is governed by both upper and lower motor neurons. **Upper motor neurons** arise in the cerebral cortex and brainstem, and project onto lower motor neurons in the



▲ **Figure 1-18.** Test for positional vertigo and nystagmus. The patient is seated on a table with the head and eyes directed forward (**A**) and then quickly lowered to supine with the head over the table edge, ~30° below horizontal. The patient's eyes are then observed for nystagmus, and the patient is asked to report any vertigo. The test is repeated with the patient's head and eyes turned 45° to the right (**B**), and again with the head and eyes turned 45° to the left.

brainstem and anterior horn of the spinal cord. They include projections from cortex to spinal cord (**corticospinal tract**), most notably the part of the corticospinal tract that crosses (decussates) in the medulla (**pyramidal tract**). The motor examination involves evaluation of muscle bulk, tone, and strength. **Lower motor neurons** project from brainstem and spinal cord to innervate skeletal muscle. Lesions of either upper or lower motor neurons produce weakness. Upper motor neuron lesions also cause increased muscle tone, hyperactive tendon reflexes, and Babinski signs, whereas lower motor neuron lesions produce decreased muscle tone, hypoactive reflexes, muscle atrophy, and fasciculations.

A. Bulk

The muscles should be inspected to determine whether they are normal or decreased in bulk. Reduced bulk (**atrophy**) usually results from denervation due to lower motor neuron (spinal cord anterior horn cell or peripheral nerve) lesions. Asymmetric atrophy can be detected

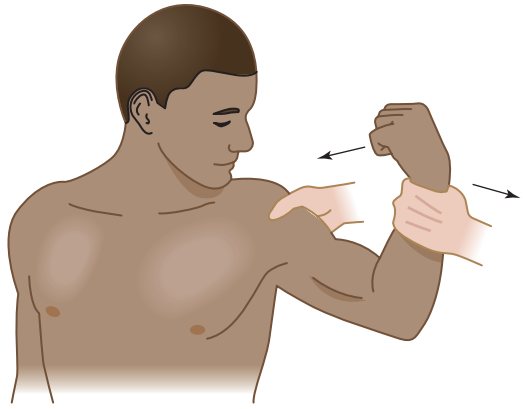
by comparing the bulk of individual muscles on the two sides by visual inspection or by using a tape measure. Atrophy may be associated with **fasciculations**—spontaneous muscle twitching visible beneath the skin.

B. Tone

Tone is resistance of a muscle to passive movement at a joint. With normal tone, there is little such resistance. Abnormally decreased tone (**hypotonia** or **flaccidity**) may accompany muscle, lower motor neuron, or cerebellar disorders. Increased tone takes the form of **rigidity**, in which the increase is constant over the range of motion at a joint, or **spasticity**, in which the increase is velocity-dependent and variable over the range of motion. Rigidity is associated classically with diseases of the basal ganglia and spasticity with diseases affecting the corticospinal tracts. Tone at the elbow is measured by supporting the patient's arm with one hand under the elbow, then flexing, extending, pronating, and supinating the forearm with the examiner's other hand. The arm should move smoothly in all directions. Tone at the wrist is tested by grasping the forearm with one hand and flopping the wrist back and forth with the other. With normal tone, the hand should rest at a 90° angle at the wrist; with increased tone the angle is >90°. Tone in the legs is measured with the patient lying supine and relaxed. The examiner places one hand under the knee, and then pulls abruptly upward. With normal or reduced tone, the patient's heel is lifted only momentarily off the bed or remains in contact with the surface of the bed as it slides upward. With increased tone, the leg lifts completely off the bed. Axial tone can be measured by passively rotating the patient's head and observing whether the shoulders also move, which indicates increased tone, or by gently but firmly flexing and extending the neck and noting whether resistance is encountered.

C. Strength

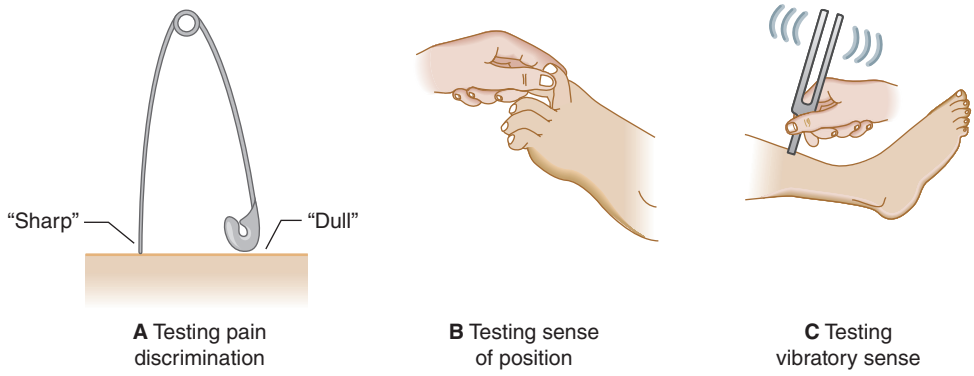
Muscle strength, or power, is graded on a scale according to the force a muscle can overcome: 5, normal strength; 4, decreased strength but still able to move against gravity plus added resistance; 3, able to move against gravity but not added resistance; 2, able to move only with the force of gravity eliminated (ie, horizontally); 1, flicker of movement; and 0, no visible muscle contraction. What is normal strength for a healthy, young person cannot be expected of a frail, elderly individual, and this must be taken into account in grading muscle strength. Strength is tested by having the patient execute a movement that involves a single muscle or muscle group and then applying a gradually increasing opposing force to determine whether the patient's movement can be overcome (**Figure 1-19**). Where possible, the examiner's opposing force should be applied using muscles similar in size to those being tested (eg, the arm for proximal and the fingers for distal limb muscles). The emphasis should be on identifying differences from side to side, between proximal and distal muscles, or between muscle groups innervated by different nerves or nerve roots. In **pyramidal weakness** (due to lesions affecting the corticospinal tract), there is preferential weakness of extensor and abductor muscles in the upper and flexor muscles in the lower extremity. **Fine finger movements**, such as rapidly tapping the thumb and index finger together, are slowed. With the arms extended, palms up, and eyes closed, the affected arm falls slowly downward and the hand pronates (**pronator drift**). Bilaterally symmetrical **distal weakness** is characteristic of polyneuropathy, whereas bilaterally symmetrical **proximal weakness** is observed in myopathy. Tests of strength for selected individual muscles are illustrated in the Appendix.



▲ **Figure 1-19.** Technique for testing muscle strength. In the example shown (biceps), the patient flexes the arm and the examiner tries to overcome this movement. (Reproduced with permission from LeBlond RF, DeGowin RL, Brown DD. *DeGowin's Diagnostic Examination*. 9th ed. New York, NY: McGraw Hill; 2009.)

▶ Sensory Function

Somatic sensation is mediated through large sensory fibers that travel from the periphery to the thalamus in the posterior columns of the spinal cord and brainstem medial lemniscus, and small sensory fibers that ascend to the thalamus in the spinothalamic tracts. Light touch sensation is conveyed by both pathways, vibration and position sense by the large-fiber pathway, and pain and temperature sense by the small-fiber pathway. Because most sensory disorders affect distal more than proximal sites, screening should begin distally (ie, at the toes and fingers) and proceed proximally, until the upper border of any deficit is reached. If the patient complains of sensory loss in a specific area, sensory testing should begin in the center of that area and proceed



▲ **Figure 1-20.** Tests of somatosensory function. (**A**) Touch (using finger or dull end of safety pin) and pain (sharp end of safety pin). (**B**) Joint position sense. (**C**) Vibration sense (using 128-Hz tuning fork). (Modified with permission from LeBlond RF, DeGowin RL, Brown DD. *DeGowin's Diagnostic Examination.* 9th ed. New York, NY: McGraw Hill; 2009.)

outward until sensation is reported as normal. Comparing the intensity of or threshold for sensation on the two sides of the body is useful for detecting lateralized sensory deficits. When sensory deficits are more limited, such as when they affect a single limb or truncal segment, their distribution should be compared with that of the spinal roots and peripheral nerves, to determine if involvement of a specific root or nerve can explain the deficit observed. Some tests of somatosensory function are illustrated in **Figure 1-20**.

A. Light Touch

Touch perception is tested by applying a light stimulus—such as a wisp of cotton, the teased-out tip of a cotton swab, or a brushing motion of the fingertips—to the skin of a patient whose eyes are closed and who is asked to indicate where the stimulus is perceived. If a unilateral deficit is suspected, the patient can be asked to compare how intensely a touch stimulus is felt when applied at the same site on the two sides.

B. Vibration

Vibration sense is tested by striking a low-pitched (128-Hz) tuning fork and placing its base on a bony prominence, such as a joint; the fingers of the examiner holding the tuning fork serve as a normal control. The patient is asked to indicate whether the vibration is felt and, if so, when the feeling goes away. Testing begins distally, at the toes and fingers, and proceeds proximally from joint to joint until sensation is normal.

C. Position

To test joint position sense, the examiner grasps the sides of the distal phalanx of a finger or toe and slightly displaces the joint up or down. The patient, with eyes closed, is asked to report any perceived change in position. Normal joint position sense is exquisitely sensitive, and the patient should detect the slightest movement. If joint position sense is diminished distally, more proximal limb joints are tested until normal position sense is encountered. Another test of position sense is to have the patient close the eyes, extend the arms, and then touch the tips of the index fingers together.

D. Pain

A disposable pin should be used to prick (but not puncture) the skin with enough force for the resulting sensation to be mildly unpleasant. The patient is asked whether the stimulus feels sharp. If a safety pin is used, the rounded end can be used to demonstrate to the patient the intended distinction between a sharp and dull stimulus. Depending on the circumstance, the examiner should compare pain sensation from side to side, distal to proximal, or dermatome to dermatome, and from the area of deficit toward normal regions.

E. Temperature

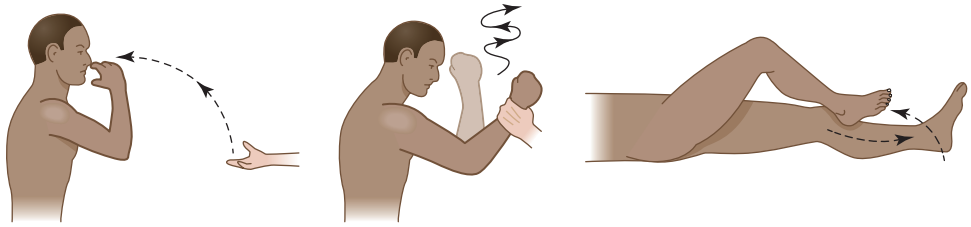
This can be tested using the flat side of a cold tuning fork or another cold object. The examiner should first establish the patient's ability to detect the cold sensation in a presumably normal area. Cold sensation is then compared on the two sides, moving from distal to proximal, across dermatomes, and from abnormal toward normal areas.

▶ Coordination

Impaired coordination (**ataxia**), which usually results from lesions affecting the cerebellum or its connections, can affect the eye movements, speech, limbs, or trunk. Some tests of coordination are illustrated in **Figure 1-21**.

A. Limb Ataxia

Ataxia is manifested by **dyssynergia** (decomposition of complex movements into their constituent parts) and



▲ **Figure 1-21.** Tests of cerebellar function: finger-to-nose test (left), test for rebound (center), and heel-knee-shin test (right). (Reproduced with permission from LeBlond RF, DeGowin RL, Brown DD. *DeGowin's Diagnostic Examination.* 9th ed. New York, NY: McGraw Hill; 2009.)

dysmetria (miscalculation of a movement's distance, direction, or speed). These can be detected by asking the patient to perform **rapid alternating movements** (eg, alternately tapping the palm and dorsum of the hand on the patient's other hand, or tapping the sole of the foot on the examiner's hand) and noting any irregularity in rate, rhythm, amplitude, or force (**dysdiadochokinesia**). In the **finger-to-nose test**, the patient moves an index finger back and forth between his or her nose and the examiner's finger; with ataxia there may be overshoot or undershoot of the target, and **intention tremor**, which is most prominent at the beginning and end of a movement. Impaired ability to check the force of muscular contraction can also often be demonstrated. When the patient is asked to raise the arms rapidly to a given height—or when the arms, extended and outstretched in front of the patient, are displaced by a sudden force—there may be overshooting (**rebound**). This can be demonstrated by having the patient forcefully flex the arm at the elbow against resistance—and then suddenly removing the resistance. If the limb is ataxic, continued contraction without resistance may cause the hand to strike the patient. Ataxia of the lower limbs can be demonstrated by the **heel-knee-shin test**. The supine patient is asked to run the heel of the foot smoothly up and down the opposite shin from ankle to knee. Ataxia produces jerky and inaccurate movement, making it impossible for the patient to keep the heel in contact with the shin.

B. Truncal Ataxia

To detect truncal ataxia, the patient sits on the side of the bed, or in a chair without lateral support, and any tendency to list to one side is noted. If the patient is asked to walk with eyes closed, they may also drift toward the side of a cerebellar lesion.

▶ Reflexes

A. Deep (Tendon) Reflexes

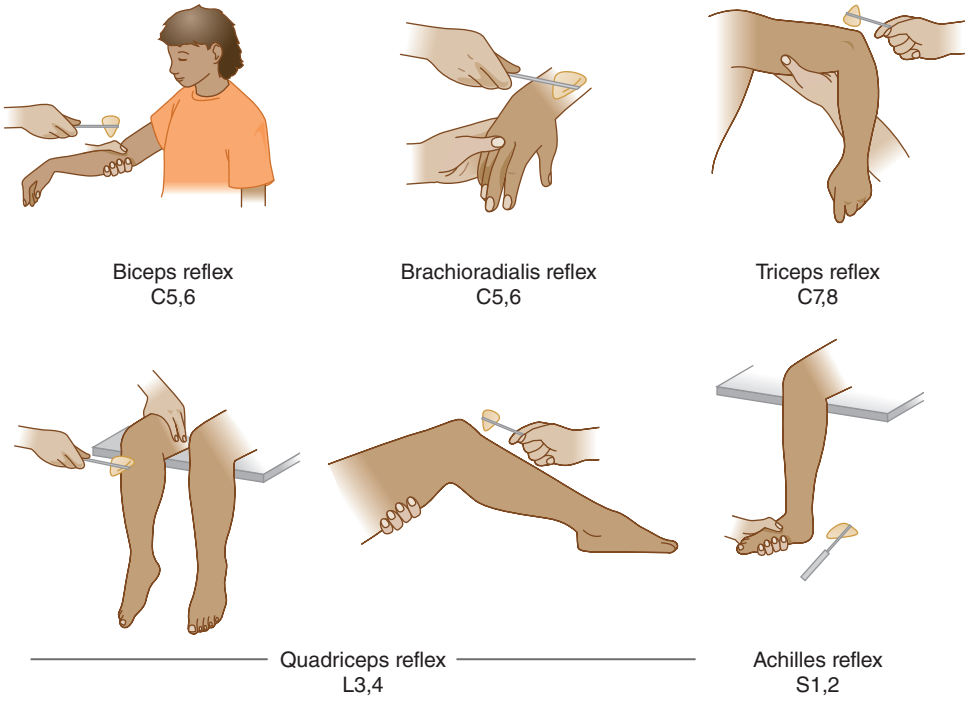
A **tendon reflex** is the reaction of a muscle to being passively stretched by percussion on a tendon. These monosynaptic reflexes require the integrity of both afferent and efferent peripheral nerves, and are normally inhibited by descending central pathways. Consequently, tendon reflexes are decreased or absent in disorders that affect any part of the reflex arc, most often polyneuropathies, and increased by lesions of the descending corticospinal tract. Tendon reflexes are graded on a scale according to the force of the contraction or the minimum force needed to elicit the response: 4, very brisk, often with rhythmic reflex contractions (**clonus**); 3, brisk but normal; 2, normal; 1, minimal; and 0, absent. In some cases, tendon reflexes are difficult to elicit, but may be brought out by having the patient clench the fist on the side not being tested or interlock the fingers and attempt to pull them apart. The main goal of reflex testing is to detect absence or asymmetry. Symmetrically absent reflexes suggest a polyneuropathy; symmetrically increased reflexes may indicate bilateral cerebral or spinal cord disease. The commonly tested tendon reflexes and the nerve roots they involve are biceps and brachioradialis (C5-6), triceps (C7-8), quadriceps (L3-4), and Achilles (S1-2). Methods for eliciting these tendon reflexes are shown in **Figure 1-22**.

B. Superficial (Cutaneous) Reflexes

The polysynaptic **superficial reflexes** are elicited by stimulating the skin, rather than tendons, and are altered or absent in disorders affecting the corticospinal tract. They include the **abdominal reflexes** (T5-T12), elicited by stroking the skin over the abdomen toward the umbilicus, which causes the umbilicus to deviate toward the stimulus, and the **cremasteric reflex** (L1-2), in which stroking the skin of the medial upper thigh results in elevation of the ipsilateral testis (**Figure 1-23**).

C. Pathologic Reflexes

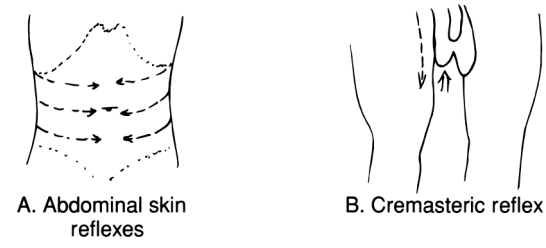
The most important of these is the **plantar reflex** (L4-S2), in which stroking the sole of the foot from its lateral border near the heel toward the great toe normally elicits plantar flexion of the toes. With corticospinal lesions, however, the great toe dorsiflexes (**Babinski sign**), which may be



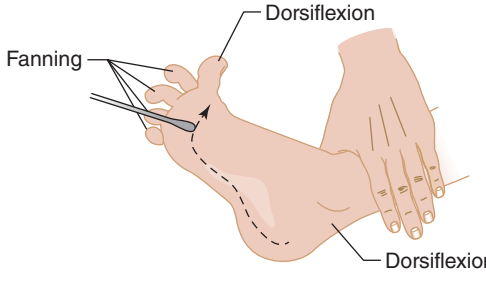
▲ **Figure 1-22.** Methods to elicit the tendon reflexes and spinal nerve roots involved. Techniques for eliciting the quadriceps reflex in both seated and supine patients are shown. (Modified with permission from LeBlond RF, DeGowin RL, Brown DD. *DeGowin's Diagnostic Examination*. 9th ed. New York, NY: McGraw Hill; 2009.)

accompanied by fanning of the toes, dorsiflexion at the ankle, and flexion at the thigh (**Figure 1-24**).

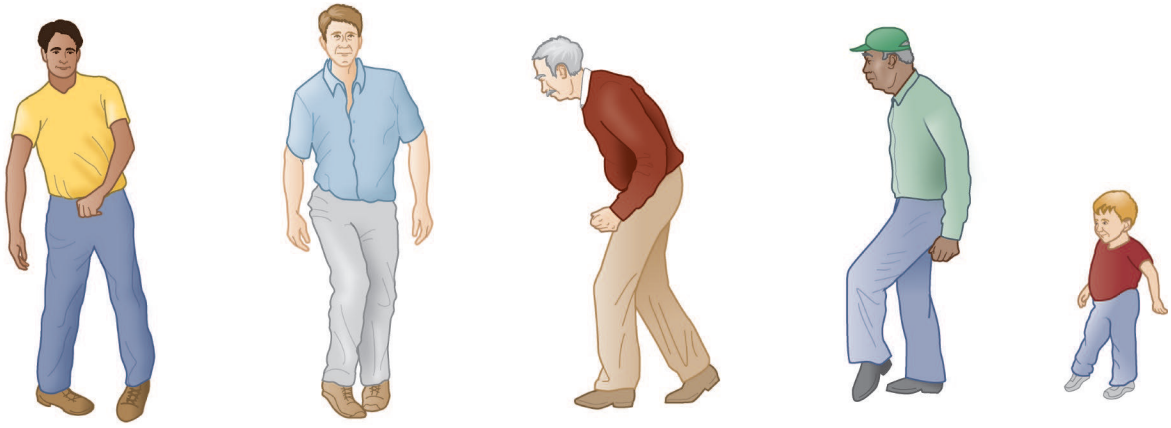
Several other reflexes are normally present in infancy, and subsequently disappear, but may reappear with aging or frontal lobe dysfunction. The **palmar grasp** reflex, elicited by stroking the skin of the patient's palm with the examiner's fingers, causes the patient's fingers to close around those of the examiner. The **plantar grasp** reflex consists of flexion and adduction of the toes in response to stimulation of the sole of the foot. The **palmomental reflex** is elicited



▲ **Figure 1-23.** Abdominal and cremasteric reflexes. Stroking the skin in the directions shown causes deviation of the umbilicus toward the stimulus (**A**) or elevation of the ipsilateral testis (**B**). (Modified with permission from LeBlond RF, DeGowin RL, Brown DD. *DeGowin's Diagnostic Examination*. 9th ed. New York, NY: McGraw Hill; 2009.)



▲ **Figure 1-24.** Extensor plantar response (Babinski sign) elicited by firmly stroking the lateral border of the sole of the foot. (Modified with permission from LeBlond RF, DeGowin RL, Brown DD. *DeGowin's Diagnostic Examination*. 9th ed. New York, NY: McGraw Hill; 2009.)



▲ **Figure 1-25.** Gait abnormalities. Left to right: hemiplegic gait (left hemiplegia), paraplegic gait, parkinsonian gait, steppage gait, dystrophic gait. (Modified with permission from *Handbook of Signs & Symptoms*. 4th ed. Ambler, PA: Lippincott Williams & Wilkins; 2009.)

by scratching the palm of the hand and results in contraction of ipsilateral chin (mentalis) and perioral (orbicularis oris) muscles. The **suck reflex** consists of involuntary sucking movements following stimulation of the lips. The **snout reflex** is elicited by gently tapping the lips and results in their protrusion. In the **rooting reflex**, stimulation adjacent to the lips causes them to deviate toward the stimulus. The **glabellar reflex** is elicited by repetitive tapping on the forehead just above the nose; normal subjects blink only in response to the first several taps, whereas persistent blinking is an abnormal response (**Myerson sign**).

▶ Stance & Gait

The patient should be asked to stand with feet together and eyes open to detect instability from cerebellar ataxia. Next, the patient should close the eyes; instability occurring with eyes closed but not open (**Romberg sign**) is a sign of sensory ataxia. The patient should then be observed walking normally, on the heels, on the toes, and in **tandem** (one foot placed directly in front of the other), to identify any of the following classic gait abnormalities (**Figure 1-25**):

1. **Hemiplegic gait**—The affected leg is held extended and internally rotated, the foot is inverted and plantar flexed, and the leg moves in a circular direction at the hip (circumduction).
2. **Paraplegic gait**—The gait is slow and stiff, with the legs crossing in front of each other (scissoring).
3. **Cerebellar ataxic gait**—The gait is wide-based and may be associated with staggering or reeling, as if one were drunk.
4. **Sensory ataxic gait**—The gait is wide based, the feet are slapped down onto the floor, and the patient may watch the feet.
5. **Steppage gait**—Inability to dorsiflex the foot, often due to a fibular (peroneal) nerve lesion, results in exaggerated elevation of the hip and knee to allow the foot to clear the floor while walking.
6. **Dystrophic gait**—Pelvic muscle weakness produces a lordotic, waddling gait.
7. **Parkinsonian gait**—Posture is flexed, starts are slow, steps are small and shuffling, arm swing is reduced, and involuntary acceleration (festination) may occur.
8. **Choreic gait**—The gait is jerky and lurching, but falls are surprisingly rare.
9. **Apraxic gait**—Frontal lobe disease may result in loss of the ability to perform a previously learned act (apraxia), in this case the ability to walk. The patient has difficulty initiating walking and may appear to be glued to the floor. Once started, the gait is slow and shuffling. However, there is no difficulty performing the same leg movements when the patient is lying down and the legs are not bearing weight.
10. **Antalgic gait**—One leg is favored over the other in an effort to avoid putting weight on the injured leg and causing pain.

NEUROLOGIC EXAMINATION IN SPECIAL SETTINGS

Although the neurologic examination is always tailored to a patient's specific situation, it is sufficiently distinctive to deserve special mention in two settings: examination of the

comatose patient and "screening" examination of a patient without neurologic complaints.

Coma

The comatose patient cannot cooperate for a full neurologic examination. Fortunately, however, a great deal of information can be derived from much more limited examination, focused on three elements: the **pupillary reaction to light**, **eye movements** induced by oculocephalic (head turning) or oculovestibular (cold water caloric) stimulation, and the **motor response to pain**. Examination of the comatose patient is discussed at length in Chapter 3, Coma.

"Screening" Neurologic Examination

In the absence of specific neurologic complaints, an abbreviated neurologic examination can be performed as part of the general physical examination.

1. **Mental status**—Observe whether the patient is awake and alert, confused, or unarousable. Test for orientation to person, place, and time. Screen for aphasia by asking the patient to repeat "no ifs, ands, or buts."
2. **Cranial nerves**—Examine the optic disks for papilledema. Test the visual fields by confrontation. Confirm the patient's ability to move the eyes conjugately in the six cardinal directions of gaze. Have the patient close the eyes tightly and show the teeth to assess facial strength.
3. **Motor function**—Compare the two sides with respect to speed of fine finger movements, strength of extensor muscles in the upper limb, and strength of flexor muscles in the lower limb, to detect corticospinal tract lesions.
4. **Sensory function**—Ask the patient to sketch out any area of perceived sensory deficit. Test light touch and vibration sense in the feet and, if impaired, determine the upper limit of impairment in both the lower and upper limbs.
5. **Reflexes**—Compare the two sides for activity of the biceps, triceps, quadriceps, and Achilles tendon reflexes, as well as the plantar responses.
6. **Coordination, stance, and gait**—Watch the patient stand and walk and note any asymmetry or instability of stance or gait.

DIAGNOSTIC FORMULATION

Principles of Diagnosis

Once the history and examination are completed, evaluation of a neurologic problem proceeds with the formulation of a provisional diagnosis. This is divided into two stages: anatomic diagnosis and etiologic diagnosis. The diagnostic process should always be guided by the **law of parsimony**, or **Occam's razor**: the simplest explanation is most likely to be correct. This means that a single, unifying diagnosis should be sought in preference to multiple diagnoses, each accounting for a different feature of the patient's problem.

Anatomic Diagnosis: Where Is the Lesion?

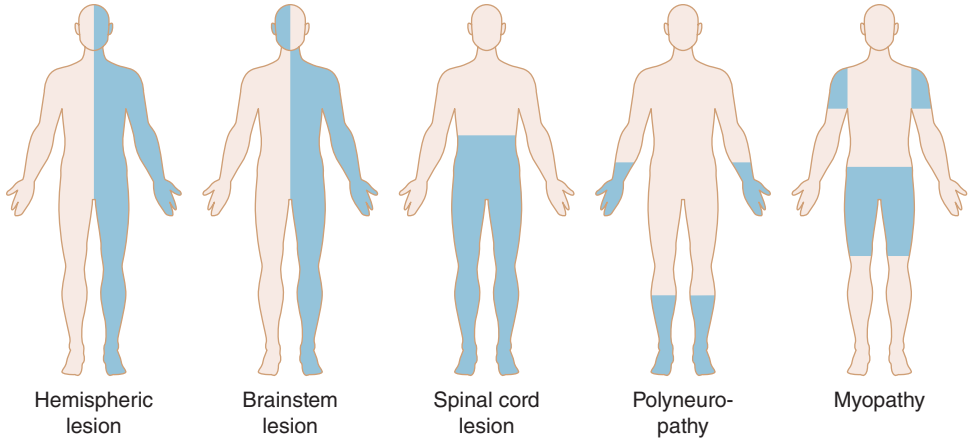
Anatomic diagnosis takes advantage of neuroanatomic principles to localize a lesion in space. The precision with which localization can be achieved varies, but it should always be possible at least to state the highest and lowest levels of the nervous system at which a lesion could produce the clinical picture under consideration.

A. Central versus Peripheral Nervous System

Making this distinction is typically the first step in anatomic diagnosis. Many symptoms and signs can be produced by both central and peripheral processes, but some symptoms and signs are more definitive. For example, cognitive abnormalities, visual field deficits, hyperreflexia, or extensor plantar responses (Babinski signs) point to the central nervous system, whereas muscle atrophy, fasciculation, or areflexia usually results from peripheral nervous system disorders.

B. Laterality

Unilateral brain lesions typically produce symptoms and signs on the opposite (contralateral) side of the body. This rule (Valsalva Doctrine) helps localize most focal cerebral lesions. However, exceptions occur. For example, hemispheric mass lesions that cause transtentorial herniation may compress the contralateral cerebral peduncle in the midbrain, producing hemiparesis on the same side as the mass. Brainstem lesions can produce crossed deficits, with weakness or sensory loss over the ipsilateral face and contralateral limbs. Thus, a unilateral lesion in the pons can cause ipsilateral facial weakness due to involvement of the facial (VII) nerve nucleus, with contralateral weakness of the arm and leg from involvement of descending motor pathways above their crossing (decussation) in the medulla. **Wallenberg syndrome**, usually due to a stroke in the lateral medulla, is associated with ipsilateral impairment of pain and temperature sensation over the face due to involvement of the descending tract and nucleus of the trigeminal (V) nerve, with contralateral pain and temperature deficits in the limbs from interruption of the lateral spinothalamic tract. Lesions of a cerebellar hemisphere produce ipsilateral symptoms and signs (eg, limb ataxia), due partly to connections with the contralateral cerebral cortex. Finally, the spinal accessory (XI) nerve receives bilateral input from



▲ **Figure 1-26.** Anatomic patterns of involvement (blue) from disorders affecting different sites in the nervous system.

the motor cortex, with ipsilateral input predominating, so a cortical lesion can produce ipsilateral sternocleidomastoid muscle weakness.

C. Anatomic Patterns of Involvement

Anatomic diagnosis of neurologic lesions can be facilitated by recognizing patterns of involvement characteristic of disease at different sites (**Figure 1-26**). **Hemispheric lesions** are suggested by contralateral motor and sensory deficits affecting face, arm, and leg, as well as by cognitive or visual field abnormalities. **Brainstem lesions** should be suspected with crossed deficits (motor or sensory involvement of the face on one side of the body and the arm and leg on the other) or cranial nerve (eg, ocular) palsies. **Spinal cord lesions** produce deficits below the level of the lesion and, except for high cervical cord lesions affecting the spinal tract and nucleus of the trigeminal (V) nerve, spare the face. The relative involvement of upper motor neurons, lower motor neurons, and various sensory pathways depends on the site and extent of the spinal lesion in the horizontal plane. **Polyneuropathies** produce distal, symmetric sensory deficits and weakness, which usually affect the lower more than the upper limbs, and are associated with areflexia. **Myopathies** (disorders of muscle) produce proximal weakness, which may affect the face and trunk as well as the limbs, without sensory loss.

▶ Etiologic Diagnosis: What Caused the Lesion?

A. Revisit the History

Once an anatomic diagnosis is reached, the next step is to identify the cause. Often the patient's prior history contains clues. Preexisting diseases such as hypertension, diabetes, heart disease, cancer, and AIDS are each associated with a spectrum of neurologic complications. Numerous medications and drugs of abuse (eg, alcohol) have neurologic side effects. The family history may point to a genetic disease.

B. Consider General Categories of Disease

Neurologic disease can be produced by the same kinds of pathologic processes that cause disease in other organ systems (**Table 1-3**). Once a neurologic problem has been localized, these categories can be used to generate a list of possible etiologies.

C. Time Course Is a Clue to Etiology

The time course of a disorder is an important clue to its etiology (see Figure 1-1). For example, only a few processes produce neurologic symptoms that evolve within minutes—typically ischemia, seizure, or syncope. Neoplastic and degenerative processes, by contrast, give rise to progressive, unremitting symptoms and signs, whereas inflammatory and metabolic disorders may wax and wane.

D. Common Diseases Are Common

Sometimes the anatomic syndrome is sufficiently distinctive that the cause is obvious. More often, however, an anatomic syndrome can have multiple etiologies. When this is the case, it is important to remember that common diseases are common and that even unusual presentations of common diseases occur more frequently than

Table 1-3. Etiologic Categories of Neurologic Disease.

Category	Examples
Degenerative	Alzheimer disease, Huntington disease, Parkinson disease, amyotrophic lateral sclerosis
Developmental or genetic	Muscular dystrophies, Arnold–Chiari malformation, syringomyelia
Immune	Multiple sclerosis, Guillain–Barré syndrome, myasthenia gravis
Infectious	Bacterial meningitis, brain abscess, viral encephalitis, HIV-associated dementia, neurosyphilis
Metabolic	Hypo/hyperglycemic coma, diabetic neuropathies, hepatic encephalopathy
Neoplastic	Glioma, metastatic carcinoma, lymphoma, paraneoplastic syndromes
Nutritional	Wernicke encephalopathy (vitamin B_1), combined systems disease (vitamin B_{12})
Toxic	Alcohol-related syndromes, intoxication with recreational drugs, side effects of prescription drugs
Traumatic	Sub/epidural hematoma, entrapment neuropathies
Vascular	Ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage

classic presentations of rare diseases. **Table 1-4** shows the relative prevalence of several neurologic diseases. It is helpful to appreciate how common different diseases are and whether they affect particular populations (ie, ages, sexes, or ethnic groups) disproportionately. For example, multiple sclerosis usually has its onset between the ages of 20 and 40 years, affects women more often than men, and preferentially affects individuals of north European descent.

INVESTIGATIVE STUDIES

After the history is taken, the general physical and neurologic examinations are completed, and a preliminary diagnosis is formulated, laboratory investigations are often undertaken to obtain additional diagnostic information. These investigations are addressed in Chapter 2, Investigative Studies.

Table 1-4. Estimated Worldwide Prevalence of Selected Neurologic Disorders (in Millions).

Migraine	959
Alzheimer disease & other dementias	46
Stroke	42
Epilepsy	23
Meningitis	9
Parkinson disease	6
Encephalitis	4
Multiple sclerosis	2
Cancer (primary CNS)	1
Motor neuron disease	0.2

Data from GBD 2015 Neurological Disorders Collaborator Group: Global, Regional, and National Burden of Neurological Disorders During 1990-2015: A Systematic Analysis for the Global Burden of Disease Study 2015, *Lancet Neurol* 2017 Nov;16(11):877-897.

Investigative Studies

2

(Continued on Next Page)

LUMBAR PUNCTURE

INDICATIONS

1. Diagnosis of meningitis, other infective or inflammatory disorders, subarachnoid hemorrhage, hepatic encephalopathy, meningeal malignancies, paraneoplastic disorders, or suspected intracranial pressure abnormalities.
2. Assessment of therapeutic response in meningitis, infective or inflammatory disorders.
3. Administration of intrathecal medications or radiologic contrast media.
4. Rarely, to reduce cerebrospinal fluid (CSF) pressure.
5. In specialized centers, assessment of biomarkers of certain degenerative diseases, especially Creutzfeldt-Jakob disease and Alzheimer disease, and of narcolepsy.

CONTRAINDICATIONS

1. **Suspected intracranial mass lesion**—Lumbar puncture can hasten incipient transtentorial herniation.
2. **Local infection** over site of puncture. Use cervical or cisternal puncture instead.
3. **Coagulopathy**—Correct clotting-factor deficiencies and thrombocytopenia (platelet count below 50,000/μL or rapidly falling) before lumbar puncture to reduce risk of hemorrhage.
4. **Suspected spinal cord mass lesion**—In this case, remove only a small quantity of CSF to avoid creating a pressure differential above and below the block, which can increase spinal cord compression.

PREPARATION

A. Personnel

With a cooperative patient, one person can perform lumbar puncture. An assistant may be helpful in patient positioning and sample handling especially if the patient is uncooperative or frightened.

B. Equipment and Supplies

The following are usually included in preassembled trays and must be sterile:

1. Gloves
2. Iodine-containing solution for sterilizing the skin
3. Sponges
4. Drapes
5. Lidocaine (1%)
6. Syringe (5 mL)
7. Needles (22- and 25-gauge)
8. Spinal needles (preferably 22-gauge) with stylets
9. Three-way stopcock
10. Manometer
11. Collection tubes
12. Adhesive bandage

C. Positioning

The lateral decubitus position is usually used (**Figure 2-1**) with the patient lying at the edge of the bed facing away from the clinician. Have the patient maximally flex the lumbar spine to open the intervertebral spaces with the spine parallel to the bed surface and hips and shoulders aligned in the vertical plane.

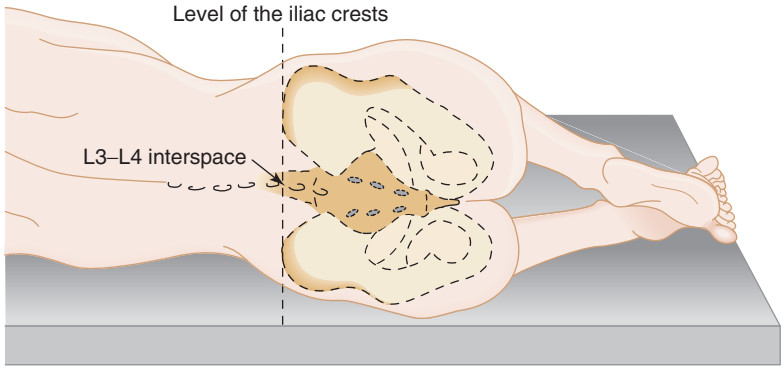
When a seated position is necessary, have the patient sit on the side of the bed, bent over a pillow on a bedside table, and reach over the bed from the opposite side to perform the procedure.

D. Site of Puncture

Most often, puncture is at the L3-L4 (level of posterior iliac crests) or L4-L5 vertebral interspace because the spinal cord (conus medullaris) terminates just above, approximately at L1-L2, in adults. Thus, with puncture below that level, there is no danger of puncturing the cord.

PROCEDURE

1. For blood and CSF glucose level comparison, draw venous blood for glucose determination. Ideally, obtain simultaneous blood and CSF samples after the patient has fasted for at least 4 hours.
2. Place necessary equipment and supplies in easy reach.
3. Wear a mask and sterile gloves.
4. Apply iodine-containing solution to sponges and wipe a wide area surrounding the interspace. Next, wipe the solution off with clean sponges.
5. Drape the area surrounding the sterile field.
6. Anesthetize the skin overlying the puncture site with lidocaine using a 5-mL syringe and a 25-gauge needle.



▲ **Figure 2-1.** Lateral decubitus position for lumbar puncture.

Next, anesthetize the underlying tissues with lidocaine using a 22-gauge needle.

7. With the stylet in place, insert the spinal needle at the midpoint of the interspace. Keep the needle parallel to the bed surface and angled slightly cephalad, or toward the umbilicus. Keep the needle bevel facing upward toward the face of the person performing the procedure.
8. Advance the needle slowly until feeling a pop from penetration of the ligamentum flavum. Withdraw the stylet to check for flow of CSF through the needle, which indicates entry into the CSF space. If no CSF appears, replace the stylet and advance the needle a short distance, continuing until CSF is present. If the needle cannot be advanced, it is likely that bone is in the way. Withdraw the needle partway, keeping it parallel to the surface of the bed, and advance it again at a slightly different angle.
9. After CSF is obtained, reinsert the stylet. Ask the patient to straighten the legs, and attach the stopcock and manometer to the needle. Turn the stopcock to allow CSF to flow into the manometer, and measure opening pressure. Pressure should fluctuate with the phases of respiration.
10. Turn the stopcock to allow CSF collection and note the appearance (clarity and color) of the fluid. Obtain as much fluid in as many tubes as needed for the tests that have been ordered. Typically, collect 1-2 mL in each of five tubes for cell count, glucose and protein determination, measurement of the CSF/serum albumin ratio (test of the blood-brain barrier) and IgG index (to exclude neuroinflammatory disorders), the Venereal Disease Research Laboratory (VDRL) test for syphilis, Gram stain, and cultures. Additional specimens may be collected for other tests, such as cryptococcal antigen, other fungal and bacterial antibody studies, polymerase chain reaction for herpes simplex virus and other viruses, oligoclonal bands (when CNS inflammation is a consideration), glutamine (if hepatic encephalopathy is suspected), biomarkers of Creutzfeldt-Jakob disease (increased 14-3-3 protein level) and Alzheimer disease (low Aβ42 and high total or phosphorylated tau), hypocretin (very low or absent in narcolepsy with cataplexy), and cytologic study. If the CSF appears bloody, obtain additional fluid so that the cell count can be repeated on the specimen in the last tube collected. Cytologic studies require at least 10 mL of CSF.
11. Replace the stopcock and manometer and record closing pressure.
12. Withdraw the needle and apply an adhesive bandage over the puncture site.
13. Previously, patients were instructed to lie prone or supine for 1-2 hours after the procedure to reduce the risk of post-lumbar puncture headache. Current evidence suggests this is unnecessary.

COMPLICATIONS

A. Unsuccessful Tap

Several conditions such as marked obesity, degenerative disease of the spine, previous spinal surgery, recent lumbar puncture, and dehydration can make lumbar puncture difficult to perform. When puncture in the lateral decubitus position is impossible, attempt the procedure with the patient in a sitting position. If the tap is again unsuccessful, have an experienced neurologist or neuroradiologist use an oblique approach, image guidance, or perform lateral cervical or cisternal puncture under image guidance.

B. Arterial or Venous Puncture

If the needle enters a blood vessel rather than the spinal subarachnoid space, withdraw the needle and use a new needle to attempt the tap at a different level. In patients with coagulopathy or taking aspirin or anticoagulants, observe carefully for signs of spinal cord compression (see Chapter 9, Motor Disorders) from spinal subdural or epidural hematoma.

C. Post-Lumbar Puncture Headache

After lumbar puncture, patients may have a mild headache that is worse in the upright position but relieved by recumbency. This will usually resolve spontaneously over hours to days. The frequency of this complication is directly related to the size of the spinal needle, but not to the volume of fluid removed. Vigorous hydration or bedrest for 1 or 2 hours after the procedure does not reduce the likelihood of headache. The headache usually responds to nonsteroidal anti-inflammatory drugs (NSAIDs) or caffeine (see Chapter 6, Headache & Facial Pain). Severe and protracted headache can be treated by an autologous blood clot patch, applied by experienced personnel. The use of an atraumatic spinal needle reduces the incidence of post-lumbar puncture headache.

ANALYSIS OF RESULTS

A. Appearance

Note the clarity and color of the CSF as it leaves the spinal needle and any changes in its appearance during the course of the procedure. CSF is normally clear and colorless. It may appear cloudy or turbid with white blood cell counts that exceed ~200/μL, but counts as low as ~50/μL may cause light scattering by the suspended cells (Tyndall effect) when the tube is held up to direct sunlight. Color can be imparted to the CSF by hemoglobin (pink), bilirubin (yellow), or rarely, melanin (black).

B. Pressure

With adults in the lateral decubitus position, lumbar CSF pressure is normally between 60 and 180-200 mm water. In children, the 90th percentile for opening pressure is 280 mm water. When lumbar puncture is performed with patients seated, they should assume a lateral decubitus posture before CSF pressure is measured. Increased CSF pressure may result from obesity, agitation, or increased intra-abdominal pressure related to position (which may be eliminated by having the patient extend the legs and straighten the back before the opening pressure is recorded). Pathologic conditions associated with the increased CSF pressure include intracranial mass lesions, meningoencephalitis, subarachnoid hemorrhage, and pseudotumor cerebri.

C. Microscopic Examination

This may be undertaken by the person who performed the lumbar puncture or in the clinical laboratory; it always includes a total and differential cell count. Gram stain for bacteria, acid-fast stain for mycobacteria, and cytologic examination for tumor cells may also be indicated. The CSF normally contains up to five mononuclear leukocytes (lymphocytes or monocytes) per microliter, no polymorphonuclear cells, and no erythrocytes unless the lumbar puncture is traumatic. Normal CSF is sterile, so that in the absence of central nervous system (CNS) infection, no organisms are observed with the above stains.

D. Bloody CSF

It is crucial to distinguish between CNS hemorrhage and a traumatic tap. If the blood clears as more fluid is withdrawn, a traumatic tap is likely. This can be confirmed by comparing red cell counts in the first and last tubes of CSF obtained; a marked decrease supports a traumatic tap.

The specimen should also be centrifuged promptly and the supernatant examined. With a traumatic lumbar puncture, the supernatant is colorless. In contrast, after CNS hemorrhage, enzymatic degradation of hemoglobin to bilirubin renders the supernatant yellow (xanthochromic). Xanthochromia may be subtle. Visual inspection requires comparison with a colorless standard (a tube of water) and is best assessed by spectrophotometric quantitation of bilirubin.

Table 2-1 outlines the time course of changes in CSF color after subarachnoid hemorrhage. Blood in the CSF after a traumatic lumbar puncture usually clears within 24 hours and does not clot, whereas after subarachnoid hemorrhage it usually persists for at least 6 days and clotting may occur. Crenation (shriveling) of red blood cells is of no diagnostic value. In addition to breakdown of hemoglobin from red blood cells, other causes of CSF xanthochromia include jaundice with serum bilirubin levels above 4-6 mg/dL, CSF protein concentrations exceeding 150 mg/dL, and rarely, the presence of carotene pigments.

White blood cells seen in the CSF early after subarachnoid hemorrhage or with traumatic lumbar puncture result from leakage of circulating whole blood. If the hematocrit and peripheral white blood cell count are within normal limits, there is ~1 white blood cell for every 1,000 red blood cells. If the peripheral white cell count is elevated, this ratio increases proportionately. In addition, for every 1,000 red blood cells present in the CSF, the CSF protein concentration increases by ~1 mg/dL.

Table 2-1. Pigmentation of the CSF After Subarachnoid Hemorrhage.

	Appearance	Maximum	Disappearance
Oxyhemoglobin (pink)	0.5-4 hours	24-35 hours	7-10 days
Bilirubin (yellow)	8-12 hours	2-4 days	2-3 weeks

PROCEDURE NOTES

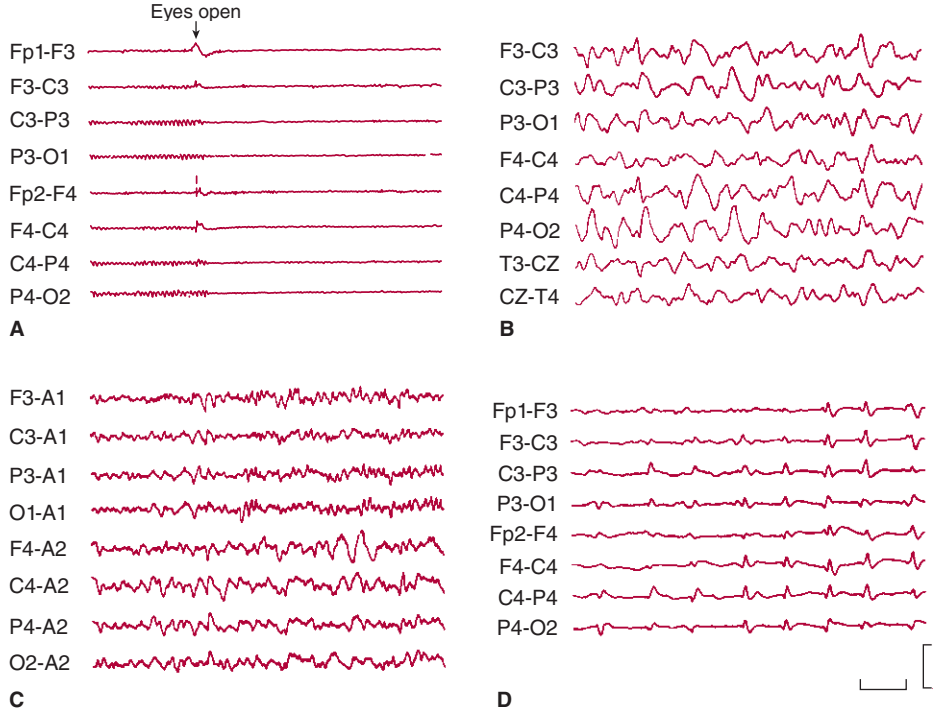
A note describing the lumbar puncture should be recorded in the patient's chart and include:

1. Date and time performed.
2. Name of person or persons performing the procedure.
3. Indication.
4. Position of patient.
5. Anesthetic used.
6. Interspace entered.
7. Opening pressure.
8. Appearance of CSF, including changes in appearance during the procedure.
9. Amount of fluid removed.
10. Closing pressure.
11. Tests ordered; for example: Tube 1 (1 mL), cell count; tube 2 (1 mL), glucose and protein levels; tube 3 (1 mL), microbiologic stains; tube 4 (1 mL), bacterial, fungal, and mycobacterial cultures.
12. Results of any studies, such as microbiologic stains, performed by the operator.
13. Complications, if any.

ELECTROPHYSIOLOGIC STUDIES

ELECTROENCEPHALOGRAPHY

Electrodes placed on the scalp record the electrical activity of the brain. Electroencephalography (EEG) is easy to perform, relatively inexpensive, and helpful in several different clinical contexts (**Figure 2-2**).



▲ **Figure 2-2.** (**A**) Normal EEG with a posteriorly situated 9-Hz alpha rhythm that attenuates with eye opening. (**B**) Abnormal EEG showing irregular diffuse slow activity in an obtunded patient with encephalitis. (**C**) Irregular slow activity in the right central region, on a diffusely slowed background, in a patient with a right parietal glioma. (**D**) Periodic complexes occurring once every second in a patient with Creutzfeldt–Jakob disease. Horizontal calibration: 1 s; vertical calibration: 200 μV in A panel, 300 μV in other panels. Electrode placements are indicated at the left of each panel and are as follows. A, earlobe; C, central; F, frontal; Fp, frontal polar; P, parietal; T, temporal; O, occipital. Right-sided placements are indicated by even numbers, left-sided placements by odd numbers, and midline placements by Z. (Reproduced with permission from Aminoff MJ. *Aminoff's Electrodiagnosis in Clinical Neurology*. 6th ed. St. Louis, MO: Elsevier/Saunders; 2012.)

EVALUATION OF SUSPECTED EPILEPSY

The EEG is useful in evaluating patients with suspected epilepsy. The presence of electrographic seizure activity (abnormal, rhythmic electrocerebral activity of abrupt onset and termination and showing an evolving pattern) during a behavioral disturbance of uncertain nature establishes the diagnosis beyond doubt. It is often not possible to obtain an EEG during a seizure, because these occur unpredictably. However, the EEG may be abnormal interictally (at times when the patient is not experiencing clinical attacks) and is therefore still useful diagnostically. The interictal presence of epileptiform activity (abnormal paroxysmal activity containing some spike discharges) is helpful. Such activity occurs occasionally in patients who have never had a seizure, but its prevalence is greater in patients with epilepsy than in normal subjects. Epileptiform activity in the EEG of a patient with episodic behavioral disturbances that could represent seizures on clinical grounds markedly increases the likelihood that attacks are indeed epileptic, thus supporting the clinical diagnosis.

CLASSIFICATION OF SEIZURE DISORDERS

The EEG findings may help in classifying a seizure disorder and thus in selecting appropriate anticonvulsant medication. For example, in patients with the typical absence of petit mal epilepsy (see Chapter 12, Seizures & Syncope), the EEG is characterized both ictally and interictally by episodic generalized spike-wave activity (see Figure 12-3). By contrast, with episodes of impaired external awareness caused by focal seizures, it may be normal or show focal epileptiform discharges interictally. During seizures, abnormal rhythmic activity of variable frequency may occur with a localized or generalized distribution, but sometimes there are no electrographic correlates. A focal or lateralized epileptogenic source is of particular importance if surgical treatment is under consideration.

ASSESSMENT & PROGNOSIS OF SEIZURES

The EEG may guide prognosis and has been used to follow the course of seizure disorders. A normal EEG implies a more favorable prognosis for seizure control, whereas an abnormal background or profuse epileptiform activity implies a poor prognosis. The EEG findings do not, however, provide a reliable guide to the subsequent development of seizures in patients with head injuries, stroke, or brain tumors. EEG findings are sometimes used to determine whether anticonvulsant medication can be discontinued in patients after a seizure-free interval of several years. Although patients with a normal EEG are more likely to be weaned successfully, such findings provide only a general guide, and patients with a normal EEG can have further seizures after withdrawal of antiepileptic medication. Conversely, no further seizures may occur despite a continuing EEG disturbance.

MANAGEMENT OF STATUS EPILEPTICUS

The EEG is of little help in managing tonic–clonic status epilepticus unless patients have received neuromuscular blocking agents and are in a coma induced by medication. The EEG is then useful in indicating the level of anesthesia and determining whether seizures are continuing. Status is characterized by repeated electrographic seizures or continuous epileptiform (spike-wave) activity. Nonconvulsive status may follow control of convulsive status. In nonconvulsive status epilepticus, the EEG findings provide the only means of making the diagnosis with confidence and in distinguishing the two main types. In absence status epilepticus, continuous spike-wave activity is seen, whereas in focal status, repetitive electrographic seizures are found.

DIAGNOSIS OF OTHER NEUROLOGIC DISORDERS

Certain neurologic disorders produce characteristic but nonspecific EEG abnormalities that help in suggesting, establishing, or supporting the diagnosis. In patients with an acute disturbance of cerebral function, for example, repetitive slow-wave complexes over one or both temporal lobes suggest a diagnosis of herpes simplex encephalitis. Similarly, the presence of periodic complexes in a patient with an acute dementing disorder suggests Creutzfeldt-Jakob disease, subacute sclerosing panencephalitis, or toxicity from lithium, baclofen, or bismuth.

EVALUATION OF ALTERED CONSCIOUSNESS

The EEG slows as consciousness is depressed, depending in part on the underlying etiology. The presence of electrographic seizure activity suggests diagnostic possibilities (eg, nonconvulsive status epilepticus) that might otherwise be overlooked. Serial records permit the prognosis and course to be followed. The EEG response to external stimulation is an important diagnostic and prognostic guide. Electrocerebral responsiveness implies a lighter level of coma. Electrocerebral silence in a technically adequate record implies neocortical death in the absence of hypothermia or drug overdose. In some seemingly comatose patients, consciousness is, in fact, preserved. Although there is quadriplegia and a supranuclear paralysis of the facial and bulbar muscles, the EEG is usually normal and helps in indicating the diagnosis of locked-in syndrome.

MAGNETOENCEPHALOGRAPHY

The magnetic field of electrocerebral activity can be recorded with specialized equipment. The magnetoencephalogram (MEG) is more sensitive than the EEG to activity arising in the cortical sulci, whereas the EEG best detects activity arising at the cortical surface. The MEG has

better spatial resolution and can localize activity with more accuracy than the EEG. It is used for localizing abnormal cerebral activity in epilepsy and in localizing the central fissure preoperatively in patients with epilepsy or brain tumors when surgery is planned.

EVOKED POTENTIALS

Noninvasive stimulation of certain afferent pathways elicits spinal or cerebral potentials, which can be used to monitor the functional integrity of these pathways but do not indicate the cause of any lesion involving them. The responses are very small compared with the background EEG activity (noise), which has no relationship to the time of stimulation. The responses to a number of stimuli are therefore recorded and averaged with a computer to eliminate the random noise.

TYPES OF EVOKED POTENTIALS

A. Visual

Monocular visual stimulation with a checkerboard pattern elicits visual evoked potentials, which are recorded from the midoccipital region of the scalp. The most clinically relevant component is the P100 response, a positive peak with a latency of ~100 msec. The presence and latency of the response are noted. Although its amplitude can also be measured, alterations in amplitude are far less helpful in recognizing pathology.

B. Auditory

Monaural stimulation with repetitive clicks elicits brainstem auditory evoked potentials, which are recorded at the vertex of the scalp. A series of potentials are evoked in the first 10 msec after the auditory stimulus; these represent the sequential activation of various structures in the subcortical auditory pathway. For clinical purposes, attention is directed at the presence, latency, and interpeak intervals of the first five positive potentials.

C. Somatosensory

Electrical stimulation of a peripheral nerve is used to elicit somatosensory evoked potentials, which are recorded over the scalp and spine. Their configuration and latency depend on the nerve that is stimulated.

INDICATIONS FOR USE

A. Detection of Lesions in Multiple Sclerosis

Evoked potentials can detect and localize lesions in the CNS. This is particularly important in multiple sclerosis, where the diagnosis depends on detecting multifocal CNS lesions. When patients have clinical evidence of only a single lesion, electrophysiologic recognition of abnormalities in other sites helps to establish the diagnosis. When patients with suspected multiple sclerosis present with ill-defined complaints, electrophysiologic abnormalities in the appropriate afferent pathways indicate the organic basis of the symptoms. Although magnetic resonance imaging (MRI) is more useful for detecting lesions, it complements evoked potential studies rather than substituting for them. Evoked potential studies monitor the function rather than anatomic integrity of the afferent pathways and can sometimes reveal abnormalities not detected by MRI (and the reverse also holds true). They also cost less than MRI. In patients with established multiple sclerosis, the evoked potential findings are sometimes used to follow the course of the disorder or its response to treatment, but their value in this regard is unclear.

B. Detection of Lesions in Other CNS Disorders

Evoked potential abnormalities occur in disorders other than multiple sclerosis; multimodal evoked potential abnormalities may be encountered in certain spinocerebellar degenerations, familial spastic paraplegia, Lyme disease, acquired immunodeficiency syndrome (AIDS), neurosyphilis, and vitamin E or B_{12} deficiency. Their diagnostic value therefore depends on the context in which they are found. Although the findings may permit lesions to be localized within broad areas of the CNS, precise localization may not be possible because the generators of many components are unknown.

C. Assessment and Prognosis After CNS Trauma or Hypoxia

In posttraumatic or postanoxic coma, bilateral absence of cortically generated components of the somatosensory evoked potential implies that cognition will not recover; the prognosis is more optimistic when cortical responses are present on one or both sides. Such studies may be particularly useful in patients with suspected brain death. Somatosensory evoked potentials have also been used to determine the completeness of a traumatic spinal cord lesion; the presence or early return of a response after stimulation of a nerve below the level of the cord injury indicates that the lesion is incomplete and thus suggests a better prognosis than otherwise.

D. Intraoperative Monitoring

The functional integrity of certain neural structures may be monitored by evoked potentials during operative procedures to permit the early recognition of any dysfunction and thereby minimize damage. When the dysfunction relates to a surgical maneuver, it may be possible to prevent or diminish any permanent neurologic deficit by reversing the maneuver.

E. Evaluation of Visual or Auditory Acuity

Visual and auditory acuity may be evaluated by evoked potential studies in patients unable to cooperate with behavioral testing because of age or abnormal mental state.

ELECTROMYOGRAPHY & NERVE CONDUCTION STUDIES

ELECTROMYOGRAPHY

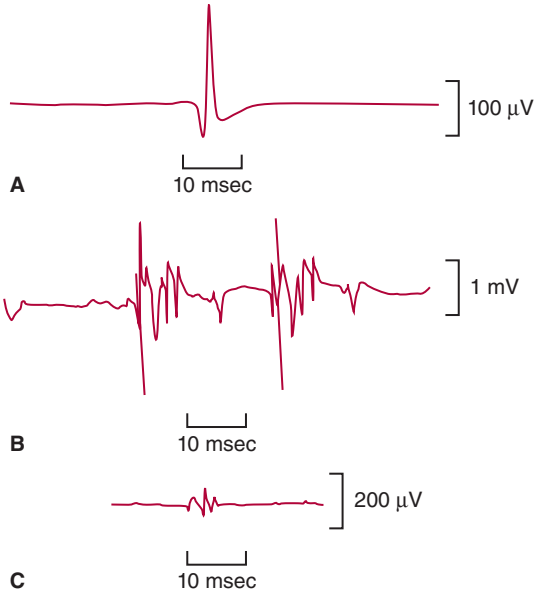
The electrical activity within a discrete region of an accessible muscle can be recorded by inserting a needle electrode into it. The pattern of electrical activity in muscle (**electromyogram** or **EMG**) both at rest and during activity has been characterized, and abnormalities have been correlated with disorders at different levels of the motor unit.

A. Activity at Rest

Spontaneous electrical activity is not present in relaxed normal muscle except in the end-plate region where neuromuscular junctions are located, but various types of abnormal activity occur spontaneously in diseased muscle. **Fibrillation potentials** and **positive sharp waves** (which reflect muscle fiber irritability) are typically—but not always—found in denervated muscle. They are sometimes also found in myopathic disorders, especially inflammatory disorders such as polymyositis. Although **fasciculation potentials**, which reflect the spontaneous activation of individual motor units, are occasionally encountered in normal muscle, they are characteristic of neuropathic disorders, especially those with primary involvement of anterior horn cells (eg, amyotrophic lateral sclerosis). **Myotonic discharges** (high-frequency discharges of potentials from muscle fibers that wax and wane in amplitude and frequency) are found most commonly in disorders such as myotonic dystrophy or myotonia congenita and occasionally in polymyositis or other, rarer disorders. Other types of abnormal spontaneous activity also occur.

B. Activity During Voluntary Muscle Contraction

A slight voluntary contraction of a muscle activates a small number of motor units. The potentials generated by the muscle fibers of individual units within the detection range of the needle electrode can be recorded. Normal motor-unit potentials have clearly defined limits of duration, amplitude, configuration, and firing rates. These limits depend on the muscle under study. In many **myopathic disorders**, there is an increased incidence of small, short-duration, polyphasic motor units in affected muscles, and an excessive number of units may be activated for a specified degree of voluntary activity. In **neuropathic disorders**, motor units are lost; the number of units activated during a maximal contraction is therefore reduced, and units fire faster than normal. In addition, the configuration and dimensions of the potentials may be abnormal, depending on the acuteness of the neuropathic process and on whether reinnervation is occurring (**Figure 2-3**). Variations in the configuration and size of individual motor-unit potentials are characteristic of **disorders of neuromuscular transmission**.



▲ **Figure 2-3.** Motor unit action potentials recorded with a concentric needle electrode. (**A**) Normal potential. (**B**) Long-duration polyphasic potential (shown twice). (**C**) Short-duration, low-amplitude polyphasic potential. (Reproduced with permission from Aminoff MJ. *Electromyography in Clinical Practice*. 3rd ed. New York, NY: Churchill Livingstone; 1998.)

C. Clinical Utility

Lesions can involve the neural or muscle component of the motor unit, or the neuromuscular junction. When the neural component is affected, the pathologic process can be at the level of the anterior horn cells or at some point along the length of the axon as it traverses a nerve root, limb plexus, and peripheral nerve before branching into its terminal arborizations. Electromyography can detect disorders of the motor units and can indicate the site of the underlying lesion. Neuromuscular disorders can be recognized when clinical examination is unrewarding because the disease is mild or because poor cooperation by the patient or the presence of other symptoms such as pain

makes clinical evaluation difficult. The electromyographic findings do not, of themselves, permit an etiologic diagnosis to be reached, and they must be correlated with the clinical findings and the results of other laboratory studies.

The electromyographic findings may provide a guide to prognosis. For example, in an acute disorder of a peripheral or cranial nerve, electromyographic evidence of denervation implies a poorer prognosis for recovery than otherwise.

In contrast to needle electromyography, the clinical utility of surface-recorded electromyography is not established.

NERVE CONDUCTION STUDIES

A. Motor Nerve Conduction Studies

The electrical response of a muscle is recorded to stimulation of its motor nerve at two or more points along its course (**Figure 2-4**). This permits conduction velocity to be determined in the fastest-conducting motor fibers between the points of stimulation.

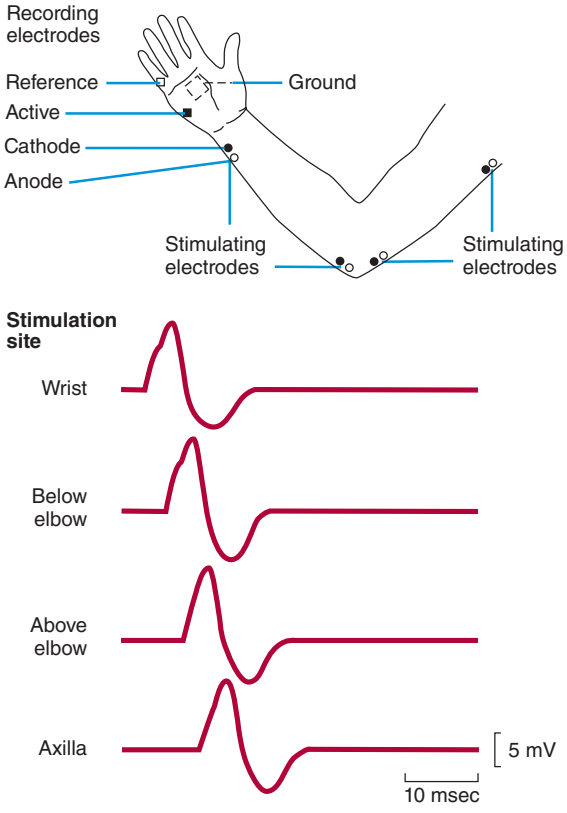
B. Sensory Nerve Conduction Studies

The conduction velocity and amplitude of action potentials in sensory fibers can be determined when these fibers are stimulated at one point and their responses are recorded at another point along the course of the nerve.

C. Indications for Use

Nerve conduction studies can confirm the presence and extent of peripheral nerve damage. They are particularly helpful when clinical examination is difficult (eg, in children). Nerve conduction studies are useful in the following contexts:

1. Determining whether sensory symptoms are caused by a lesion proximal or distal to the dorsal root ganglia (in the latter case, sensory conduction studies of the involved fibers will be abnormal) and whether neuromuscular dysfunction is due to peripheral nerve disease.
2. Detecting subclinical involvement of other peripheral nerves in patients with a mononeuropathy.
3. Determining the site of a focal lesion and providing a guide to prognosis in patients with a mononeuropathy.
4. Distinguishing between a polyneuropathy and a mononeuropathy multiplex. This is important because the causes of these conditions differ.
5. Clarifying the extent to which disabilities in patients with polyneuropathy relate to superimposed compressive focal neuropathies, which are common complications.
6. Following the progression of peripheral nerve disorders and their response to treatment.



▲ **Figure 2-4.** Arrangement for motor conduction studies of the ulnar nerve. Responses of the abductor digiti minimi to supramaximal stimulation of the nerve at different sites are recorded with a surface electrode. (Reproduced with permission from Aminoff MJ. *Electromyography in Clinical Practice*. 3rd ed. New York, NY: Churchill Livingstone; 1998.)

7. Indicating the predominant pathologic changes in peripheral nerve disorders. In demyelinating neuropathies, conduction velocity is often markedly slowed and conduction block may occur; in axonal neuropathies, conduction velocity is usually normal or slowed only mildly, sensory nerve action potentials are small or absent, and electromyography shows evidence of denervation in affected muscles.
8. Detecting subclinical hereditary disorders of the peripheral nerves in genetic and epidemiologic studies.

F-RESPONSE STUDIES

Stimulation of a motor nerve causes impulses to travel **antidromically** (toward the spinal cord) as well as **orthodromically** (toward the nerve terminals) and leads a few

anterior horn cells to discharge. This produces a small motor response (the F wave) considerably later than the direct muscle response elicited by nerve stimulation. The F wave is sometimes abnormal with lesions of the proximal portions of the peripheral nervous system, such as the nerve roots. F-wave studies may be helpful in detecting abnormalities when conventional nerve conduction studies are normal.

REPETITIVE NERVE STIMULATION

DESCRIPTION

The size of the electrical response of a muscle to supramaximal electrical stimulation of its motor nerve correlates with the number of activated muscle fibers. Neuromuscular transmission is tested by recording (with surface electrodes) the response of a muscle to supramaximal stimulation of its motor nerve either repetitively or by single shocks or trains of shocks at selected intervals after a maximal voluntary contraction.

NORMAL RESPONSE

In normal subjects, little or no change occurs in the size of the compound muscle action potential after repetitive stimulation of a motor nerve at 10 Hz or less or with a single stimulus or a train of stimuli delivered at intervals after a 10-second voluntary muscle contraction. Preceding activity in the junctional region influences the amount of acetylcholine released and thus the size of the end-plate potentials elicited by the stimuli. Although the amount of acetylcholine released is increased briefly after maximal voluntary activity and is then reduced, normally more acetylcholine is released than is necessary to bring the motor end-plate potentials to the threshold for generating muscle-fiber action potentials.

RESPONSE IN DISORDERS OF NEUROMUSCULAR TRANSMISSION

A. Myasthenia Gravis

In myasthenia gravis, the reduced release of acetylcholine that follows repetitive firing of the motor neuron prevents compensation for the depleted postsynaptic acetylcholine receptors at the neuromuscular junction. Accordingly, repetitive stimulation, particularly between 2 and 5 Hz, may lead to depressed neuromuscular transmission, with a **decrement** in the compound muscle action potential recorded from an affected muscle. Similarly, an electrical stimulus of the motor nerve immediately after a 10-second period of maximal voluntary activity may elicit a muscle response that is slightly larger than before, indicating that more muscle fibers are responding. This postactivation facilitation of neuromuscular transmission is followed by a longer depression that is maximal from 2-4 minutes after the conditioning period and lasts up to 10 minutes or so. During this period, the compound muscle action potential is reduced in size.

Decrementing responses to repetitive stimulation at 2-5 Hz can also occur in congenital myasthenic syndromes.

B. Myasthenic Syndrome and Botulism

In Lambert–Eaton myasthenic syndrome, defective release of acetylcholine at the neuromuscular junction leads to a very small compound muscle action potential elicited by a single stimulus. With repetitive stimulation at rates of up to 10 Hz, the first few responses may decline in size, but subsequent responses increase, and their amplitude is eventually several times larger than the initial response. Patients with botulism exhibit a similar response to repetitive stimulation but the findings are somewhat more variable, and not all muscles are affected. **Incremental responses** in Lambert–Eaton syndrome and botulism are more conspicuous with high rates of stimulation and may result from the facilitation of acetylcholine release by the progressive accumulation of calcium in the motor nerve terminal.

TESTS OF AUTONOMIC FUNCTION

Autonomic and small-fiber function tests evaluate the control of heart rate, blood pressure, and sweating. Both sympathetic and parasympathetic pathways are assessed. Five simple noninvasive tests of cardiovascular reflexes may be adequate for assessing diabetic (and presumably other) autonomic neuropathies: the heart rate responses to (1) the Valsalva maneuver, (2) standing, and (3) deep breathing; and the blood pressure responses to (4) standing and (5) sustained handgrip. Definite autonomic neuropathy is indicated by an abnormality in two or more tests. Sweating is tested separately. In the thermoregulatory sweat test, the patient is warmed with a radiant heat cradle to increase body temperature by 1°C while the skin is covered with a powder that changes color when moist. This permits the presence and distribution of sweating to be characterized. The sympathetic skin response, that is, the change in voltage at the skin surface following a single electrical stimulus, also can be recorded. This depends on the electrical activity arising from sweat glands and on the reduced electrical resistance of the skin with sweating. Quantitative sudomotor axon reflex testing (QSART) assesses postganglionic sympathetic function quantitatively but requires sophisticated and expensive equipment.

POLYSOMNOGRAPHY

DESCRIPTION

The investigation of sleep disorders requires the recording during sleep and wakefulness of multiple physiologic variables, typically EEG and submental EMG activity, eye movements, respiratory activity, nasal or oral airflow, oxygen saturation, and electrocardiogram activity; a video recording is also made of the patient. Other variables, such as penile tumescence, may be measured depending on the reason for the study.

INDICATIONS FOR USE

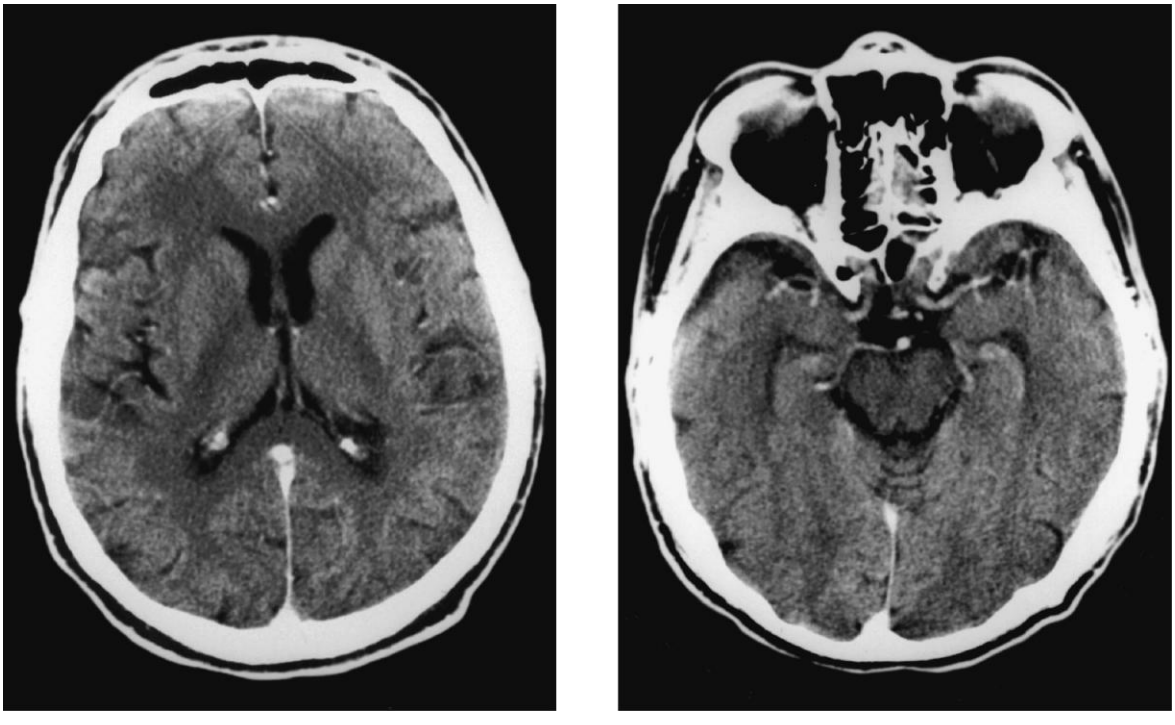
1. Diagnosis of sleep-related breathing disorders and their response to various therapeutic maneuvers.
2. Evaluation and diagnosis of patients with suspected narcolepsy. Multiple sleep latency testing is also required, evaluates the time required to fall asleep, and consists of five nap opportunities at 2-hour intervals.
3. Evaluation of periodic limb movements of sleep.
4. Evaluation of insomnia or hypersomnia of uncertain cause.
5. Evaluation of sleep-related symptoms in patients with epilepsy or neuromuscular disorders.
6. Evaluation of organic causes of erectile dysfunction.

CRANIAL IMAGING STUDIES

COMPUTED TOMOGRAPHY

DESCRIPTION

Computed tomographic (**CT**) scanning is a noninvasive, computer-assisted, radiologic means of examining anatomic structures (**Figure 2-5**). It detects structural intracranial abnormalities with precision, speed, and facility. It is thus of particular use in evaluating patients with acute neurologic disorders or focal neurologic deficits in whom a structural lesion is suspected, and patients with suspected stroke or head injuries. Intravenous administration of an iodinated contrast agent improves the detection and definition of vascular lesions and those associated with a disturbance of the blood–brain barrier. Contrast-enhanced scans provide more information than unenhanced scans in patients with known or suspected primary or secondary



▲ **Figure 2-5.** Contrast-enhanced CT brain scans from a 62-year-old man, showing the normal anatomy. Images are at the level of the lateral ventricles (left) and midbrain (right) (same patient as in Figure 2-6).

brain tumors, arteriovenous malformations (AVMs), aneurysms, cerebral abscesses, chronic isodense subdural hematomas, or infarctions. Because the contrast agents may affect the kidneys adversely, they should be used with discrimination. Other adverse effects of the contrast agents in common use are pain, nausea, thermal sensations, and rare anaphylactoid reactions that include bronchospasm and death.

INDICATIONS FOR USE

A. Stroke

Noncontrast CT is the standard imaging procedure for patients presenting with a suspected acute ischemic episode. CT scan can distinguish infarction from intracranial hemorrhage; it is particularly sensitive in detecting intracerebral hematomas (see Figure 13-20), the location of which may provide a guide to their cause. CT scan occasionally demonstrates a nonvascular cause of the patient's clinical deficit, such as a tumor or abscess.

B. Tumor

CT scans can indicate the site of a brain tumor, the extent of any surrounding edema, whether the lesion is cystic or solid, and whether it has displaced midline or other normal anatomic structures. It also demonstrates any acute hemorrhagic component. Magnetic resonance imaging (discussed later) is, however, the preferred method for the detection and characterization of cerebral neoplasms.

C. Trauma

CT scans are important for detecting traumatic intracranial (epidural, subdural, subarachnoid, or intracerebral) hemorrhage and bony injuries. They also provide a more precise delineation of associated fractures than do plain x-rays.

D. Dementia

CT scanning may indicate the presence of a tumor or hydrocephalus (enlarged ventricles), with or without accompanying cerebral atrophy. The occurrence of hydrocephalus without cerebral atrophy in demented patients suggests normal pressure or communicating hydrocephalus. Cerebral atrophy (ie, enlarged ventricles and sulci) can occur in demented or normal elderly subjects.

E. Subarachnoid Hemorrhage

In patients with subarachnoid hemorrhage, the CT scan indicates the presence of blood in the subarachnoid space and may even suggest the source of the bleeding (see Figure 6-5). If the CT scan findings are normal despite clinical findings suggestive of subarachnoid hemorrhage, the CSF should be examined to exclude hemorrhage or meningitis. CT angiography (see later) may demonstrate an underlying vascular malformation or aneurysm.

MAGNETIC RESONANCE IMAGING

DESCRIPTION

MRI involves no ionizing radiation. The patient lies within a large magnet that aligns some of the hydrogen protons in the body along the magnet's axis. The protons resonate when stimulated with radiofrequency energy, producing a signal that is dependent on the concentration of mobile hydrogen nuclei (or nuclear-spin density) and the tissues in which they reside. The position and intensity of these radiofrequency emissions are recorded and mapped by a computer. Spin–lattice (T1) and spin–spin (T2) relaxation times are mainly responsible for the relative differences in signal intensity of the various soft tissues; these parameters are sensitive to the state of water in biologic tissues. Pulse sequences with varying dependence on T1 and T2 selectively alter the contrast between soft tissues (**Figure 2-6**).

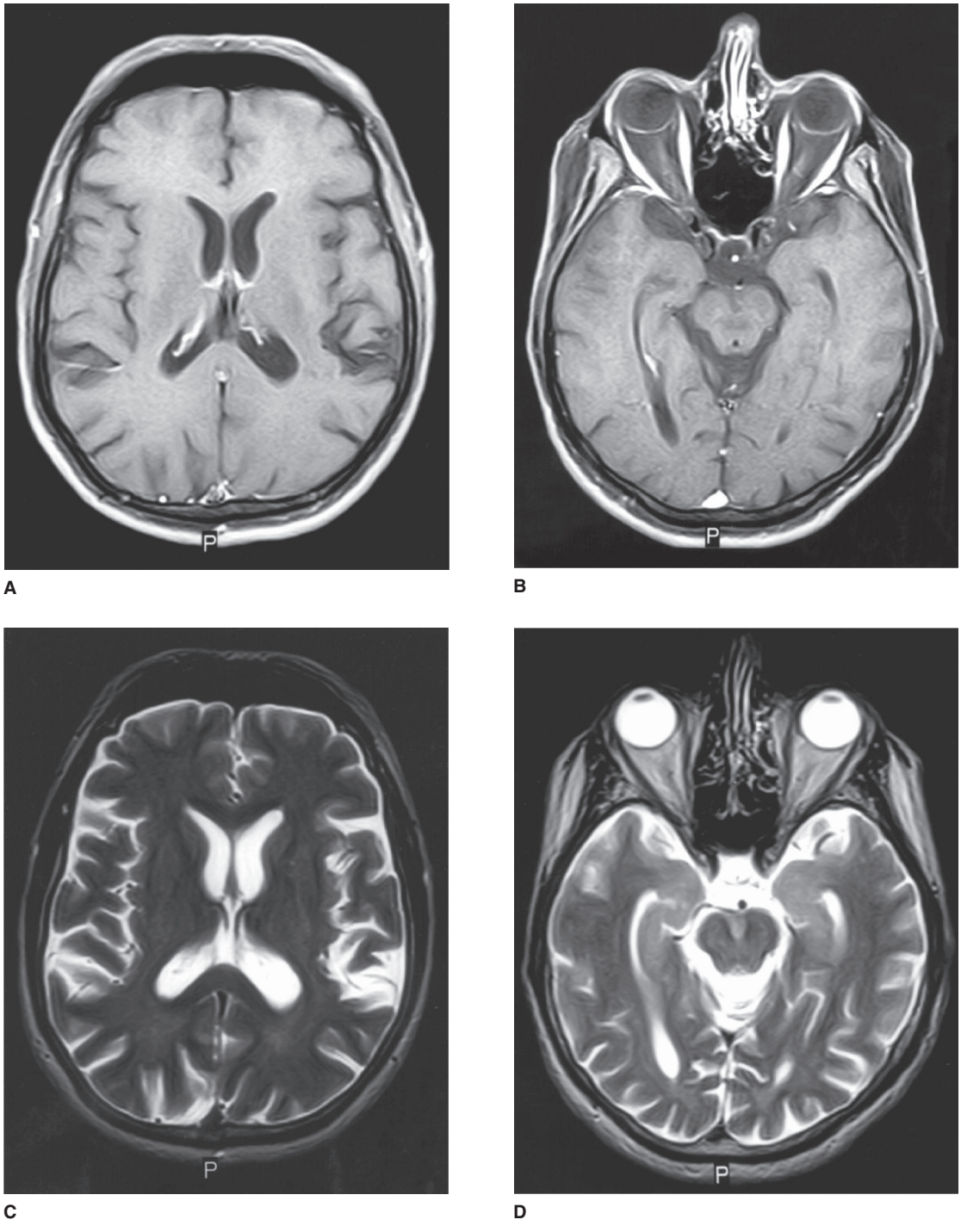
The soft-tissue contrast available with MRI makes it more sensitive than CT scanning in detecting certain structural lesions. MRI provides better contrast than CT scans between the gray and white matter of the brain. It is superior for visualizing abnormalities in the posterior fossa and spinal cord, for subacute and chronic hemorrhage, and for detecting lesions associated with multiple sclerosis or those that cause seizures. In addition to its greater sensitivity, it is also free of bony artifact and permits multiplanar (axial, sagittal, and coronal) imaging with no need to manipulate the position of the patient. Because there are no known hazardous effects, MRI studies can be repeated in a serial manner if necessary. Occasional patients cannot tolerate the procedure without sedation because of claustrophobia or cannot safely enter the magnet because of implanted ferromagnetic devices.

Gadopentetate dimeglumine (gadolinium-DPTA) is an effective MRI contrast agent that is stable and well-tolerated intravenously. It is useful in identifying small tumors that, because their relaxation times are similar to those of normal cerebral tissue, may be isointense on unenhanced MRI. It also helps to separate solid tumor from surrounding edema, identify leptomeningeal disease, and provide information about the blood–brain barrier. Gadolinium has been associated with nephrogenic systemic fibrosis in patients with renal insufficiency, so it should be used judiciously in this setting.

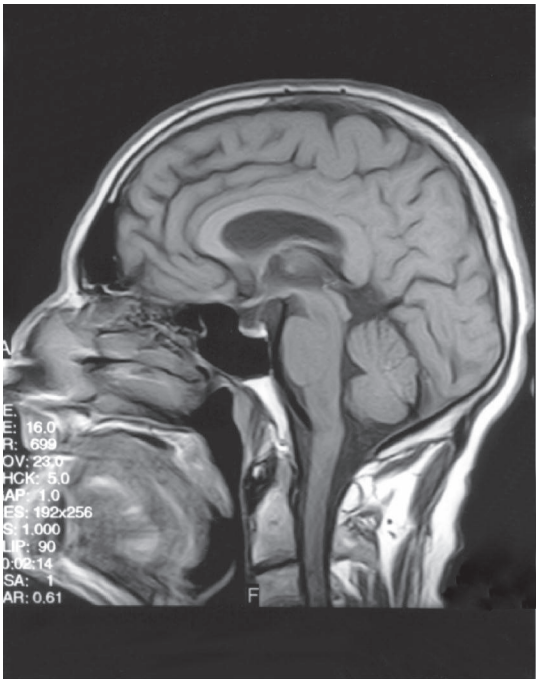
INDICATIONS FOR USE & COMPARISON WITH CT SCAN

A. Stroke

Within a few hours of vascular occlusion, cerebral infarcts may be detected by MRI. Breakdown in the blood–brain barrier (several hours after onset of cerebral ischemia) permits



▲ **Figure 2-6.** Brain MR images from a 62-year-old man, showing the normal anatomy. (**A** and **B**) Gadolinium-enhanced T1-weighted (CSF dark) images; (**C** and **D**) T2-weighted (CSF white) images. Images are at the level of the lateral ventricles (**A** and **C**) and midbrain (**B** and **D**).



E

▲ **Figure 2-6.** (*Continued*) A midsagittal T1-weighted image is shown in (**E**). Brain images are from the same patient as in Figure 2-5.

the intravascular content to be extravasated into the extracellular space. This can be detected by T2-weighted imaging and **fluid-attenuated inversion-recovery (FLAIR)** sequences. Diffusion-weighted MRI also has an important role in the early assessment of stroke, as is discussed later, whereas CT scans may be unrevealing for up to 48 hours. Thereafter, the advantage of MRI over CT scanning lessens, except that MRI detects smaller lesions and provides superior imaging of the posterior fossa.

Nevertheless, to determine quickly whether hemorrhage has occurred, CT scanning without contrast is usually the preferred initial study in acute stroke. Hematomas of >2-3 days' duration, however, are better visualized by MRI. Although MRI can detect and localize vascular malformations, angiography is necessary to define their anatomic features and plan effective treatment. In cases of unexplained hematoma, a follow-up MRI obtained 3 months later may reveal the underlying cause, which is sometimes unmasked as the hematoma resolves.

B. Tumor

Both CT scans and MRI are useful in detecting brain tumors. MRI is the preferred technique because of its greater soft tissue sensitivity, the absence of bone artifacts at the vertex or in the posterior fossa, and the ability to employ advanced imaging techniques such as MR spectroscopy and diffusion and perfusion imaging that better characterize a lesion. MRI or CT scan may detect secondary effects of tumors, such as cerebral herniation, but MRI provides more detailed and sensitive anatomic information. Neither technique, however, can determine the type of a tumor with certainty.

C. Trauma

In the acute phase after head injury, CT scan is preferable to MRI because it requires less time, is superior for detecting intracranial hemorrhage, and may reveal bony injuries. Similarly, spinal MRI should not be used in the initial evaluation of patients with spinal injuries because nondisplaced fractures are often not visualized. For follow-up purposes, however, MRI is helpful for detecting parenchymal pathology of the brain or spinal cord.

D. Dementia

In patients with dementia, either CT scan or MRI can help in demonstrating treatable structural causes, but MRI is more sensitive in demonstrating abnormal white matter signal and associated atrophy.

E. Multiple Sclerosis

Lesions in the cerebral white matter or the cervical cord are best detected by MRI, as lesions may not be visualized on CT scans. The lesions on MRI may have signal characteristics resembling those of ischemic changes, however, and clinical correlation is therefore always necessary. Gadolinium-enhanced MRI permits lesions of different ages to be distinguished. This ability facilitates the diagnosis of multiple sclerosis: The presence of lesions of different ages suggests a multiphasic disease, whereas lesions of similar age suggest a monophasic disorder, such as acute disseminated encephalomyelitis.

F. Infections

MRI is sensitive in detecting white matter edema and probably permits earlier recognition of focal areas of cerebritis and abscess formation than CT scan. Diffusion MR imaging is particularly helpful in detecting areas of reduced diffusion, typical of purulent abscess and encephalitis.

CONTRAINDICATIONS

MRI is contraindicated by the presence of intracranial ferromagnetic aneurysm clips, metallic foreign bodies in the eye, demand-mode pacemakers, and cochlear implants. Many implanted devices are also contraindications for MRI. Patients requiring close monitoring are probably best

studied by CT if possible. Furthermore, MRI is difficult in patients with claustrophobia, extreme obesity, uncontrolled movement disorders, or respiratory disorders that require assisted ventilation or carry any risk of apnea. Advances in MRI-compatible mechanical ventilators, pacemakers, and monitoring equipment, however, now allow many critically ill patients to be scanned safely.

DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING

This technique, in which contrast within the image is based on the microscopic motion of water protons in tissue, provides information that is not available on standard MRI or CT. It is particularly important in the assessment of stroke because it can discriminate cytotoxic edema (which occurs in strokes) from vasogenic edema (found with other types of cerebral lesion) and thus reveals cerebral ischemia early and with high specificity. Diffusion-weighted MRI permits reliable identification of acute cerebral ischemia during the first few hours after onset, before it is detectable on standard MRI. This is important because it reveals the true volume of infarcts prior to treatment with thrombolytic agents. However, because diffusion-weighted imaging will be positive in the setting of cytotoxic edema of any cause (eg, brain abscess, highly cellular tumors), clinical correlation is always required. When more than one infarct is found on routine MRI, diffusion-weighted imaging permits the discrimination of acute from older infarcts by the relative increase in signal intensity of the former.

DIFFUSION TENSOR MAGNETIC RESONANCE IMAGING

This technique produces neural tract images by measuring the anisotropic motion of water in tissue. It is important in determining the severity and extent of cerebral involvement after head injury, localizing brain tumors, and planning surgical procedures. White matter pathways and alterations may be detected that are not seen on conventional MRI.

PERFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING

Blood flow through the brain may be measured using either an injected contrast medium (eg, gadolinium) or an endogenous technique (arterial spin labeling, in which the patient's own blood provides the contrast). Cerebral blood-flow abnormalities can be recognized, and the early reperfusion of tissues after treatment can be confirmed. Cerebral ischemia may be detected very soon after clinical onset. Comparison of the findings from diffusion-weighted and perfusion-weighted MRI may have a prognostic role and is currently under study. The distinction of reversible from irreversible ischemic damage is important in this regard. Perfusion-weighted imaging also contributes in distinguishing between various types of brain tumors such as gliomas and metastases.

SUSCEPTIBILITY-WEIGHTED MAGNETIC RESONANCE IMAGING

Susceptibility-weighted MRI is a gradient echo technique that is exquisitely sensitive to alterations in local magnetic field generated by blood, calcium, and air. It has become a routine sequence in most MRI protocols, and is used to detect macro- and microhemorrhages typical of amyloid, hemorrhagic metastases, superficial siderosis, traumatic brain injury, and thrombosed vessels. It is also sensitive to deoxyhemoglobin, which exists primarily in normal venous structures, but also in slow flowing arterial vessels distal to emboli.

POSITRON EMISSION TOMOGRAPHY

Positron emission tomography (PET) is an imaging technique that uses positron-emitting radiopharmaceuticals, such as ^{18}F-fluoro-2-deoxy-D-glucose or ^{18}F-L-dopa, to map brain biochemistry and physiology. PET thus complements other imaging methods that provide primarily anatomic information, such as CT scan and MRI, and may demonstrate functional brain abnormalities before structural abnormalities are detectable. PET has proved useful in several clinical settings and is now combined with CT or MR scanners in hybrid machines. When patients with medically refractory epilepsy are being considered for surgical treatment, PET CT scan can identify focal areas of hypometabolism in the temporal lobe as likely sites of the origin of seizures. PET can also be useful in the differential diagnosis of dementia, because common dementing disorders such as Alzheimer disease and frontotemporal dementia exhibit different patterns of abnormal cerebral metabolism. In vivo imaging of amyloid-β (Aβ) with PET facilitates the early diagnosis of Alzheimer disease and provides prognostic information for patients with mild cognitive impairment. PET can help distinguish between clinically similar movement disorders, such as Parkinson disease and progressive supranuclear palsy, and can provide confirmatory evidence of early Huntington disease. It may also be of value in grading gliomas, selecting tumor biopsy sites, and distinguishing recurrent tumors from radiation-induced brain necrosis. It has been an important tool with which to investigate the functional involvement of different cerebral areas in behavioral and cognitive tasks and is used frequently in patients with suspected metastatic disease. However, PET is more expensive than MR or CT alone and requires administration of radioactive isotopes, thus exposing subjects to radiation.

SINGLE-PHOTON EMISSION COMPUTED TOMOGRAPHY

In single-photon emission computed tomography (SPECT), chemicals containing isotopes that emit single photons are administered intravenously or by inhalation to image the brain. SPECT has been used, in particular, to measure perfusion, to investigate receptor distribution, and to detect areas of increased metabolism such as occurs with seizures.

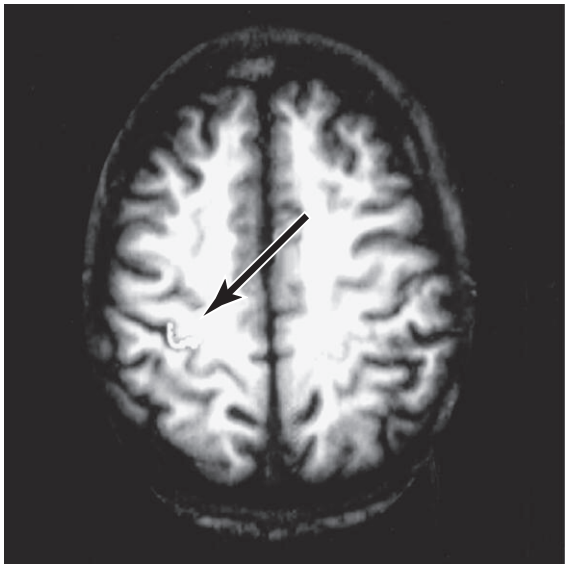
A specific contrast agent (^{123}I ioflupane) used with SPECT detects dopamine transporters (DaT) and helps to distinguish parkinsonian syndromes from essential tremor when this is clinically difficult. A DaT scan is also used to confirm a diagnosis of Parkinson disease in patients with ambiguous symptoms.

FUNCTIONAL MAGNETIC RESONANCE IMAGING

Functional MRI (**fMRI**) involves pulse sequences that change in signal intensity in response to alterations in the oxygen concentration of venous blood (blood oxygen level–dependent [BOLD]-fMRI), which correlate with focal cerebral activity. Studies are performed with the subject at rest and then after an activation procedure so that the change in signal intensity reflects the effect of the activation procedure on local cerebral blood flow (**Figure 2-7**). Studies are also performed without a stimulus ("resting state fMRI") to interrogate the brain's functional organization. fMRI studies are indicated for preoperative functional mapping of sensorimotor and language areas in the evaluation of patients with brain tumors, as well as in some cases of epilepsy or vascular malformations.

MAGNETIC RESONANCE SPECTROSCOPY

Magnetic resonance spectroscopy may provide important information about the chemical composition of tissue. Proton magnetic resonance spectroscopy (^{1}H-MRS) can determine levels of *N*-acetylaspartate (exclusive to neurons) or choline, creatinine, and lactate (glia and neurons). Measurements of brain concentrations of these metabolites may be useful in detecting specific tissue loss in Alzheimer disease or other neurodegenerative disorders; in distinguishing brain tumors from non-neoplastic lesions such as abscesses and in classifying brain tumors; in identifying certain inborn errors of metabolism and leukodystrophies; in prognostication of hypoxic-ischemic brain injury; and in localizing the source of seizures in temporal lobe epilepsy. Phosphorus magnetic resonance spectroscopy (^{31}P-MRS) may be useful in the evaluation of metabolic muscle diseases.



▲ **Figure 2-7.** A functional MR brain image obtained from a patient during rapid finger tapping of the left hand. An increase in relative blood flow in the region of the right motor strip is imaged (arrow) and superimposed on a T1-weighted MR scan. (Reproduced with permission from Waxman SG. *Correlative Neuroanatomy*. 23rd ed. Norwalk, CT: Appleton & Lange; 1996.)

ARTERIOGRAPHY

DESCRIPTION

The intracranial circulation is visualized most satisfactorily by arteriography, in which the major vessels to the head are opacified and radiographed after injection of contrast material through an arterial or venous catheter. Specifically, a catheter is introduced into the femoral or brachial artery and passed into one of the major cervical vessels. A radiopaque contrast material is then injected through the catheter, allowing the vessel (or its origin) to be visualized. Access to the cranial vessels with a catheter also allows for the delivery of certain therapies. The technique, generally performed after noninvasive imaging by CT scan or MRI, has a definite (~1%) morbidity and mortality associated with it and involves considerable exposure to radiation. It is contraindicated in patients who are allergic to the contrast medium. Stroke may result as a complication of arteriography. Moreover, after the procedure, bleeding may occur at the puncture site, and the catheterized artery (usually the femoral artery) may become occluded, leading to distal ischemic complications. The puncture site and the distal circulation must therefore be monitored.

INDICATIONS FOR USE

The major indications for cerebral arteriography are:

1. Diagnosis of **intracranial aneurysms, arteriovenous malformations** (**AVMs**), or **fistulas**. Although these lesions can be visualized by CT scan or MRI, their detailed anatomy and the vessels that feed, drain, or are otherwise implicated in them cannot reliably be defined by these other means. Moreover, arteriography is required for interventional procedures such as embolization, the injection of occlusive polymers, or the placement of detachable balloons or coils to treat certain vascular anomalies.
2. Detection and definition of the underlying lesion in patients with **subarachnoid hemorrhage** who are considered good operative candidates (see Chapter 6, Headache & Facial Pain).
3. Detection and management of vasospasm after subarachnoid hemorrhage.
4. Emergency embolectomy in the setting of ischemic stroke due to large-vessel occlusion. In addition, arteriography can define vascular lesions in patients with **transient cerebral ischemic attacks** or **strokes** if surgical treatment such as carotid endarterectomy is being considered.
5. Evaluation of small vessels, when vasculitis is under consideration.
6. Evaluation of **space-occupying intracranial lesions**, particularly when CT scanning or MRI is unavailable. There may be displacement of the normal vasculature, and in some tumors neovasculature may produce a blush or stain on the angiogram. Meningiomas are supplied from the external carotid circulation. Presurgical embolization of certain tumors reduces their blood supply and decreases the risk of major bleeding during resection.

MAGNETIC RESONANCE ANGIOGRAPHY

Several imaging techniques to visualize blood vessels by MRI depend on the physical properties of flowing blood, thereby allowing visualization of vasculature without the use of intravenous contrast. These properties include the rate at which blood is supplied to the imaged area, its velocity and relaxation time, and the absence of turbulent flow. Magnetic resonance (MR) angiography is a noninvasive technique that is cheaper and less risky than conventional angiography. It has been most useful in visualizing the cervical carotid and proximal portions of the intracranial arterial circulation, as well as the dural venous sinuses. The images are used to screen for stenosis or occlusion of vessels and for large atheromatous lesions. It has particular utility in screening for venous sinus occlusion. Resolution is inferior to that of conventional angiography, and occlusive disease may not be recognized in vessels with slow flow. Moreover, intracranial MR angiograms may be marred by saturation or susceptibility artifacts that result in irregular or discontinuous signal intensity in vessels close to bone. Although current techniques allow visualization of AVMs and aneurysms >3 mm in diameter, conventional angiography remains the "gold standard." Finally, MR angiography may reveal dissection of major vessels: Narrowing is produced by the dissection, and cross-sectional images reveal the false lumen as a crescent of abnormal signal intensity next to the vascular flow void.

CT ANGIOGRAPHY

CT angiography is a minimally invasive procedure that requires a CT scanner capable of acquiring numerous thin, overlapping sections quickly after intravenous injection of a bolus of contrast material. Because the images are acquired within 5-10 seconds, CTA is less likely than MR angiography to be affected by patient movement. A wide range of vessels can be imaged with the technique.

CT angiography of the carotid bifurcation is used increasingly in patients with suspected disease of the carotid arteries. It can also be used for intracranial imaging and can detect stenotic or aneurysmal lesions. However, sensitivity is reduced for aneurysms <3 mm, and the method cannot adequately define aneurysmal morphology in the preoperative evaluation of patients. It is sensitive in visualizing the anatomy in the circle of Willis, the vasculature of the anterior and posterior circulations, and intracranial vasoocclusive lesions, but it may not reveal plaque ulceration or disease of small vessels. It is a reliable alternative to MR angiography, but both techniques are less sensitive than conventional angiography.

In patients with acute stroke, CT angiography provides important information complementary to conventional CT scan studies, revealing the site and length of vascular occlusion and the contrast-enhanced arteries distal to the occlusion as a reflection of collateral blood flow. CT perfusion, in which the relative blood flow to an area of the brain is measured as iodinated contrast passes through over time, can provide additional information regarding the proportion of ischemic to infarcted tissue in this setting.

SPINAL IMAGING STUDIES

PLAIN X-RAYS

Plain x-rays of the spine can reveal congenital, traumatic, degenerative, or neoplastic bony abnormalities or narrowing (stenosis) of the spinal canal. Degenerative changes become increasingly common with advancing age, and their clinical relevance depends on the context in which they are found.

MYELOGRAPHY

Injecting iodinated contrast medium into the subarachnoid space permits visualization of part or all of the spinal subarachnoid system. The cord and nerve roots, which are silhouetted by the contrast material, are visualized indirectly. CSF leaks can be documented and localized. The procedure is relatively safe but carries the risk of headache, vasovagal reactions, persistent CSF leak, nausea, and vomiting. Rarely, confusion and seizures occur. Other rare complications include traumatically induced herniated intervertebral disks due to poor technique and damage to nerve roots.

The contrast agent is absorbed from the CSF and is excreted by the kidneys; ~75% is eliminated over the first 24 hours. While current water soluble agents do not cause arachnoiditis, tonic–clonic seizures have sometimes occurred when large amounts of contrast enter the intracranial cavity. Contrast myelography is usually followed by a CT scan of the spine while the medium is still in place. This shows the soft tissue structures in or about the spinal cord and provides information complementary to that obtained by the myelogram (see later).

Myelography has largely been replaced by MRI and CT scanning but it is still sometimes performed, particularly in patients with spinal hardware precluding useful MRI studies and in those with suspected CSF fistula.

COMPUTED TOMOGRAPHY

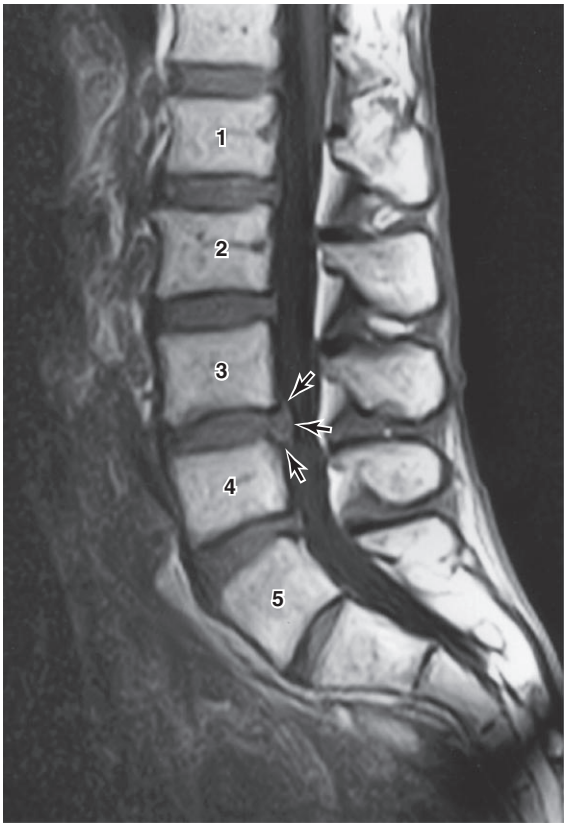
CT scanning without myelography is a routine procedure, but scanning may also be performed immediately after a myelogram, especially one that fails to reveal any abnormality or provides poor visualization of the area of interest. The myelogram may fail to detect a laterally placed disk protrusion, for example, while CT scan easily reveals such a lesion. CT scanning is also useful in visualizing more fully the area above or below an almost complete block in the subarachnoid space and in evaluating patients with spinal injuries.

CT scan is most helpful in defining the bony anatomy of the spine. It is performed routinely after trauma to exclude cervical spine fractures when spinal injury cannot be excluded on clinical grounds. CT scanning may show osteophytic narrowing of neural foramina or the spinal canal in patients with cervical spondylosis and may show spinal stenosis or disk protrusions in patients with neurogenic claudication. In patients with neurologic deficits, however, MRI is generally preferred because it provides more useful information about the spinal canal, neural foramina, and spinal cord.

MAGNETIC RESONANCE IMAGING

Spinal MRI is the best method for visualizing the spinal canal and its contents, and—in most cases—it provides the information obtained previously by myelography. Imaging of the spinal canal by MRI is direct and noninvasive.

Spinal MRI is indicated in the urgent evaluation of patients with suspected spinal cord compression. It permits differentiation of solid from cystic intramedullary lesions. MRI is the preferred imaging method for visualizing cord cavitation and detecting any associated abnormalities at the craniocervical junction. Congenital abnormalities associated with spinal dysraphism are also easily visualized by MRI. In patients with degenerative disk disease, MRI is an important means of detecting cord or root compression (**Figure 2-8**). However, abnormal MRI findings in the lumbar and cervical spine are common in asymptomatic subjects, especially in middle or later life, and care must therefore be exercised in attributing symptoms such as back pain to anatomic abnormalities that may be coincidental. When a spinal AVM (dural fistula) is suspected but MRI is unrevealing, a myelogram is sometimes helpful, but spinal angiography is often undertaken without proceeding to myelography.



▲ **Figure 2-8.** Spinal MRI showing disk herniation at the L3-L4 level (arrows).

NEUROMUSCULAR IMAGING STUDIES

MRI and ultrasound imaging of peripheral nerves may provide complementary information to clinical examination and electrodiagnostic studies, for example in nerve entrapment syndromes or after nerve injury, but the clinical role of these imaging studies is still being defined. MRI measures of muscle volume and composition and of edema are also being studied, as is their clinical application in patients with muscle disease. Muscle ultrasound is helpful in the identification of specific muscles for chemodenervation procedures, and its role in other clinical contexts is under study. In patients with myopathies, it may reveal atrophy and increased echogenicity, and the distribution of abnormalities may suggest specific disorders. In inclusion body myositis, for example, there is increased echogenicity of the flexor digitorum profundus relative to the flexor carpi ulnaris.

ULTRASONOGRAPHY

In **2D (B-mode) ultrasonography**, echoes reflected from anatomic structures are plotted on an oscilloscope screen in two dimensions. The resulting brightness at each point reflects the density of the imaged structure. The technique has been used to image the carotid artery and its bifurcation in the neck, permitting evaluation of the extent of extracranial vascular disease. Blood flowing within an artery does not reflect sound, and the lumen of the vessels therefore appears black. The arterial wall can be seen, however, and atherosclerotic lesions can be detected. Note that with severe stenosis or complete occlusion of the internal carotid artery, it may not be possible to visualize the carotid artery bifurcation.

The velocity of blood flow through an artery can be measured by **Doppler ultrasonography**. Sound waves within a certain frequency range are reflected off red blood cells, and the frequency of the echo provides a guide to the velocity of the flow. Any shift in frequency is proportional to the velocity of the red cells and the angle of the beam of sound waves. When the arterial lumen is narrowed, the velocity of flow increases; increased frequencies are therefore recorded by Doppler ultrasonography. Spectral analysis of Doppler frequencies is also used to evaluate the anatomic status of the carotid artery.

Transcranial Doppler studies can be used to detect intracranial arterial lesions or vasospasm (eg, after subarachnoid hemorrhage) and to assess the hemodynamic consequences of extracranial disease of the carotid arteries.

Duplex instruments perform a combination of both B-mode imaging and Doppler ultrasonography, thereby simultaneously providing information about the structure and the hemodynamics of the circulation in a color-coded format. The technique is commonly used to screen asymptomatic patients at high risk of carotid artery disease. Depending on the quality of the study, a CT angiogram may be necessary to confirm the extent and severity of disease. Symptomatic patients with suspected atheromatous lesions of the cervical carotid artery are best studied by MR or CT angiography to determine whether carotid endarterectomy is indicated. Duplex ultrasound is also useful for follow-up after carotid endarterectomy or stenting to detect recurrent stenosis. The role of ultrasonography in neuromuscular disease, referred to earlier, is currently under study.

BIOPSIES

BRAIN BIOPSY

Biopsy of brain tissue is sometimes useful when less invasive methods, such as imaging studies, fail to provide a diagnosis. Brain lesions most amenable to biopsy are those that can be localized by imaging studies; are situated in superficial, surgically accessible sites; and do not involve critical brain regions, such as the brainstem or the areas of cerebral cortex involved in language or motor function. Cerebral disorders that can be diagnosed by biopsy include primary and metastatic brain tumors, inflammatory conditions such as vasculitis or sarcoidosis, infectious disorders such as brain abscess, and certain degenerative diseases such as Creutzfeldt–Jakob disease, although MRI has largely supplanted biopsy in the diagnosis of this disorder.

MUSCLE BIOPSY

Histopathologic examination of a biopsy specimen of a weak muscle can indicate whether the weakness is neurogenic or myopathic. In neurogenic disorders, atrophied fibers occur in groups, adjacent to groups of larger uninvolved fibers. In myopathies, atrophy occurs in a random pattern; the nuclei of muscle cells may be centrally situated, rather than in their normal peripheral location; and fibrosis or fatty infiltration may also be found. Examination of a muscle biopsy specimen may also permit certain inflammatory diseases of muscle, such as polymyositis, to be recognized and treated.

In some patients with a suspected myopathy, although the electromyographic findings are normal, examination of a muscle biopsy specimen reveals the nature of the underlying disorder. Conversely, electromyographic abnormalities

suggestive of a myopathy are sometimes found in patients in whom the histologic or histochemical studies fail to establish a diagnosis of myopathy. The two approaches are therefore complementary.

NERVE BIOPSY

Nerve biopsy is not required to establish a diagnosis of peripheral neuropathy. The nature of any neuropathologic abnormalities, however, can sometimes suggest the underlying cause, such as a metabolic storage disease (eg, Fabry disease, Tangier disease), infection (eg, leprosy), inflammatory change, vasculitis, or neoplastic involvement. The findings are not always of diagnostic relevance, and nerve biopsy itself can be performed only on accessible nerves. It is rarely undertaken on more than a single occasion.

ARTERY BIOPSY

In patients with suspected giant cell arteritis, temporal artery biopsy may help to confirm the diagnosis, but the pathologic abnormalities are usually patchy in distribution. Therefore, a normal study should not exclude the diagnosis or lead to withdrawal of treatment.

SKIN BIOPSY

In patients with suspected small-fiber neuropathy, punch skin biopsy may be performed to determine the number, density, and length of small nerve fibers in the epidermis. The most common biopsy site is the lateral calf, for which normative values have been established. However, these values appear insensitive in ethnic Chinese patients, and better diagnostic standards are required for different patient populations.