The Neurologic Diagnosis

A Practical Bedside Approach

Jack N. Alpert

Second Edition

Springer

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In memory of Morris B. Bender, a superlative clinical neurologist of the twentieth century, who stimulated my lifelong interest in the manifestations, evaluation, and diagnosis of patients with neurologic diseases. His influence permeates this text.

Foreword

Assessment of neurological complaints, a high percent of a family practitioner and internist's practice, requires an accurate history and a careful neurologic examination. As Dr. Alpert expertly discusses in detail, the history provides clues to the clinical diagnosis, while the complementary neurologic examination localizes the lesion(s). Dr. Alpert is able to distil out from his over four decades of a busy practice and from his excellent teaching of medical students and neurological trainees a logical, readable, and provocative approach to each neurological complaint. In a chapter of 42 cases of *Diagnostic Dilemmas*, one's clinical acumen is challenged with practical questions and astute observations.

By discussing neurological disorders in terms of ten *Neuroanatomic Diagnoses*, Dr. Alpert compartmentalizes neurologic diseases into convenient and manageable discrete entities. By building upon the unique anatomy and physiology of each unit, greater logic is made in one's deductive reasoning for a diagnostic conclusion. Special emphasis is given to the *Six Major Decussations* with clinical correlations, as with strokes, autonomic disorders, neuromuscular diseases, and the poorly responsive patient. A separate chapter on *Common Symptoms in the Neurology Clinic* is a potpourri of frequently seen and rare cases which will challenge the beginner and the experienced practitioner of neurology. This textbook is highly recommended to the serious student of clinical neurosciences, be they medical students, trainees, or practitioners.

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Preface

The second edition of this book retains the same emphasis on the simplification of making a neurologic diagnosis. The unique diagnostic principles of neurology are based on the requirement of an anatomic definition of the disease before a differential diagnosis can be offered. This process often disrupts the thinking of medical students and residents and certainly adds to the confusion of the practicing physician, thus providing the necessity for neurologic expertise and consultations. The explosion of efficacious treatment options for common neurologic diseases and disorders such as headache, epilepsy, multiple sclerosis, Parkinson's disease, sleep disorders, and stroke mandates an accurate diagnosis which depends on a thorough history and meticulous neurologic examination. This initial, critical, first step is the focus of this text.

The first eight chapters provide core knowledge of neuroanatomy and diagnostic principles. They include several updates on clinical-neuroanatomic correlations so that a rereading, although repetitive to some extent, should remain useful. Chapter 9 now includes a brief review of the muscular dystrophies with several added challenging cases. A new Chap. 10 on myelopathies not provided in the first edition adds brief discussions of a group of diseases which uniquely target the spinal cord. Although some are uncommon or rare, it is important to be mindful of them. As multiple sclerosis often begins with myelopathic features, the discussion of one case furnishes an opportunity for elaboration of new diagnostic criteria according to the recent (2017) revisions of McDonald's criteria. These are briefly summarized. A full review will require a return to source material.

Chapter 11 remains focused on the practical diagnosis of common neurologic diseases and disorders. The *International Classification of Headache Disorders (ICHD), third edition* reported in *Cephalalgia* (2013) supplies the substrate for a reexamination of these entities. Positron emission tomography (PET) imaging of the brain during migraine, relatively unknown among most medical practitioners and some neurologists, is now included. The section on vertigo has been enlarged by the addition of new cases as well as modified by the clarification and explication of relatively new clinical signs. The section on epilepsy incorporates the International League Against Epilepsy (ILAE) classification of epilepsies published in *Epilepsy*

(2017). The transition from the old terminology will undoubtedly be resisted but, nevertheless, eventually accepted, likely over many years since the prior classification in 1981 held force for decades. Discussion of psychogenic factors has been expanded and incorporates principles of differentiating psychogenic non-epileptic seizures (PNES) or pseudoseizures from seizures and psychogenic pseudosyncope (PPS) from syncope. The section on sleep disorders has broadened and will include elements of the most recent International Classification of Sleep Disorders 3rd Edition 2014. Understanding these conditions is increasingly recognized as furnishing important clinical clues for diagnoses, such as recognizing rapid eye movement (REM) sleep behavior disorder as a prelude to Parkinson's disease, as well as providing treatment opportunities for the maintenance of overall health.

In Chap. 12, Diagnostic Dilemmas, recently discovered neurologic diseases are introduced such as autoimmune encephalitis, chronic traumatic encephalopathy, and the neurologic complications of Zika virus infections. Advances in the neurologic armamentarium for the diagnosis of Parkinson's disease, particularly the non-motor manifestations, are explored. This chapter is also expanded by several new challenging case reports of rare diseases. In Chap. 13, additional syndromes have been added, always intriguing for many neurologists, since they add an element of historical interest.

The relevance of the neurologic examination has been questioned by many physicians, including some experienced neurologists. There have even been statements that simply reviewing an MRI scan with a neuroradiologist could easily be more valuable. Forgotten, astonishingly, is the reality that the majority of patients visiting most neurologic clinics have normal studies. Just think of migraine, epilepsy, Parkinson's disease, sleep and neuromuscular disorders, as well as neuro-otologic conditions whose diagnoses depend on a thorough history and neurologic examination. Additionally, the benefit of a soothing touch which may convey interest and empathy by the caring, thoughtful examiner provides a form of treatment by reducing the discomfort of anxiety. Abandonment of this gift which is bequeathed to all physicians is a developing tragedy of modern medicine.

A video has been provided which focuses on the standard neurologic examination methods as well as special techniques which may have been forgotten or omitted from current neurological training. (It is available as electronic supplementary material on this book's page on the Springerlink.com website. Those without a subscription to Springerlink.com can still view the ESM material for free.)

Certainly, superb training programs which focus on stroke may differ significantly from those which concentrate on neuromuscular diseases.

In summary, it is my hope that this text will expand the horizons of the reader beyond that with which he is so familiar.

Houston, TX, USA Jack N. Alpert

Acknowledgments

Without the patience and encouragement of my wife, Ruth, this book could never have been completed. Donna J. Williams was my invaluable, conscientious, and superb transcriptionist. A number of neurologists, who provided excellent advice for the first edition, which is an integral element of this text, include Drs. Frank Yatsu, Stanley Appel, Randolph Evans, James Grotta, Ernesto Infante, Frank Perez, Victor Rivera, and Loren Rolak. Michael Griffin, my editorial advisor, insisted on a well-disciplined, correctly documented manuscript and prodded me to complete the text without excessive delay. I appreciate everyone's influence and guidance.

Contents

Chapter 1
Introduction

Neurology has made major advances over the last few decades in understanding some of the complexities of neuroanatomic structures and their physiologic ramifications. This has resulted in the development of efficacious treatment options for common neurologic disorders such as epilepsy and migraine and for previously debilitating diseases, for example, myasthenia gravis and multiple sclerosis. Nevertheless Neurology has been bedeviled with an unjustified accusation that diseases of the nervous system are observable but untreatable. This misconception has been handed down through generations of medical students because of the dearth of sufficient instruction in the early years of medical school.

Furthermore, it is commonly asserted that neurologic diseases are uniquely incurable. This fallacious argument, often promulgated by poorly educated physicians, conveniently forgets that most illnesses are incurable. For instance, are there cures for people with asthma, diabetes, hypertension, coronary artery disease, and rheumatoid arthritis, just to name a few? Some examples of curable diseases are infectious diseases which can be eradicated by antibiotics or run a natural course of spontaneous recovery. Gallstones, appendicitis, and some forms of cancer can be cured, usually through excision of the abnormal tissue.

Only when physicians have been in practice for a few years do they recognize the importance of neurologic symptoms and their inability to analyze them. In fact, the majority of symptoms that affect the body, other than the chest and abdomen, have neurologic sources or neurologic ramifications. Furthermore, patients with unexplained chest and abdominal pain may benefit from a neurologic consultation. Thus, common complaints such as loss of consciousness, impairment of memory and speech, headache, dizziness, numbness, paresthesias, weakness, neck pain, pain of the extremities, and low back pain require a clinical assessment, not necessarily neurophysiological and neuroimaging procedures.

Modern technology with CT and MRI scans, angiography, electromyography, and electroencephalography are wonderful adjuncts to making a diagnosis. They cannot be substituted for the initial assessment. Here is an example:

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Case report A 55-year-old man arrives in the emergency room with left-sided weakness after a motor vehicle accident. His car was struck from the passenger side where he was sitting. He has a medical history of diabetes and hypertension. A neurologic examination disclosed a blood pressure of 150/110. STAT blood sugar was 280 mg/dl. Neurologic abnormalities included a moderate left hemiparesis, arm greater than leg, left hyperreflexia with left Hoffmann and Babinski signs, and impaired rapid alternating movements of the left arm. There was no sensory loss. A prompt CT scan of the brain revealed prominent subcortical ischemic changes, right greater than left. A subsequent MRI scan of the brain confirms vascular pathology because of multiple scattered T2 hyperintensities. The patient was admitted to a stroke unit and a neurological consultant was requested. The neurologist promptly ordered an MRI scan of the cervical spine which revealed a herniated disk, C3–C4 on the left side, compressing the spinal cord. Surgery was performed and the patient recovered completely.

Lessons:

1. Hemiparesis is not a localizing abnormality other than supporting the presence of central nervous system disease.
2. The past medical history, in this case diabetes and hypertension, leads the attending physician astray.
3. CT or MRI abnormalities in the wrong location promote inaccurate diagnoses.

Neuroanatomy frightens the fledgling medical student. For the beginner, there are numerous, unfathomable tracts criss-crossing at different locations in brain and spinal cord. How can one distinguish lesions of the medial lemniscus from the lateral spinothalamic tract? The presence of a "long tract sign," such as a Babinski sign, indicates a lesion of the corticospinal tract which is a few feet in length. As the tract extends from the frontal cortex to the caudal portion of the spinal cord, additional abnormal signs are required for the precise localization of pathology.

The predominant principle of this text will be an emphasis on the existence of only ten neuroanatomic diagnoses. The second chapter will introduce this concept. A simplification, however, does not obviate the necessity of acquiring at least a modest knowledge of neuroanatomy. After a discussion of methods to obtain a neurologic history and perform a neurologic examination, four subsequent chapters will focus on the major elements of neuroanatomy and their clinical relevance. Chaps. 9 and 10 will focus on neuromuscular diseases and myelopathy. A separate chapter will review the common neurologic symptoms of an outpatient clinic, applicable both to general medicine and neurology. Each subtopic will be dealt with cursorily since the purpose of this text is only to provide an overview of the diversity of neurologic disorders. In Chap. 12, Diagnostic Dilemmas, a variety of case reports will be presented to expose the reader to the wide spectrum of neurologic diseases. As neurologic syndromes and terminology are so ingrained in medical lore, a separate, final chapter to review them is obligatory.

Chapter 2
The Ten Neuroanatomic Diagnoses

This chapter aims merely to introduce the student to the unique diagnostic method used by neurologists. Detailed discussion of anatomic pathways, abnormal findings and differential diagnosis is provided in subsequent chapters. Sections on case reports will allow the student or physician to utilize the principles discussed in the foregoing chapters.

The immediate linkage of symptoms and signs to the differential diagnosis is the common approach in the practice of internal medicine. For the neurologist this practice is fraught with hazards and contains the seeds of misdiagnosis. A neuroanatomic diagnosis is a required preliminary step. In addition, there are numerous misconceptions about neurologic symptoms and signs which trigger errors when making a neuroanatomic localization. The consequences are often unnecessary, exorbitant expenditures for inapplicable neuroimaging or neurophysiologic testing and inappropriate referrals. This results in delayed care, sometimes with serious adverse consequences.

Most medical students are worried, if not terrified, about making an inaccurate localization of a neurologic disease. There is a plethora of tracts and "centers" of function which supposedly require the acquisition and recall of detailed anatomic minutia. In fact, only a rough localization to one of ten anatomic sites is required for practical purposes. An inaccurate selection of one of these diagnoses will make a differential diagnosis nearly impossible. This choice does require a sufficient knowledge of neuroanatomy and neurophysiology which will be reviewed in subsequent chapters. The outline below is a summary of essential diagnostic principles.

Ten neuroanatomic sites to choose from:

1. Cerebral
2. Extrapyramidal
3. Brainstem/Cerebellum
4. Spinal cord
5. Root

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6. Plexus
7. Nerve
8. Neuromuscular junction
9. Muscle
10. Meninges

Common Neurologic Signs: Localizing Value

Central Nervous System Disease (CNS), Peripheral Nervous System (PNS) and Muscle Disease (M)

1. Pathologic signs indicating CNS disease with localizing value
   (a) Dementia: Cerebral
   (b) Aphasia: Cerebral
   (c) Seizure: Cerebral
   (d) Abnormalities of mood, personality and behavior associated with abnormal neurologic signs: Cerebral
   (e) Homonymous hemianopsia: Cerebral
   (f) Abnormal involuntary movements/postures: Extrapyramidal
   (g) Abnormal eye movements and/or pupils localizing to: Brainstem or Cerebellum
   (h) Crossed findings, ipsilateral cranial nerve and contralateral long tract: Brainstem
   (i) Sensory levels: Spinal cord, rarely Brainstem
2. Pathologic signs indicating CNS disease but nonlocalizing within the CNS
   (a) Hemiparesis
   (b) Hemisensory loss
   (c) Hemiataxia
   (d) Unilateral hyperreflexia including unilateral Hoffmann's sign
   (e) Babinski sign
   (f) Eye movement abnormalities of Cerebral, Brainstem or Cerebellar origin
   (g) Position sense loss exceeding loss of vibration perception
3. Pathologic signs (nonlocalizing) of CNS or PNS/M origin
   (a) Dysarthria
   (b) Dysphagia
   (c) Monoparesis, paraparesis, triparesis, quadriparesis, and crossed paresis
   (d) Dysdiadochokinesis (impaired rapid alternating movements)
   (e) Positive Romberg
   (f) Gait disorders

4. Common differential diagnoses
    (a) Autoimmune
    (b) Demyelinating
    (c) Degenerative
    (d) Degenerative, structural/compressive
    (e) Developmental
    (f) Genetic
    (g) Infectious
    (h) Inflammatory
    (i) Metabolic
    (j) Neoplasm
    (k) Nutritional
    (l) Toxic
    (m) Trauma
    (n) Vascular
5. The paroxysmal disorders
    (a) Headache and facial pain
    (b) Seizure and syncope
    (c) Sleep disorders
    (d) Transient ischemic attack (requires anatomic definition)
    (e) Transient global amnesia
    (f) Vestibular disorders (requires anatomic definition)
    (g) Muscle pain (cramps, spasms)

Cerebral

The five pathognomonic signs of cerebral hemisphere disease are dementia or a confusional state, abnormalities of mood, personality and behavior associated with abnormal neurologic signs, aphasia, seizure, and homonymous hemianopsia. The absence of these abnormalities does *not* exclude cerebral disease but must allow for other possibilities.

> Pathognomonic signs of cerebral disease are dementia/confusion, aphasia, seizure, homonymous hemianopsia, and abnormalities of mood, personality and behavior accompanied by abnormal neurologic signs.

Case 1 A 67-year-old retired male accountant is brought to the Emergency Department at 10:00 p.m. because of slurred speech and confusion. He is unable to give a coherent history. His wife says that she noticed slurred speech shortly after dinner followed promptly by confusion and asking the same question repeatedly. He

has diabetes controlled by diet only and has just recovered from a severe gastroenteritis causing prolonged watery diarrhea.

Neurologic examination: The patient is oriented to person, year, not month or place. Speech is severely dysarthric but content and syntax are normal. He is able to add 14 + 6 but not 14 + 17. He spells "hand" forward but not backward. Short-term recall is one of three words given after 3 min have elapsed. He has impaired rapid alternating movements of both hands and is clumsy when removing his shirt. He has a mild postural tremor and asterixis.

The third-year medical student's diagnosis: Cerebrovascular accident (CVA) in the left middle cerebral artery distribution.

Neurologist's diagnosis: Encephalopathy, probably metabolic.

Laboratory data: Serum sodium is 162 mEq/L and BUN 70 mg/dl.

Final diagnosis: Encephalopathy secondary to hypernatremia caused by volume contraction due to severe diarrhea.

Lessons:

The differential diagnosis of cerebral hemisphere disease depends on whether it is unilateral or bilateral.

1. The first task is to determine whether there is focal or diffuse disease, in this case unilateral or bilateral cerebral disease.
2. Confusion indicates bilateral cerebral dysfunction.
3. Dysarthria is nonlocalizing. Aphasia indicates a dominant hemisphere lesion.
4. Acalculia and errors reversing words are usually not focal signs. Occasionally, they can be part of an aphasia.
5. Short-term recall deficits indicate bilateral cerebral dysfunction.
6. Impaired rapid alternating movements are of localizing value when unilateral. This impairment occurs with any motor system involvement, corticospinal, cerebellar, or extrapyramidal. Proprioception loss and weakness from any etiology may be the source of this finding.
7. Postural tremor and asterixis may occur with any metabolic encephalopathy.

Summary:

The term CVA is no longer an acceptable diagnosis. A stroke is an infarction or hemorrhage, not an "accident."

This patient has an acute encephalopathy which indicates bilateral cerebral dysfunction. Bilateral cerebral dysfunction can be due to a slowly progressive disorder such as Alzheimer's disease which would not be characterized as an encephalopathy. The term encephalopathy implies a rapidly developing confusional state. An acute cerebral ischemic event rarely produces an encephalopathy. Furthermore, the term CVA is no longer an acceptable diagnosis. A stroke is an infarction or hemorrhage, not an "accident."

Categories of diseases which are likely to cause an encephalopathy include metabolic alterations, infections such as an encephalitis, nutritional disorders, toxic substances or drugs, and trauma.

Case 2 A 73-year-old man reports the sudden onset of left-sided weakness beginning 2 weeks ago with a mild increase in weakness since then. He has a history of diabetes and hypertension.

Examination: Blood pressure 150/100, left hemiparesis with greatest involvement of hand and foot, left hyperreflexia including a left Hoffmann's and Babinski signs.

MRI (brain): Multiple subcortical T2 hyperintensities typical of vascular disease but no discrete infarction.

MRA (head and neck): 60% stenosis of right internal carotid artery and 85% stenosis of left internal carotid artery.

Neurologic consultation is requested with regard to treatment options of the vascular lesions. The neurologist takes additional history as a neurologic review of systems is mandatory for every patient even if seemingly irrelevant. The patient reports a 2-year history of periodic severe neck pain with occasional radiation to the left shoulder. The neurologist's examination shows no other findings. Recognizing that a hemiparesis is a nonlocalizing sign of central nervous system disease, an MRI of the cervical spine is obtained. This reveals an extramedullary mass at C3–C4 on the left side compressing the spinal cord. Extramedullary tumors, outside the spinal cord and within the dura, are nearly always benign such as a schwannoma or meningioma.

Diagnosis: Cervical myelopathy secondary to a schwannoma with spinal cord compression at C3–C4.

Treatment: Cervical laminectomy and resection of the neoplasm. The patient makes a complete recovery.

Lessons:

A hemiparesis may occur with cerebral, brainstem, or spinal cord disease.

1. Take a complete history. A seemingly irrelevant symptom may be pertinent. Pain radiating to the shoulder may be radicular, particularly common with a schwannoma.
2. Recognize that a spastic hemiparesis localizes the disease only to the central nervous system, specifically cerebral, brainstem and spinal cord, the location of the corticospinal tract.
3. The differential diagnosis of spinal cord disease associated with a 2-year history of neck pain begins first with structural degenerative disease. Neoplasm would be a secondary choice, but nevertheless it is always a diagnostic consideration.
4. MRI scans usually show the pathology when a myelopathy is present.

Case 3 A 66-year-old man with coronary artery disease undergoes coronary artery bypass surgery (CABG). Thirty-six hours later he becomes acutely anxious and appears confused to the nurse who requests a sedative for her patient. A well-trained, careful medical resident decides to evaluate the patient before prescribing a sedative.

Neurologic examination: The patient asks the resident, "When will I be displaced?" then says, "I mean discharged." The patient is alert, has fluent speech, and is oriented to person, place, and month. When asked to state the year he repeats the month. On the fourth request to state the year he responds correctly. When asked to repeat "no ifs, ands or buts," he replies "no ifs, ands, and buts." The remainder of a complete neurologic examination is normal.

Laboratory findings: The EKG monitor shows intermittent atrial fibrillation. CT (head) reveals a small, ill-defined hypodensity in the left temporal lobe.

Diagnosis: Left cerebral infarction, temporal lobe, due to cardioembolism to a branch of the left middle cerebral artery. Atrial fibrillation, a common complication after heart surgery, is the etiology [1].

Lessons:

Aphasia is often misinterpreted as confusion. Aphasia suggests stroke whereas confusion implies metabolic, toxic or hypoxic-ischemic factors.

1. Accurate distinction between confusion and aphasia is critical. Confusion means bilateral cerebral dysfunction and therefore metabolic, toxic or hypoxic-ischemic etiologies. Aphasia indicates a stroke in this clinical setting.
2. The first clue to a neurologic disorder is acute anxiety occurring many hours after surgery, a not unusual occurrence in a patient with the sudden onset of aphasia. This prompts a neurologic evaluation.

Anxiety and agitation often occur with the acute onset of aphasia.

3. The patient exhibits a *paraphasia* which, in this case, is the substitution of the word "displaced" for "discharged." This is a semantic (verbal) paraphasia. A phonemic paraphasia would be, for example, to say "plor" instead of "floor" or "fleet" instead of "street." He demonstrates perseveration which is giving the same response despite a new question being asked. Additionally, the patient is unable to repeat a simple phrase. These three findings, paraphasia, perseveration, and poor repetition are characteristic of aphasia although perseveration may also occur in demented patients. See detailed discussion of aphasia in Chap. 4.
4. The presence of aphasia ordinarily indicates a left cerebral lesion. Only about 50% of left-handed individuals are right hemisphere dominant. Since about 10% of the population is left-handed there is about a 5% chance of a right cerebral lesion.
5. The acute onset of a focal cerebral deficit in a patient who just underwent coronary artery bypass surgery is nearly always an infarction. The most common etiology in the postoperative period is cardioembolism associated with atrial fibrillation. Atrial fibrillation occurs in one third of post-CABG patients.
6. Thus, a single word, "displaced," prompts a diagnosis of cardioembolism to the left middle cerebral artery due to postoperative atrial fibrillation!

> Signs of aphasia are paraphasias, dysnomia, abnormal speech fluency, and poor repetition.

7. The common diagnostic hallmarks for aphasia include one or more of these findings: paraphasias, dysnomia, abnormal speech fluency, and poor repetition. Any one of these findings indicates the likelihood of focal disease and thus rules out a solely metabolic or toxic etiology.

Extrapyramidal [2]

> There are three motor systems: corticospinal, extrapyramidal, and cerebellar mediating initiation of movement, maintenance of posture, and coordination, respectively.

There are three motor systems, corticospinal, extrapyramidal, and cerebellar. The corticospinal tract mediates initiation of movement, and the cerebellar system, coordination of movement. The extrapyramidal system is responsible for the maintenance of posture. Lesions of the extrapyramidal system cause abnormal involuntary movements and abnormal postures. This system is represented mainly by specific nuclei, the basal ganglia, which are located in deep subcortical regions. The primary nuclei are the caudate, globus pallidus, subthalamus, and putamen. An

additional structure, the substantia nigra, is located in the midbrain. Lesions in these regions result in abnormal postures or abnormal involuntary movements. Examples include Parkinson's disease, chorea, hemiballism, athetosis, and dystonia. These disorders will be discussed in the chapter on neurologic examination.

Lesions of the extrapyramidal system cause abnormal involuntary movements such as ballism, athetosis, chorea, dystonia, and tremor.

Case 4 An 85-year-old woman complains of sudden involuntary movements of the right arm which began 5 days ago. They occur every few minutes. At about the same time she noted blurred vision affecting the right eye. She has a history of hypertension controlled with a diuretic.

Examination: Neurologic examination discloses a right homonymous hemianopsia. There are abrupt flinging movements of the right arm over her head.

MRI (head) reveals infarctions in the left occipital lobe and in the region of the left subthalamic nucleus. The MRA (head and neck) discloses a severe left posterior cerebral artery stenosis.

Diagnosis: Left subthalamic nucleus and occipital lobe infarctions due to atheromatous disease causing severe stenosis with subsequent thrombosis in the proximal portion of the left posterior cerebral artery.

Lessons:

1. Branches of the left posterior cerebral artery supply the left subthalamic nucleus, thalamus, portions of the midbrain, inferior temporal and occipital lobes.

Ballism produces sudden movements at proximal joints, chorea affects distal musculature, athetotic movements are writhing, and dystonia is marked by abnormal postures.

2. Hemiballism is a flinging irregular movement at proximal joints, especially shoulder and hip, classically thought to be due to a lesion in the subthalamic nucleus, but now found to be associated with other basal ganglia lesions.
3. Differential diagnoses of the patient's involuntary movements include chorea, athetosis, and dystonia.
4. Choreiform movements are rapid, jerky movements of the extremities primarily involving distal musculature.
5. Athetosis is characterized by slow, writhing movements of the extremities.
6. Dystonic movements are persistent or intermittent maintenance of an abnormal posture.

7. The patient describes visual loss in only one eye, a relatively common complaint of patients with homonymous hemianopsias. The temporal field loss is larger and more apparent to the patient.
8. Treatment of the involuntary movements with a dopamine antagonist is useful, and the syndrome usually subsides over several weeks to a few months.

Case 5 A 70-year-old man complains of running into walls. For the last 3 months, while walking in the corridors at work, he involuntarily picks up speed and has to catch himself by aiming at the nearest door or wall. He has no other complaints. When specifically queried about turning in bed or getting out of a chair he reports that he has slowed down.

Examination: The patient has a flat affect and his shoulders droop. He walks with a stooped posture and leans forward. He crosses his legs slowly. Tapping the bridge of his nose elicits repeated blinking. A normal individual may blink once or twice but not persistently and uninterruptedly. There is mild cogwheel rigidity and no tremor.

Diagnosis: Parkinson's disease.

Lessons:

1. The patient describes a festinating gait, an uncontrollable increase in speed in an attempt to catch up with his center of gravity.
2. He has a flat affect, hypomimia, which is also known as masked facies. This is a decreased mobility of facial musculature. Yet the patient has a positive glabellar reflex, known as Myerson's sign, which is a rapid, sustained blinking when the bridge of the nose is tapped. Thus reflex responses can be increased in the presence of lack of mobility.
3. Bradykinesia is exhibited by the patient slowly crossing his legs.
4. Thus pure observation on entering the examination room makes the diagnosis. Paying attention to the patient's facial mobility and leg movements furnishes the two primary diagnostic clues.

Brainstem/Cerebellum [3]

Crossed findings and abnormal eye movements typify brainstem lesions.

The cardinal features of diseases affecting the brainstem are: (1) crossed findings and (2) specific types of abnormal eye movements. Examples of the former include right facial weakness and left hemiparesis, right third nerve palsy and left hemiparesis (Weber's syndrome), ipsilateral gaze palsy, and contralateral hemiparesis, i.e., gaze to the right with a right hemiparesis (Foville's syndrome) and a third nerve lesion with contralateral tremor or choreiform movements (Benedikt's syndrome).

Most forms of pathologic nystagmus occur with brainstem lesions and less often pure cerebellar lesions. The direction of nystagmus refers to its quick phase. Quick phases of nystagmus that are pure rotatory, multidirectional, oblique, disconjugate, or vertical indicate brainstem/cerebellar pathology. An important exception is drug toxicity which most often causes horizontal, gaze-evoked nystagmus. This means left-beating nystagmus on left lateral gaze and right-beating nystagmus on right lateral gaze. Nystagmus in the vertical plane may also occur with drug toxicity.

Peripheral vestibular disease typically produces horizontal, direction-fixed nystagmus with a slight rotatory element.

If the quick phases of nystagmus are horizontal and unidirectional with any ocular deviation, an eighth nerve or semicircular canal lesion may be present. The proviso is the absence of other neurologic symptoms or signs which would indicate central nervous system disease. A left eighth nerve lesion, for instance, produces direction-fixed, contralateral (right-beating), horizontal nystagmus with a slight rotatory element which is counterclockwise and most prominent on right lateral gaze, usually present on up and down gaze and least often on left lateral gaze. The reverse occurs with a right eighth nerve lesion.

Pendular nystagmus, equal velocity in both directions, is usually congenital.

Pendular nystagmus is usually of congenital origin. Manifestations are nystagmus which has equal velocities in both directions which means no separation into quick and slow phases. There may be also jerk nystagmus with quick and slow phases which vary in intensity with changes of eye position. This nystagmus is accentuated by visual fixation, and there is commonly a null point, a location where it disappears. The patient seldom has symptoms. The etiology is unknown.

Case 6 A 62-year-old man complains of difficulty swallowing of 3 days' duration. At the onset of this problem he was briefly dizzy and had numbness in his mouth. He describes the dizziness as a tilting of the horizon, a visual illusion. He walked unsteadily. There was rapid improvement except for residual difficulty swallowing liquids. His past medical history includes hypertension and hypercholesterolemia. Medications are lisinopril and atorvastatin.

Examination: The patient has mild horizontal, gaze-evoked nystagmus. This means quick phases of nystagmus to the right on right lateral gaze and to the left on left lateral gaze. The left pupil is 2 mm and the right is 3 mm with both reacting briskly to light. The right palpebral fissure is larger than the left. The left face is warmer than the right. The left corneal response is absent. The left soft palate elevates

poorly. There is mild left heel-to-shin ataxia. There is slight impairment of pinprick sensibility on the right side of the body.

Dysphagia, vertigo, diplopia, and facial numbness are common symptoms of brainstem ischemia.

Diagnosis: Brainstem infarction, left dorsolateral medulla, secondary to a left vertebral artery occlusion with ischemia in the left posterior inferior cerebellar artery distribution. The diagnosis is confirmed by MRI and MRA scans.

Lessons:

1. This patient has a partial Wallenberg's syndrome.

Nystagmus due to CNS lesions is most often secondary to brainstem lesions, less often pure cerebellar pathology.

2. He has a left Horner's syndrome manifested by miosis, ptosis, and anhidrosis (warmth) on the left side. The sympathetic system begins in the hypothalamus, descends through the brainstem, coalesces in the dorsolateral medulla before it passes down the spinal cord. See Chap. 8 on autonomic nervous system.
3. Horizontal gaze-evoked nystagmus indicates involvement of vestibular nuclei.
4. The absent left corneal response indicates involvement of the left spinal tract and nucleus of the fifth cranial nerve. Numbness in the mouth at the onset of the stroke is caused by the same lesion.

Cerebellar ataxia often occurs with lesions outside the cerebellum proper.

5. Left heel-to-shin ataxia is consistent with involvement of the left inferior cerebellar peduncle (restiform body). Of note is the common presence of ataxia without intrinsic cerebellar disease.
6. Weakness of the left soft palate indicates involvement of the nucleus ambiguus on the left side which contains the motor portion of the tenth cranial nerve.
7. Hypesthesia on the right side of the body points to involvement of the lateral spinothalamic tract on the left side.

There are quick and slow eye movement systems. Saccades (quick) are used to scan the environment. Visual pursuit (slow) follows a moving target. The vestibular system generates slow eye movements when the head is turned quickly.

A brief comment about the two main eye movement systems is now required. The quick or saccadic system is used to place the fovea on the object of interest when scanning the environment. An example of the use of saccades is inspecting parts of a stationary object such as a painting. The slow system includes visual tracking such as following the course of a plane through the sky. The vestibular system also generates a slow phase with quick head movement, part of the vestibulo-ocular reflex arc. The cerebellar flocculus and vermis play a role in generating slow eye movements.

The crossed findings of brainstem lesions are usually cranial nerve involvement on one side and hemiparesis or hemihypesthesia on the other.

A voluntary, contralateral saccade begins with a signal produced, for example, in the right frontoparietal eye fields, descends to the contralateral left PPRF (paramedian pontine reticular formation) after crossing the midline between the midbrain and pons. The left PPRF generates a saccade to the left by sending fibers to the left sixth nucleus and the right third nucleus. The left sixth nerve innervates the left lateral rectus and the right third nerve innervates the right medial rectus muscle. The medial longitudinal fasciculus (MLF) connects the left PPRF to the right third nucleus. There are interneurons in the abducens nucleus which receive input from the ipsilateral PPRF and send fibers across the midline to form the contralateral MLF. Thus, the MLF is responsible for ipsilateral adduction.

Case 7 A 52-year-old man is brought to the emergency room after the sudden onset of diplopia, vertigo, and vomiting followed by right-sided weakness. He has a 10-year history of hypertension and smokes one pack of cigarettes per day. He has had his hypertension under control with amlodipine.

Examination: Examination reveals a blood pressure of 160/100 and he has bilateral carotid bruits. The eyes are deviated to the right and he is unable to look to the left. He has a right spastic hemiparesis.

Laboratory studies: Carotid Dopplers show bilateral 60–70% stenoses of the internal carotid arteries. A CT scan of the brain is normal.

Diagnosis: Left pons ischemia secondary to basilar artery disease.

Lessons:

1. Diplopia, vertigo, and vomiting are characteristic symptoms of brainstem ischemia.
2. Eye deviation to the right is compatible with either a right cerebral or a left pontine (PPRF) lesion.

3. A right hemiparesis can be due to a left cerebral, internal capsule, midbrain, pontine or medullary lesion. Below the decussation of the pyramids at the cervical medullary junction, a right hemiparesis is caused by a right-sided spinal cord lesion.

> The oculomotor pathway between frontoparietal eye fields and the PPRF decussates at the pontomesencephalic junction.

4. Right cerebral ischemia would produce eye deviation to the right and a left hemiparesis, but left pontine ischemia would explain the findings because of involvement of the left PPRF and left basis pontis (corticospinal tract). Thus, when a patient looks at his weak side he most likely has a contralateral pontine lesion. The oculomotor pathway will be reviewed in detail in Chap. 6.

> Carotid artery stenoses are unrelated to brainstem ischemia.

5. Carotid stenoses are unrelated since the vertebrobasilar system supplies the pons.
6. A powerful risk factor for carotid stenosis is smoking.

Spinal Cord Lesions (Myelopathies)

Myelopathies can be manifested by pure involvement of motor or sensory pathways but commonly a combination of both (see Fig. 2.1).

Case 8 A 33-year-old woman complains of scalding her left foot without realizing it when testing her bath water 1 week ago. The burn is healing well, but she has an uncomfortable tingling sensation on the left leg. A thorough review of neurologic symptoms elicits what the patient describes as a "minor problem," blurred vision O.D. when running her usual 5 miles before going to work. This began 1 year ago. The patient has insulin-dependent diabetes mellitus. She takes no medication other than insulin.

> Impaired color vision is often the first sign of optic nerve disease.

Neurologic examination: The patient has impaired color vision O.D. with a visual acuity of 20/20. She has impaired rapid alternating movements of the right arm

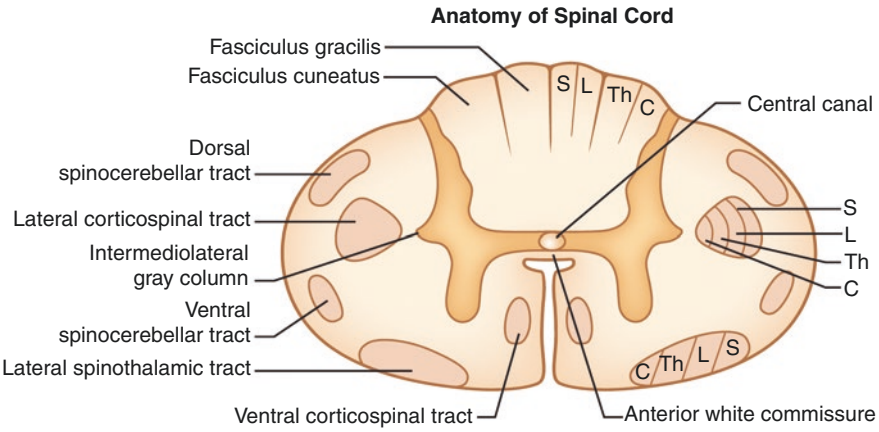

Fig. 2.1 Cross-section of the spinal cord at T2. The three major tracts are shown with their lamination. *C* cervical, *T* thoracic, *L* lumbar, *S* sacral. The lateral corticospinal and lateral spinothalamic tracts have the same pattern. The intermediolateral gray column contains sympathetic system neurons

(dysdiadochokinesis), 4+/5 strength of right interossei and wrist extensors, absent vibratory perception at right toes, ankle, and knee and she makes a few position sense errors at the right toes. She has right Hoffmann's and right Babinski signs. There is a sensory level of pain and temperature at T4 on the left side.

MRI of the cervical spine shows an intramedullary lesion (within cord) as opposed to extramedullary (outside cord, inside dura) and extradural (outside dura).

Diagnosis (by radiologist): Intramedullary neoplasm versus multiple sclerosis.

Diagnosis: Cervical myelopathy with partial Brown-Séquard's syndrome and optic neuropathy O.D. secondary to multiple sclerosis.

An MRI of the brain shows four periventricular T2 and FLAIR hyperintensities, perpendicular to the ventricles. These findings on brain MRI support the diagnosis of multiple sclerosis.

Lessons:

1. *The inadvertent discovery*. A thorough review of systems elicits a history of visual impairment with exercise. Awaiting the patient's spontaneous complaint is unsatisfactory and never an excuse for being unaware of a diagnostic symptom. The symptoms and neurologic findings are sufficient to make a diagnosis without an MRI scan as the patient has two lesions separated in space and time, confirmed by bedside examination. This is the hallmark of multiple sclerosis.

Temporary impairment of neurologic function with fever or exercise is Uhthoff's sign, common with patients who have multiple sclerosis.

2. The patient has Uhthoff's sign, a temporary impairment of neurologic function associated with exercise or fever and common with multiple sclerosis.

Optic nerve disease often causes deficits in color perception (color desaturation); yet visual acuity may remain 20/20.

3. Optic neuropathy is present because of impaired color vision even though visual acuity is normal. Depending on visual acuity to diagnose optic nerve disease is not acceptable.
4. Loss of temperature sensation on one side of the body may be the initial symptom of a myelopathy. Patients are often aware of this problem prior to loss or impairment of pinprick sensibility. Both pain and temperature are mediated through the lateral spinothalamic tract.
5. Unilateral distal weakness usually occurs with corticospinal tract involvement in any of its three locations, cerebral, brainstem, and spinal cord.

Dysdiadochokinesis (impaired rapid alternating movements) occurs with lesions affecting any of the three motor systems, corticospinal, extrapyramidal, and cerebellar.

6. Dysdiadochokinesis (impaired rapid alternating movements) is a common sign of impairment of any of the three motor systems, corticospinal tract, extrapyramidal system, and cerebellar system. In this case it is due to involvement of the corticospinal tract in the spinal cord.
7. Vibration sense loss out of proportion to proprioception (position sense) is a typical pattern with any lesion located at or below the thalamus. Conversely, position sense loss with preserved vibration sense is common with cerebral hemisphere lesions.
8. Asymmetric Hoffmann's signs are abnormal whereas bilateral symmetrical Hoffmann's signs can be normal. A clearly unilateral Hoffmann's sign indicates pathology affecting the corticospinal tract whether cerebral, brainstem, or spinal cord.
9. Babinski signs, unilateral or bilateral, are always abnormal and indicate central nervous system disease involving the corticospinal tract, cerebral, brainstem or spinal cord.

When spinal cord disease is suspected there must be a search for a sensory level.

10. A discrete sensory level is usually diagnostic of myelopathy and may be one to several levels below the location of the lesion. When spinal cord disease is suspected there must be a careful search for this level.

Brown-Séquard's syndrome occurs with spinal cord lesions. There is ipsilateral impairment of motor function, vibration/position sense, increased reflexes with Babinski sign, and contralateral loss of pain and temperature.

11. Brown-Séquard's syndrome is manifested by ipsilateral abnormalities of motor function with weakness and spasticity, increased reflexes, Babinski sign, loss of vibration/position sense and contralateral impairment of pain/temperature. There is contralateral impairment of pain and temperature sensation because of the already decussated lateral spinothalamic fibers.
12. Lastly, multiple sclerosis involves only the central nervous system. Initial involvement with most patients affects the optic nerve, brainstem, or spinal cord.

Motor dysfunction exhibits a predilection for involvement of the legs with monoparesis or paraparesis of spinal cord origin. This may occur with either cervical or thoracic lesions. Triparesis or quadriparesis obviously occurs only with cervical lesions. Bilateral arm weakness alone, "man-in-the-barrel" syndrome, is a rare occurrence which may be a manifestation of high cervical cord lesions. It should be emphasized that weakness is usually most prominent in distal musculature and increased tone of spastic type is a common associated feature. Acute spinal cord lesions may produce greater proximal weakness and loss of muscular tone.

High cervical spinal cord lesions, C1–C4, often cause symptoms in both arms.

The typical sensory symptom is a sensory level to pain and temperature due to involvement of the lateral spinothalamic tract in either cervical or thoracic cord. Although the prototypical sign is a sensory level one or two segments below the level of the lesion, a thoracic sensory level may occur with cervical lesions. Involvement of the dorsal column, fasciculus gracilis and cuneatus, causes ipsilateral loss of vibration and occasionally position sense. Nearly always, vibration sense to a 128 cps tuning fork is lost first, similar to neuropathies. Consequently, depending on proprioception to evaluate this system is not acceptable. Sensory loss may begin in the legs and gradually rises as the lesion progresses. High cervical cord lesions, C1–C4, may result in motor and sensory symptoms involving both arms. The sensory loss may uniquely include so-called "cortical" sensory signs such as astereognosis, poor two-point discrimination and agraphesthesia. Position sense loss may exceed vibratory impairment.

The essential principle is to think cervical myelopathy or radiculopathy first and neuropathy second with bilateral arm symptomatology.

Case 9 A 76-year-old man is admitted to the hospital because of difficulty walking. He complains of dizziness and arthritis of the knees. He adds a history of urinary urgency and frequency. Past medical history is remarkable for hypertension. A recent medical examination shows a normal size prostate. The Emergency Room physician examines the patient in the supine position. Examination reveals normal eye movements, strength, and sensation. Reflexes are 3+ and symmetrical and no pathologic reflexes are found.

A neurology consultant queries the patient in some depth about his dizziness. The patient denies vertigo and lightheadedness, but he feels unsteady and his knees are "stiff."

The neurologic examination is performed best with the patient sitting.

Neurologic examination: Neurologic examination with the patient sitting reveals normal strength but prominent spasticity. Reflexes are 3+, symmetrical and bilateral sustained ankle clonus is obtained. The patient is encouraged to walk and, after briefly refusing, walks stiffly with circumduction of his legs. The neurologist suspects a myelopathy. An MRI scan of cervical and thoracic spine reveals severe cervical spinal stenosis with cord compression at C4–C5.

Diagnosis: Cervical myelopathy secondary to cervical spinal stenosis.

The patient undergoes a cervical laminectomy and both "dizziness and arthritis" resolve over 3 months.

Lessons:

Dizziness has numerous meanings including poor balance, vertigo, blurred vision, lightheadedness, anxiety, and therefore multiple etiologies.

1. Dizziness is a term requiring detailed interrogation of the patient. This patient complains of dizziness but his symptom is due to a gait disorder.
2. The neurologic examination is best performed in the sitting position unless the patient is unable to support himself.
3. Arthritis is a commonly used term which cannot be blindly accepted as accurate without thorough investigation.
4. Unilateral or bilateral sustained clonus and unilateral unsustained clonus are pathologic and indicate involvement of the corticospinal tracts. Symmetrical unsustained clonus is normal.

5. Spasticity is detected by a free interval when passively moving a limb followed by increased resistance to further attempted movement, then a quick giving way (clasp-knife reaction).
6. Pure bilateral corticospinal tract involvement of the legs points to a myelopathy which may be cervical or thoracic.
7. An MRI of the cervical and thoracic spine covers the entire spinal cord. The lumbar region need not be imaged unless there are signs of lumbar root disease (radiculopathy). This will save the patient's insurer a few thousand dollars.
8. Cervical myelopathy secondary to spinal stenosis frequently presents with only involvement of the motor system.

Autonomic dysfunction is common with spinal cord disease. The abnormalities may involve the pupil, blood pressure, bowel, bladder and sexual function.

Autonomic nervous system involvement is common, particularly urinary tract symptoms. Urinary urgency due to a small spastic bladder is the first development. Urinary retention and overflow incontinence is a late development. Constipation is the almost invariable manifestation of bowel dysfunction and is frequently overlooked in view of its commonplace occurrence. The sympathetic nervous system is represented in the intermediolateral cell column of the spinal cord. Hence orthostatic hypotension and Horner's syndrome may be important elements of spinal cord disease, usually intramedullary. Cervical lesions between C1 and T2 can cause Horner's syndrome, an excellent localizing sign. The sympathetic fibers exit at C8, T1–T2 levels. Sexual dysfunction, mainly impotence, may occur.

Radiculopathy [4]

Radiating pain is the cardinal manifestation of radiculopathy whereas spinal cord pathology is much less likely to cause pain unless sensory nerve roots are secondarily affected. When nerve root pain extends from the neck to below the elbow or from the back to below the knee, nerve root origin is likely. When pain radiates from the neck down to the shoulder into the upper arm, or low back pain extends to hip or upper thigh, then pain of muscular origin must also be considered. Pain aggravated solely with arm and leg movement at a specific joint suggests muscle or joint pathology. Radicular pain into one or both arms may be provoked by prolonged (1–3 min) head extension which narrows the cervical intervertebral foramina. Head turning is less likely to provoke radicular pain. Head flexion maintained for a few minutes gradually relieves the pain. This is a practical and simple diagnostic bedside technique.

The primary symptom of radiculopathy is pain which radiates below the elbow or knee. Pain which radiates only to the upper arm or thigh is less certainly radicular.

Focal weakness, fasciculations, and atrophy may occur. In fact, fasciculations are most often observed with cervical and lumbar root pathology since diseases which affect the anterior horn cell, such as amyotrophic lateral sclerosis (ALS), are rare. Reflexes affected by the involved nerve root may be decreased. Quite often, however, deep tendon reflexes are not affected.

Fasciculations occur with root and anterior horn cell disease primarily.

Well-defined sensory loss in the involved dermatome is infrequent. Paresthesias are common. Vibration and proprioception loss is extremely rare since many nerve roots would have to be affected to cause this type of sensory deficit.

Case 10 A 57-year-old man complains of the acute onset of severe right hip and groin pain followed by right leg weakness. He is able to walk only with assistance. He has had chronic low back pain for 2 years, obtaining relief with periodic use of ibuprofen. The patient's past medical history is negative and he takes no medication.

Neurologic examination: Strength of iliopsoas and quadriceps is 4/5, anterior tibialis 4+/5, and there is no knee reflex on the right side. The patient has sensory loss to pinprick along the right medial calf.

MRI (Lumbar): There is a large herniated disk at L5–S1 which is centrally located. A 2-h glucose tolerance test reveals a fasting glucose of 105 mg/dl and a 2-h glucose of 220 mg/dl.

Diagnosis: Lumbosacral plexopathy due to diabetes.

This syndrome has been called diabetic amyotrophy. Iliopsoas musculature is innervated by L1–L3 roots. The knee jerk is L2–L4. The medial calf sensory loss is due to involvement of the saphenous branch of the femoral nerve. All of these findings indicate involvement of the femoral nerve and the peroneal nerve (anterior tibialis weakness), a branch of the sciatic nerve. Plexus lesions affect multiple nerves. The patient achieves good control of his diabetes and is treated with analgesics and physical therapy. He recovers in 6 months.

Lessons:

1. Groin pain is unusual in radiculopathies and immediately raises a warning flag about the significance of the MRI findings.
2. The herniated disk is at a level below the location of the abnormal signs.

3. Iliopsoas weakness implies involvement of L1–L3 nerve roots. The absent knee reflex is consistent with L2–L4 pathology.
4. Perhaps the most helpful finding is numbness on the medial calf indicating involvement of the saphenous nerve. This is a sensory branch of the femoral nerve and is seldom involved in lumbar radiculopathies.
5. Anterior tibialis weakness indicates involvement of the peroneal nerve, a branch of the sciatic nerve, and thus rules out a purely femoral neuropathy.
6. Diabetic lumbosacral plexopathies are not uncommon, may occur as the first sign of diabetes and frequently cause excruciating pain which is often difficult to control. It carries a good prognosis for recovery over 6 months.

See Figs. 2.2 and 2.3 for a review of the brachial and lumbosacral plexus anatomy.

Plexopathy [4]

The brachial plexus incorporates C4–T1 roots and extends from the spinal column to the axilla. Lesions which affect the brachial plexus must, by definition, affect more than one peripheral nerve. Shoulder and arm pain may occur and this can be aggravated by arm movement. Reflexes are decreased. There may be patchy sensory loss especially to pin and touch. Trauma of various origins is the most common

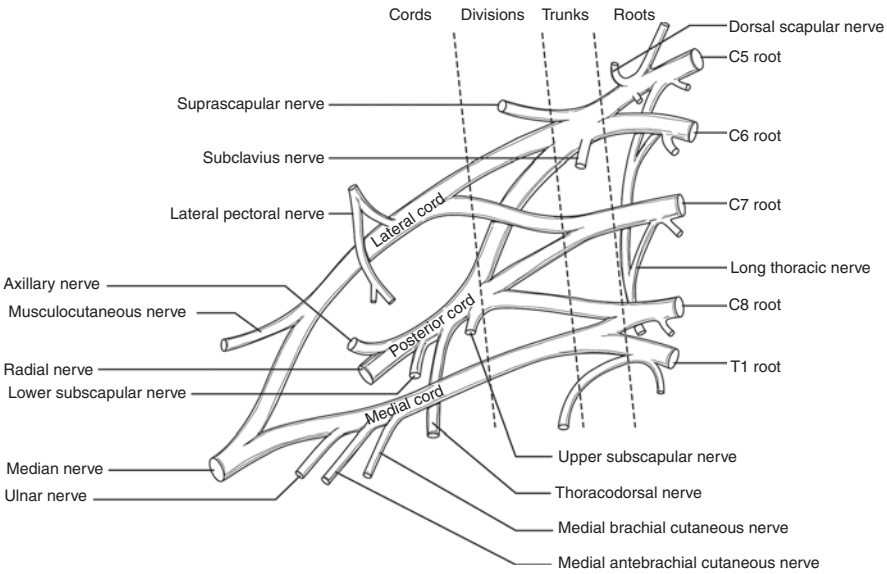

Fig. 2.2 Brachial plexus

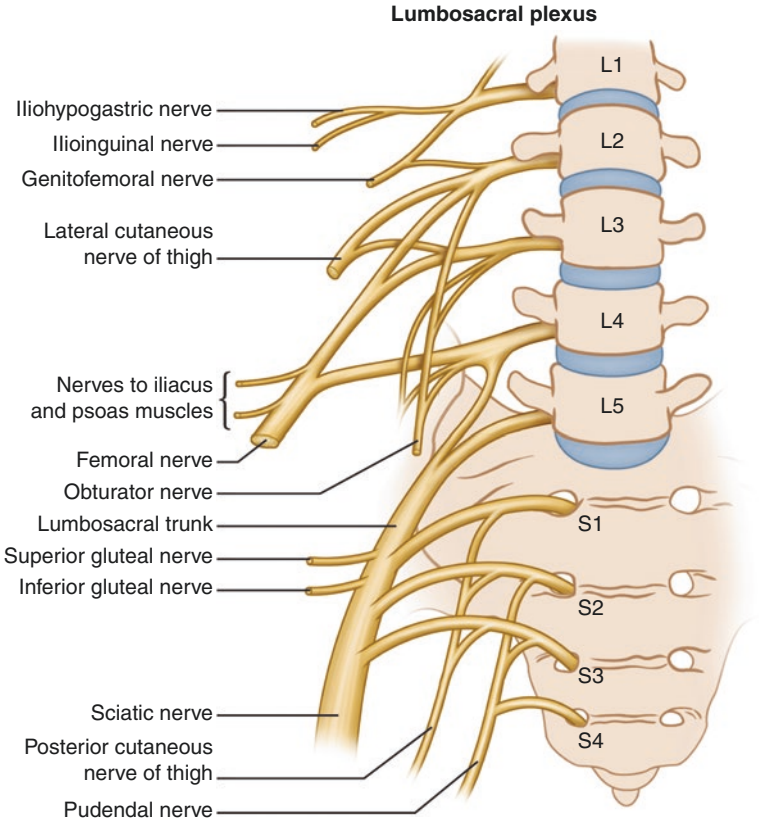

Fig. 2.3 Lumbosacral plexus

etiology and malignant neoplasm such as carcinoma of the lung is the next in frequency. Viral etiology is the least common.

The brachial plexus incorporates C4–T1 roots and the lumbosacral plexus T12–S4 roots.

The lumbosacral plexus includes T12–S4 roots and is located within the psoas major muscle. As with brachial plexopathy more than one nerve is affected. Pain and weakness in more than one nerve distribution and decreased reflexes are the most common findings. Sensory loss may be present in more than one nerve originating from the lumbar plexus but this is usually a minor presenting sign. Diabetes is a common etiology.

Diabetes is a common cause of lumbosacral plexopathy which may precede its diagnosis.

Case 11 A 60-year-old man complains of progressive difficulty walking over a period of 2 years. He states that this is a problem of arthritis manifested by aching in the thighs and calves. In addition, he reports that he has poor circulation in his legs and this was discovered by his previous doctor who has just retired. The patient has type II diabetes and coronary artery disease.

His new family physician does a "focused" examination and finds no dorsalis pedis pulses. He notes pain with hip rotation. Hip X-rays disclose osteoarthritis in both hips. He then refers the patient to a vascular surgeon and an orthopedic surgeon. Studies disclose evidence for small vessel disease in both legs and minor osteoarthritis in both hips. Physical therapy is prescribed.

The patient returns to his family physician 1 month later. He walks in with some difficulty because of bilateral footdrop. A neurology consultation is requested.

One additional month later the patient is brought in to the neurologist's office in a wheelchair. The patient reports rapid worsening of both circulation and arthritis. Moreover, he is now bothered by poor circulation in his hands.

The neurologist takes a full history. He questions the patient about his diagnosis of poor circulation. Initially, the patient states that his previous doctor diagnosed it but eventually divulges his symptoms which are numbness and tingling. He adds that his arthritis is causing muscle aches and weakness. The patient's examination is remarkable for absent reflexes in arms and legs. There is 3/5 strength of anterior tibialis, gastrocnemius, interossei, and wrist extensors. Strength of iliopsoas and quadriceps is 4/5. The patient has no vibratory perception at toes, ankles, and knees. He makes position sense errors at the toes. There is distal sensory loss to pain and temperature in all extremities.

CIDP causes diffuse weakness, distal greater than proximal.

Diagnosis: Chronic inflammatory demyelinating polyneuropathy (CIDP).

Laboratory studies: An electromyogram (EMG) and nerve conduction study reveals marked slowing of nerve conduction velocities. A lumbar puncture is remarkable for a protein of 85 mg/dl but is otherwise normal.

Treatment: Intravenous immunoglobulin restores the patient to near normal over 8 months.

Lessons:

Numbness and paresthesias are neurologic not vascular symptoms.

1. Never accept the patient's diagnosis.
2. Poor circulation does not cause numbness and tingling. These symptoms are typical of involvement of the sensory portion of either the central or peripheral nervous systems. The localization depends on the pattern of loss. In this case the distal portions of all extremities are involved, most compatible with neuropathy.
3. Weakness does not occur with arthritis unless there is an associated neurologic disorder. This patient's weakness is prominent in distal musculature, common with involvement of any portion of the central and peripheral nervous systems except focal radiculopathy and plexopathy. The pattern in this case involves all extremities which suggests neuropathy. Absent reflexes clinch the diagnosis.
4. An incomplete initial history by the family physician triggers referral to the wrong specialists which results in enormous extra costs and increased patient disability.

Neuropathy [5]

The most common neuropathy is bilateral, begins in the feet, and is usually symmetrical or nearly so. Tingling, burning, wet or cold sensations or a feeling of walking on gravel are just some of the descriptive terms used by patients. Involvement of the hands may occur soon afterward or be delayed by years depending on the etiology of the neuropathy. The sensory signs depend on whether it is mainly a small fiber neuropathy (pain and temperature) or large fiber (vibration, position, and touch).

> Distal weakness, sensory loss, and hyporeflexia support the diagnosis of neuropathy.

Strength is usually lost first in distal musculature. Combined sensorimotor neuropathies are common but the sensory symptoms and signs usually predominate. Reflexes are decreased or absent. Rarely, there are pure motor neuropathies such as multifocal motor neuropathy and some acute inflammatory demyelinating polyneuropathies (AIDP) known as Guillain-Barré syndrome, an autoimmune disorder. Although Guillain-Barré syndrome can be mostly a motor neuropathy which produces an ascending paralysis, sensory symptoms are common. Autonomic dysfunction, such as tachycardia, hypertension, and urinary retention, is not infrequent. CIDP is a sensorimotor neuropathy which may begin insidiously and progress steadily over months to years. It manifests itself with neurologic signs often quite similar to AIDP.

> The Romberg test is positive most often with neuropathy, less often with vestibular dysfunction, infrequent with most spinal cord lesions, and rare with cerebellar pathology.

When neuropathies significantly involve large fibers, vibration and position sense loss with an ataxic gait, aggravated in the dark, is often the result. Eye closure in the shower, typically when shampooing, may precipitate falls. A positive Romberg and poor tandem gait are frequent abnormalities. Probably the most common cause of a positive Romberg is a neuropathy followed by acute vestibular disease and, third, a myelopathy. Cerebellar pathology may cause a positive Romberg probably due to lesions involving vestibular-cerebellar pathways. That cerebellar disease can cause a positive Romberg is controversial.

Meralgia paresthetica is a compressive neuropathy which causes variable degrees of pain, paresthesias, and numbness on the lateral thigh.

Focal neuropathies occur due to trauma and compressive lesions. The median nerve is easily compressed at the carpal tunnel. The ulnar nerve is frequently subjected to trauma in the cubital tunnel at the elbow. The femoral nerve can be affected in a mother due to a stretch injury during childbirth. The lateral femoral cutaneous nerve of the thigh can be compressed under the inguinal ligament. This diagnosis is meralgia paresthetica, a very common disorder often mistaken for radiculopathy and has subjected patients to needless laminectomies. The peroneal nerve can be compressed in the popliteal fossa which causes a dropped foot and "steppage" gait.

Case 12 A 68-year-old man complains of progressive leg weakness, painful and stiff muscles over the previous 3 months. He has difficulty climbing stairs. For the last year he has been impotent, complains of a dry mouth, and has constipation. Past medical history is unremarkable.

Neurologic examination: The patient has mild bilateral ptosis. Strength of iliopsoas is 4/5, deltoid 4+/5, and infraspinatus 4+/5, bilaterally. Reflexes in the legs are absent.

Diagnosis: Lambert–Eaton syndrome, a disorder of the neuromuscular junction.

Lessons:

1. Unfortunately, not every patient presents a history diagnostic of a specific anatomic site of pathology.
2. Proximal weakness usually indicates a myopathy or a lesion of the neuromuscular junction.
3. Ptosis suggests myasthenia gravis.
4. Absent reflexes are most compatible with a neuropathy, not myasthenia gravis.
5. Autonomic nervous system dysfunction is present since the patient has impotence, constipation and a dry mouth. This is not expected in either myopathy or myasthenia gravis.

6. This mixed picture occurs with Lambert–Eaton syndrome, a neuromuscular junction disorder. It is caused by an insufficient release of acetylcholine at the presynaptic terminal and 50% of patients have an underlying malignancy.

Neuromuscular Junction [4]

Discussion of the neuromuscular junction must deal with a differential diagnosis since there are just three main disorders to consider.

> Neuromuscular junction disorders such as myasthenia gravis and Lambert–Eaton syndrome usually cause proximal more than distal weakness.

First and foremost is myasthenia gravis. There are numerous presentations, some of which include eyelid droop due to weak levator palpebrae superioris muscles and extraocular muscle palsies causing fluctuating diplopia even, at times, during the same examination. Pseudointernuclear ophthalmoplegia and gaze paretic nystagmus or nystagmoid jerks are not uncommon. Pseudointernuclear ophthalmoplegia refers to isolated medial rectus weakness caused by pure muscular weakness due to myasthenia gravis. An internuclear ophthalmoplegia is caused by a lesion of the MLF in the pons or midbrain ipsilateral to the medial rectus weakness. Weakness of neck musculature may cause a persistent head flexion posture associated with weakness of neck extensor muscles. More often there is weakness only of head flexion. Acute respiratory failure with a prior history of neglected neurologic symptoms is a rare presentation. Dysarthria, dysphagia, facial and extremity weakness are additional common symptoms. All of the symptomatology is likely to worsen later in the day or when the patient is fatigued. Perhaps a key to the diagnosis is the invariable presence of normal mental status, reflex, and sensory examinations. The etiology is an autoimmune disorder due to the production of antiacetylcholine receptor antibodies which destroy the acetylcholine receptors located on the postsynaptic terminal. The antibodies arise from a hyperplastic thymus or thymoma.

> Ptosis, extraocular muscle weakness, dysphagia, dysarthria, fatigue, facial and proximal extremity weakness are common in patients with myasthenia gravis.

Lambert–Eaton syndrome is a rare disorder due to inadequate release of acetylcholine from the presynaptic terminal. It is more common in men. Typical symptoms as described in Case Report 12 include proximal weakness, paresthesias, and autonomic dysfunction such as impotence and hypohidrosis. About 50% of patients

have small cell carcinoma of the lung. There is production of antibodies directed against voltage-gated calcium channels in the peripheral nerve terminals. This results in inadequate release of acetylcholine into the synaptic cleft from the presynaptic terminal. Hence, repetitive nerve stimulation results in an incremental response with the amplitude usually increasing by 2–20 times.

Lambert–Eaton syndrome is associated with proximal weakness, autonomic dysfunction, hyporeflexia, and rarely ptosis.

The third important disorder of the neuromuscular junction is the toxic effect of botulism and aminoglycoside antibiotics. Botulism prevents release of acetylcholine from the presynaptic terminal. Antibiotic-induced neuromuscular disease is related to excessively high drug levels which most often occur with renal failure. This also results in a decreased release of acetylcholine from the presynaptic terminal. Postjunctional membrane sensitivity to acetylcholine is also reduced.

Myopathy [6]

Myopathies usually cause proximal weakness but there are important exceptions such as inclusion body myositis and myotonic dystrophy.

The key to the diagnosis of myopathy is the usual absence of sensory complaints. Myopathies are ordinarily slowly progressive disorders. The history should focus on how the weakness affects the patient. Is there difficulty raising the arms to comb their hair? Is climbing steps the main problem or is it opening jars? Are eye movements, chewing, and swallowing affected?

The examination most often reveals proximal muscle weakness. However, distal weakness is not rare and occurs in some myopathies such as myotonic dystrophy and inclusion body myositis. A major diagnosis to consider on the basis of anatomy is involvement of the anterior horn cell such as in amyotrophic lateral sclerosis (ALS) or one of its variants, spinal muscular atrophy. Fasciculations, often associated with atrophy, are hallmarks of anterior horn cell disease and radiculopathy but not present in myopathy. A disorder of the neuromuscular junction, particularly myasthenia gravis, must be excluded although progressive weakness which is not variable during the day would be quite uncommon.

Wasting and decreased to absent reflexes can be present but are usually late in the course of a myopathy. Painful cramps are not unusual. Autonomic dysfunction such as a disorder of bladder function does not occur.

Case 13 A 51-year-old woman complains of neck, hip, and knee pain. For 3 months she reports that the pain has prevented her from getting out of a chair and even off

the toilet. Additionally, she has numbness and tingling of both feet. She has had rheumatoid arthritis for 12 years and has numerous joint deformities affecting the wrists, proximal interphalangeal joints, and knees. She has been on long-term treatment with low-dose prednisone and methotrexate.

Examination: Neurologic examination reveals several abnormalities which include absent reflexes in the legs and loss of vibration perception at the toes. Strength of head flexion is 4+/5, iliopsoas 4/5, quadriceps 4+/5, and anterior tibialis 4/5.

What is causing her disability?

Neurologic diagnoses:

1. Steroid myopathy.
2. Neuropathy associated with rheumatoid arthritis.

Laboratory data: EMG confirms both diagnoses as there are polyphasic low amplitude muscle potentials in proximal leg musculature which are typical for myopathy. There are also mildly slow nerve conduction velocities with occasional fibrillations in the anterior tibialis muscle which are characteristic for neuropathy.

Lessons:

1. Proximal weakness is common in myopathy and infrequent in neuropathy.

> Weakness of head flexion and less often head extension are often affected in myopathy.

2. Testing head flexion and extension is essential when myopathy is suspected as these muscles are often involved. Myasthenia gravis, acute inflammatory demyelinating polyneuropathy, and chronic inflammatory demyelinating polyneuropathy also commonly affect these muscles.
3. The patient's disability relates to strength but not sensory symptoms.
4. The patient has a neuropathy because of absent reflexes, distal sensory loss to vibration perception, and weak distal musculature.
5. In summary, this patient has two diseases, certainly not unusual in this clinical setting.

Meningeal Disease [5]

Case 14 An 89-year-old man complains of neck and severe low back pain for the last 2 weeks. After a 10-min evaluation a harried primary care physician refers him to an orthopedic surgeon. An MRI scan reveals marked spinal stenosis as well as severe stenosis of neural foramina at levels L3–L4 and L4–L5. He is referred for

physical therapy. The pain resolves gradually over 3–4 days but 1 week later suddenly increases and is unbearable.

A neurology consultation is requested before considering a lumbar laminectomy. The neurologist takes a full history. The low back pain is nonradiating. The neck pain is nearly as severe. Just prior to the onset of his symptoms the patient now recollects that he had brief double vision lasting about 2 h. He had forgotten about it.

Examination: Neurologic examination reveals asymmetric pupils, O.S. 4 mm with a 1+/4 reaction to light, and O.D. 2.5 mm with a 4+/4 reaction to light. The patient's neck is mildly stiff on flexion but not with head turning.

A CT scan (brain) shows blood in the subarachnoid spaces. Angiography demonstrates a left posterior communicating artery aneurysm.

Lessons:

1. It is essential to take a complete neurologic history even when the patient has low back pain. Questions regarding memory, speech, vision, etc., may yield diagnostic information as it did in this case.
2. Low back pain which does not radiate is not a common presenting symptom for spinal stenosis or a herniated disk. Radicular pain is ordinarily present with either condition.
3. Never accept as fact another doctor's diagnosis without personal investigation. A physician may have a stellar reputation but who has not made mistakes?
4. Neck and low back pain are symptoms which are not unusual in patients who have a subarachnoid hemorrhage.
5. The large pupil with a slow reaction to light supports compression of the left third nerve by an aneurysm, typically internal carotid or posterior communicating. The pupillary fibers are superficial and most often the first sign with aneurysms in this location since they are easily compressed.

Low back pain without radiation is more often of muscular origin rather than a herniated disk or spinal stenosis. Unusual causes include subarachnoid hemorrhage, rigidity of Parkinson's disease and metastatic bone disease.

The diagnosis of meningeal irritation may appear simple since most patients have flagrant neurologic symptoms and signs. There are many patients, however, who have subtle presenting manifestations. Of necessity, this section will focus on differential diagnoses, cerebrospinal fluid studies, and practical management issues but not on treatment since, as previously noted, radical changes will likely occur in the future.

Acute meningeal disease is due to either infection or hemorrhage. Leptomeningeal carcinomatosis usually develops gradually.

Five percent of patients with subarachnoid hemorrhage have normal CT scans. Therefore, in that event, a lumbar puncture is required to exclude hemorrhage as well as evaluate for infection.

Case 15 A 38-year-old woman complains of periodic impairment of speech for 1 week. An outpatient evaluation included a carotid Doppler study which revealed a high-grade left internal carotid artery stenosis. CT scan (head) was normal.

A neurology consultant elicits additional history after the review of all neurologic symptoms. The patient reports a mild (2/10) intermittent occipital headache for 4 weeks easily relieved with acetaminophen. She did not mention it to her primary care physician because she felt it was insignificant. Her physician did not question her about headache. The headache had increased in severity over a few days just prior to this evaluation.

Neurologic examination: Neurologic examination is significant for bilateral high cervical carotid bruits. She makes an occasional semantic (verbal) paraphasia such as calling her elbow a bone and her wrist a knee. There is mild end nuchal rigidity, i.e., her neck is initially supple but toward the end of passive flexion there is increased resistance. As noted above a CT scan of the brain was normal.

Nuchal rigidity can be a subtle finding present only with full head flexion.

The initial impression of the neurologist is suspected subarachnoid hemorrhage possibly due to a left middle cerebral artery aneurysm.

The studies performed included a lumbar puncture which revealed bloody fluid. When centrifuged, the supernatant was xanthochromic (yellowish). This secured the diagnosis of subarachnoid hemorrhage. The protein was 102 mg/dl, glucose 70 mg/dl, red blood cells 17,000/cu mm and wbc 1320/cu mm with 90% neutrophils. Angiography demonstrated band-like constrictions of both internal carotid arteries at the C2, C3 level associated with bilateral moderate stenoses. In addition, there was a left middle cerebral artery aneurysm. An MRI of the brain revealed a small left temporal lobe infarction.

Lessons:

1. Subarachnoid hemorrhage is not necessarily an acute catastrophic event.
2. Angiography disclosed fibromuscular dysplasia which is associated with cerebral aneurysms.
3. This patient's aphasia and temporal lobe infarction may have been due to vasospasm associated with subarachnoid hemorrhage, embolism from a thrombus in the aneurysm to a distal middle cerebral artery branch or embolism from fibromuscular dysplasia which has caused a left internal carotid artery stenosis. Vasospasm is the most likely etiology since embolism from a thrombus in an aneurysm is not as common and stroke caused by fibromuscular dysplasia is rare.

4. Normal CT scans of the head occur in 5% of patients with subarachnoid hemorrhage and one cannot depend on it to make a diagnosis. A lumbar puncture is essential.

Cerebrospinal fluid xanthochromia (yellow) is detected about 10 h after hemorrhage. This is found in the supernatant after centrifuging bloody CSF. It persists for 2–4 weeks.

5. A traumatic tap is excluded because of the presence of xanthochromia present in the supernatant after centrifuging of spinal fluid. Xanthochromia is due to the presence of bilirubin which causes the yellowish color and is present approximately 10 h after the hemorrhage has occurred. Xanthochromia persists for 2–4 weeks. Increased bilirubin due to liver disease produces a yellowish color but a serum bilirubin of 10 mg/dl or more is required before the spinal fluid changes color. Markedly elevated spinal fluid protein, greater than 150 mg/dl, may also produce a faint degree of xanthochromia. In the first few hours after subarachnoid hemorrhage the spinal fluid often appears pink which is due to oxyhemoglobin.

A second method of ruling out a traumatic tap is comparing the red blood cells to the white blood cells. The ratio in blood is 700:1, respectively. If this ratio is decreased, meaning an increased wbc count due to inflammation, a diagnosis of subarachnoid hemorrhage is supported.

Case 16 A 72-year-old man enters the emergency room because of a 12-h history of headache and horizontal double vision. This began the previous night. At that time he had a severe occipital headache and double vision when looking to the left. In addition, he reports a chronic cough with production of yellowish sputum over the last few weeks. His past medical history is remarkable for hypertension and heavy smoking.

Examination: Examination reveals a blood pressure of 230/120 and temperature of 102 °F. He has rales at the left base. There is mild nuchal rigidity. Funduscopic examination shows blurred optic disks bilaterally, absent venous pulsations, and one flame-shaped hemorrhage at the right optic disk margin. Vision is normal. The patient has a left lateral rectus paresis due to left sixth nerve involvement. A CT scan of the brain is ordered stat, but the unit has just broken down. The medical resident's thoughts are as follows: The funduscopic picture suggests papilledema. Furthermore, the sixth nerve palsy is an early sign of increased intracranial pressure. If that is the case, is there a risk of uncal herniation by doing a lumbar puncture?

What do these neurologic signs mean and what is the best management:

1. Nuchal rigidity and fever indicate meningeal disease, in this instance, hemorrhage or infection.

2. A high fever over 101 °F usually indicates infection.
3. A sixth nerve palsy is an early sign of increased intracranial pressure.

> Ophthalmoscopic findings in papilledema include: blurred disk margins, especially temporal side, absent venous pulsations and hemorrhages at the disk margins.

4. Papilledema is present. The three major findings of papilledema include:
   (a) Blurred optic disk margins. Initially the nasal margin is blurred followed later by the temporal margin. Nasal blurring is also a common normal variation and, therefore, the temporal margin is the focus of attention.
   (b) Venous pulsations are absent in papilledema, but approximately 5–10% of normal people have no visible venous pulsations.
   (c) Hemorrhages at the disk margins are virtually diagnostic of papilledema. The hemorrhages are usually splinter or flame-shaped.
5. The risk of uncal or tonsillar herniation, especially in the absence of a cerebral, brainstem or cerebellar lesion on a clinical basis, is negligible.

A lumbar puncture is performed. There are 800 wbc/cu mm, 95% of which are neutrophils. The glucose is 30 mg/dl with a simultaneous blood sugar of 110 mg/dl, significantly less than the two-thirds of the blood sugar which would be expected in normals. The protein is 120 mg/dl, markedly elevated. The gram stain shows gram-positive organisms. Appropriate treatment is initiated for bacterial meningitis.

Synopsis

1. Technique of making a neurologic diagnosis
   (a) Anatomic localization
   (b) Differential diagnosis determined by anatomic localization
2. Anatomic diagnosis
   (a) Cerebral dysfunction, right, left, bilateral, or encephalopathy
   (b) Extrapyramidal
   (c) Brainstem/cerebellum
   (d) Spinal cord (myelopathy)
   (e) Root (radiculopathy)
   (f) Plexus (plexopathy)
   (g) Nerve (neuropathy)
   (h) Neuromuscular junction
   (i) Muscle (myopathy)
   (j) Meninges

3. Characteristic and diagnostic features of:

   (a) Cerebral disease

      (i) Aphasia
      (ii) Dementia
      (iii) Seizures
      (iv) Homonymous hemianopsia
      (v) Abnormalities of mood, personality and behavior associated with abnormal neurologic signs

   (b) Extrapyramidal disease

      (i) Abnormal involuntary movements/postures
      (ii) Hypokinetic or hyperkinetic
      (iii) Gait disorder can be the sole manifestation

   (c) Brainstem/cerebellar

      (i) Crossed findings, e.g., right facial weakness and left hemiparesis
      (ii) Abnormal eye movements and/or pupils indicating this localization
      (iii) Pure cerebellar system signs which occur with brainstem and/or cerebellar pathology

   (d) Myelopathy

      (i) Sensory level
      (ii) Monoparesis, paraparesis, triparesis, cruciate paresis (e.g., right arm and left leg), quadriparesis, and hemiparesis
      (iii) Associated signs include spasticity, asymmetric hyperreflexia, Babinski signs, and asymmetric Hoffmann's signs

   (e) Radiculopathy

      (i) Root pain and/or paresthesias typically affecting one limb
      (ii) Decreased reflex and focal weakness in root distribution
      (iii) Sensory symptoms/abnormalities in dermatome pattern

   (f) Plexopathy

      (i) Disorder affecting multiple roots ordinarily in only one limb
      (ii) Motor signs predominate
      (iii) Pain often severe

   (g) Neuropathy

      (i) Ordinarily begins in both feet unless there is localized entrapment
      (ii) Decreased to absent reflexes
      (iii) Early signs may be distal sensory loss to temperature and pin (small fiber) and/or diminished vibratory perception distally (large fiber). Position sense loss is a much later development (large fiber).
      (iv) Light touch loss distally is virtually diagnostic

(h) Neuromuscular junction (myasthenia gravis)

(i) Fluctuating weakness worse later in the day
(ii) Extraocular muscle weakness, dysarthria, dysphagia, and especially head flexion/extension weakness. Proximal muscles are preferentially affected.

(i) Myopathy

(i) Weakness commonly proximal and often involving head flexion and/or extension
(ii) Distal weakness may occur, mostly notably in myotonic dystrophy and inclusion body myositis
(iii) No change in reflexes and no sensory loss

Multiple Choice Questions

1. A 47-year-old woman complains of a 1 week history of left leg weakness. The neurologic examination discloses mild weakness of all muscles of the left leg. The right ankle jerk is 1+ and the left is 2 + .

   Which one or more of these locations could be the site of the lesion?

   (a) Cerebral
   (b) Cerebellum
   (c) Spinal cord
   (d) Root
   (e) Nerve
   (f) Neuromuscular junction

2. A 77-year-old man has the sudden onset of slurred speech 24 h after a transurethral resection of the prostate. He has diabetes and hypertension.

   Neurologic examination reveals a blood pressure of 170/110 and a left carotid bruit. The patient is oriented to person only. His speech is dysarthric. He remembers 1 of 3 words after 1 min has elapsed.

   (a) Where is the lesion?

   (i) Left cerebral hemisphere
   (ii) Right cerebral hemisphere
   (iii) Brainstem
   (iv) Bilateral cerebral hemispheres

   (b) What test should be ordered urgently?

   (i) CT scan (brain)
   (ii) Carotid Doppler
   (iii) CBC, electrolytes, blood urea nitrogen, glucose
   (iv) MRI (brain) and MRA (head and neck)

3. A 41-year-old man is admitted to the hospital because of acute onset of vertigo and vomiting. He has diabetes and smokes one pack of cigarettes per day.

   Neurologic examination reveals a blood pressure of 150/100. He has horizontal gaze-evoked nystagmus.

   Where is the lesion?

   (a) Semicircular canals
   (b) Brainstem
   (c) Eighth nerve
   (d) Temporal lobe
   (e) Brainstem or eighth nerve

4. If the lesion is in the brainstem, what are the two most likely etiologies?

   (a) Vascular
   (b) Infectious
   (c) Neoplasm
   (d) Demyelinating
   (e) Metabolic

5. An 80-year-old man complains of progressive weakness and clumsiness of the left arm of 2 months duration.

   Examination discloses mild weakness of interossei and wrist extension, impaired rapid alternating movements of the left arm, 3+ reflexes in the left arm and 2+ in the right arm.

   Where is the most likely site of the lesion?

   (a) Cerebral
   (b) Brainstem
   (c) Cerebellum
   (d) Spinal cord
   (e) Nerve

6. A 55-year-old woman complains of severe right anterior thigh pain which is aggravated by prolonged sitting and relieved by walking. This began insidiously about 8 months ago and is progressing in severity. She has developed weakness over the last 2 weeks and finds it difficult to climb stairs.

   Neurologic examination: Strength of right iliopsoas and quadriceps is 4+/5. There are prominent fasciculations over the anterior thigh. The right knee reflex is 1+ and the left is 3 + . Where is the lesion?

   (a) Cerebral
   (b) Spinal cord
   (c) Root
   (d) Plexus
   (e) Nerve

7. In the case described in No. 6, what etiology should be considered and why?

   (a) Neoplasm
   (b) Structural/degenerative
   (c) Degenerative
   (d) Inflammation
   (e) Infectious

8. A 40-year-old man has a 3 day history of rapidly progressive slurred speech and difficulty swallowing liquids. He has insulin-dependent diabetes mellitus.

   Neurologic examination: The patient has dysarthria, bilaterally sluggish palate movements but a normal gag response and mild weakness of head flexion. Where is the lesion?

   (a) Cerebral
   (b) Brainstem
   (c) Cranial nerve
   (d) Neuromuscular junction

9. What is the etiology of the case described in No. 8?

   (a) Vascular
   (b) Autoimmune
   (c) Neoplasm
   (d) Demyelinating

10. What is the most important factor for an accurate neurologic diagnosis?

    (a) Past medical history
    (b) Family history
    (c) Present illness and neurologic examination
    (d) Neuroimaging
    (e) Blood test results

Answers

1. (a) and (c).

   Leg weakness will occur with all of the diagnoses except cerebellum. Nerve, root, or plexus lesions produce a decreased not an increased reflex. Neuromuscular junction disorders do not affect reflexes and usually cause proximal weakness. The increased ankle reflex indicates involvement of the corticospinal tract which is cerebral, brainstem, or spinal cord. Brainstem disease cannot be excluded but without brainstem signs is very unlikely.

2. (a) iv.

   Disorientation and poor short-term recall indicate bilateral cerebral dysfunction (encephalopathy). Dysarthria is nonlocalizing. Carotid bruits are not relevant in this case.

   When there is bilateral cerebral dysfunction a search for metabolic derangement comes first. Abnormalities of electrolytes are not rare after transurethral prostate resection. This patient has hyponatremia.

   (b) iii.

3. (b).

   The nystagmus has two directions which indicate brainstem or cerebellar disease. Eighth nerve or semicircular canal lesions are unidirectional. Cerebral lesions do not cause nystagmus except as a manifestation of a seizure.

4. (a) and (d).

   Vascular disease is suspected because of diabetes and a smoking history. Multiple sclerosis is possible since he is in the right age range (20–50 years) and the brainstem is often affected.

5. (a).

   A brainstem lesion is possible but usually affects other functions commonly eye movements and causes crossed findings, especially when progressing in severity. Cerebellar lesions cause neither weakness nor asymmetric reflexes. Spinal cord disease is possible but usually involves a leg first. Nerve pathology would decrease the reflexes. Distal weakness associated with poor coordination and hyperreflexia of an arm is most consistent with a cerebral lesion. Impaired rapid alternating movements occur with involvement of any of the three motor systems, corticospinal, extrapyramidal, and cerebellar. The steadily progressive worsening suggests neoplasm.

6. (c).

   Cerebral disease does not cause fasciculations or pain and usually affects distal musculature. Spinal cord pathology does not cause pain sitting and relief standing. Also it seldom produces severe pain. Plexus lesions are painful but the pain persists in any position. It also affects more than one nerve. Fasciculations and pain are characteristic features of radiculopathy.

7. (a) and (b).

   The focal findings suggest L3–L4 radiculopathy. This slow progressive course raises the possibility of a benign neoplasm such as meningioma or schwannoma but not the elimination of pain with walking. A herniated disk explains the alteration in pain with changes of position although the usual course is not one of steady progression. Neuroimaging will determine the diagnosis.

8. (d).

   Cerebral disease seldom affects swallowing. Brainstem lesions usually cause crossed findings, abnormal eye movements and affect long tracts such as the corticospinal and lateral spinothalamic tracts. Bilateral palate weakness due to a medullary lesion is not in a single arterial distribution. Thus a brainstem infarction is extremely unlikely. Cranial nerve involvement might explain the findings but the etiology, Guillain-Barré syndrome, rarely presents in this fashion. This patient has a disease affecting the neuromuscular junction, myasthenia gravis.

9. (b).

   Myasthenia gravis is the prototypical neuromuscular junction disorder. It is caused by antiacetylcholine receptor antibodies which attack the acetylcholine receptor site on the postsynaptic membrane.

10. (c).

    The past medical history may aid in the differential diagnosis but many patients with diabetes, for example, may develop cancer, demyelinating disease, or degenerative disease. The family history is much less likely to be of value for similar reasons. Neuroimaging is precise but if the wrong structure is imaged, it is of no value. Blood test results are valuable if the ones selected pertain to the differential diagnosis. The present illness and neurologic examination are likely to lead to an accurate neuroanatomic diagnosis and thus to the appropriate diagnostic tests.

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Chapter 3
The Neurologic History Holds the Diagnostic Keys

Obtaining a complete history by employing a methodical, unhurried approach is the key to an accurate diagnosis. The initial focus must be on the anatomic localization which invariably determines the differential diagnosis. Paresthesias of the left leg, for example, may indicate a compressive peroneal neuropathy, lumbar radiculopathy from a herniated disk, spinal cord disease, or a right cerebral lesion. This type of diagnostic dilemma is a frequent reason to request a neurologist's opinion. An MRI scan of the lumbar spine may be completely normal, dumbfounding the patient's physician. Conversely, a herniated disk with nerve root compression may be treated surgically without alleviation of the patient's symptoms which are due to a brain tumor. Furthermore, it is quite common to find a herniated disk which is asymptomatic. Needless to say, technology with all of its benefits has major limitations. It resolves numerous difficulties of a differential diagnosis but can easily lead to inappropriate treatment by an unwary physician.

Amongst experienced neurologists there is a fear, with some justification, that current neurology residents are better trained in interpretation of MRI scans and pharmacological applications than obtaining a history sufficient to make an accurate anatomic diagnosis. The chief complaint followed by a detailed history of the present illness remains the bedrock necessity of a precise diagnosis. In an outpatient setting perhaps 75–90% of the time spent with the patient should focus on this history. Physicians are often confronted by patients who rapidly spew forth symptoms that he or she feels are valuable. They may censor out critical information due to fear of time constraint. Scarcity of time will therefore undermine the physician's ability to care for his patient as well as interfere with the doctor–patient relationship. Administrative mandates of time allotment for an office visit have already reduced the quality of care. Is there time for demonstrating empathy which will allow the patient to more easily divulge the symptomatology that may be the key to the diagnosis and efficacious treatment?

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The following comments will digress from the specific field of neurology, but instead review my personal opinions of interviewing a patient. The physician should be groomed and dressed in a style which is compatible with the geographic location of the practice and the type of patient population. Significant deviation may engender distrust or focus on the physician to the detriment of free communication.

Entry into the room should not be rushed but deliberate and direct. Use of the patient's first name on first meeting may be appreciated by some patients but sound discourteous to others. The decision about how to greet the patient in the future should be made after the first visit. Although a woman may not expect a handshake at first meeting, that tradition is fast becoming obsolete and rightly so. The initial physically firm grasp with eye contact sets the stage for a frank discussion of all symptoms. The door must then be closed to ensure privacy.

The physician and the patient should be seated comfortably in a chair which will give the patient a sense that the doctor will spend some time listening to him before moving on to an examination or, for that matter, out of the room. Today, many patients simply jump on the examining table expecting only a cursory review of symptoms and are often astonished at a relaxed interview. Since the neurologic history is likely to be lengthy, probably 15–30 min for an initial visit, it is best for the physician to be seated facing the patient to enable him to watch for expressions that may tip off the relative importance of some symptoms. Keeping one's head down or turned to a computer screen may be a turnoff for many patients. How does one express interest without eye contact? Despite improved documentation and efficiency the consequence is rising patient dissatisfaction and often a search for alternative therapies which provide a soothing physical touch and ample time for communication. Chewing gum is obviously unacceptable as it implies boredom with "just another patient." Irritating habits such as tapping one's finger or pen indicates impatience which is likely to either irritate or intimidate some people. Frequent interruptions disrupt the patient's thinking and prepared organization for the visit. This may provoke omission of major portions of the history. On the other hand, gentle prodding back to essentials may be necessary in many cases. Comments that I have found useful for verbose patients who are circumstantial or tangential in their replies are: "Please slow down as you are going a little too fast for me." and "Could you describe your main problem again so I can understand it more completely?" A few smiles often relaxes and encourages the patient to be candid.

The history of the present illness remains the foundation of an accurate neurologic diagnosis. Emphasis must be placed on the chief complaint. Here are a few interesting examples from my practice followed by brief explanations (see Table 3.1).

Explanations

1. Any symptom which is repetitive, stereotyped and with brief duration of a few seconds to a few minutes may potentially be of epileptiform origin. This can be a movement, sensation, or psychic experience.
2. Movement or gait disorders require a thorough inquiry about other normal movements such as turning in bed, turning around while walking, getting out of a chair, writing, and using eating utensils.

Table 3.1 Analysis of the chief complaint [1]

Interesting examples of chief complaints	Follow-up questions by an experienced neurologist	Answers	Diagnosis
My teeth periodically chatter even if I am not cold	For how long do they chatter?	1 or 2 min	Simple partial seizures of the jaw caused by a convexity meningioma
I sometimes have to run to catch up with myself	Do you have difficulty getting out of a chair?	Yes	Parkinson's disease with festinating gait or propulsion
Mother becomes very thirsty and does not know it (history from daughter)	How do you know she is thirsty?	She licks her lips frequently	Complex partial seizures with automatism, idiopathic
I cannot chew chicken	Why not?	My jaws ache	Temporal arteritis with jaw claudication
My hands feel as though they are dipped in wax	Do you have any problem identifying coins in your pocket?	Yes	Cervical myelopathy due to a meningioma compressing the dorsal portion of the spinal cord at C3–C4
I have to test the bath water temperature with my right leg	Why not your left leg?	I have scalded it	Thoracic myelopathy due to multiple sclerosis
When my friend told me she had breast cancer, I collapsed and fell on the floor	Have you suddenly collapsed at other times?	Yes, when I am told a joke	Cataplexy, a near constant finding in patients with narcolepsy
My brain is turning at the base of my skull	When does this occur and how long does it last?	It always occurs in bed, sometimes when I turn over and it lasts less than 1 min	Benign paroxysmal positional vertigo
When I laugh, the back of my head hurts	Do you have any difficulty walking?	Yes, I have arthritis and my legs are getting stiff	Chiari Malformation Type 1 causing spasticity due to spinal cord compression
I hear the same phrase spoken even after changing the TV channel	Do you have any trouble understanding conversation?	Yes, that seems to have been a problem developing over the last few months	Glioma, left posterior temporal region, associated with auditory perseveration
I found a hand lying on my stomach one night when I woke up early	Was anyone with you at the time?	No, my husband was out of town at a meeting	Right cerebral infarction with the syndrome of autotopagnosia
I see Mickey Mouse flying into my left eye	How often do you see him and for how long on each occasion?	It has been occurring a few times a week for the last 2 weeks and I see him for about 15 s	Simple partial seizures with formed visual hallucinations due to a right cerebral infarction, parietotemporal

3. A history obtained only from family members is likely to include their interpretation of the patient's symptoms which may not be accurate. The basis for their conclusion should be clarified.
4. Jaw pain may be due to local pathology in the teeth, gums or temporomandibular joint, neuropathic pain such as the knife-like electrical pain of trigeminal neuralgia or ischemic pain of muscular origin which occurs with prolonged, repetitive muscular activity. In the absence of trauma ischemic pain must be considered in this case. Inflammatory disease of the internal maxillary artery is a relatively common feature of temporal arteritis.
5. The key word here is "bilateral," hence suspected spinal cord disease. The second element is inability to feel texture yet perceive pain, temperature, and light touch. This is termed "astereognosis," an uncommon but well-described consequence of damage to the posterior columns.
6. As an isolated symptom, impairment of temperature perception is nearly always due to a myelopathy with localized pathology affecting the contralateral lateral spinothalamic tract.
7. The sudden collapse without prodromal symptoms has also been called a "drop attack" which is associated with several disorders such as cataplexy, vertebrobasilar disease, complete heart block, Ménière's disease with otolithic crisis and basilar migraine. These diseases require specific questions to ascertain the diagnosis.
8. "Turning" is the key word. Although not invariably the case it implies vertigo. A brief duration of vertigo, less than 1 min, is typical of benign paroxysmal positional vertigo. Provocation with movement is another feature and will be discussed in Chap. 10.
9. Laughing, coughing, sneezing, or any strain will trigger a momentary increase in intracranial pressure which is transmitted throughout the brain and spinal cord. In this instance the cerebellar tonsils are displaced downward and are impacted on the foramen magnum causing pain. Arthritis is so common that many patients use that term to describe a variety of symptoms which may include spasticity.
10. Complex abnormalities of audition suggest central nervous system disease. Impaired comprehension, an element of aphasia, with intact hearing supports the diagnosis of a dominant hemisphere posterior temporal lobe lesion, nearly always left side.
11. Inability to recognize a part of one's own body is called "autotopagnosia" which is generally associated with a nondominant hemisphere lesion.
12. Formed visual hallucinations, such as Mickey Mouse in this case, are known to be associated with temporal lobe lesions. Unformed visual hallucinations such as geometric shapes occur with occipital lobe pathology. The signal feature here is the localization to the left eye which implies the left visual field, hence a probable focal lesion rather than an organic psychosis. Thus a right temporal lobe lesion is likely. Stereotypical brief events with preservation of consciousness indicates a simple partial seizure.

For a neurologist the chief complaint is best given without the past medical history or irrelevant comments on race or ethnicity. In any of the above-cited examples would it be immediately essential to know that the patient was diabetic, hypertensive, or that he or she was Asian-American or African-American? Why not use the most revealing exact words of the patient? The past medical history can be expanded upon in the section of past medical history. Ethnicity can be added to the social history if deemed relevant although it is seldom pertinent for diagnostic purposes. Can a 45-year-old Native American man with hypertension have a brain tumor? Certainly. Can a diabetic African-American woman with painful paresthesias of one arm have a herniated cervical disk rather than neuropathy? Absolutely and most probable. Diabetic neuropathies ordinarily are symptomatic in the feet first.

A typical example of misdiagnosis with superb although uninformed medical care follows:

Case 1 A 79-year-old man complains of three "blackouts" in the last 2 weeks. He fell twice as his legs "gave way." He did not lose consciousness and denies memory loss, impaired speech, numbness, tingling or subsequent weakness. There was no tongue biting or urinary incontinence. He momentarily lost his vision.

Past medical history includes diabetes, morbid obesity with a body mass index of 40, and hypothyroidism. Medications are metformin, losartan, and levothyroxine. He smokes one pack of cigarettes per day.

Neurologic Examination Blood pressure 110/70. Pulse 88, regular. He has bilateral high-pitched mid-cervical carotid bruits. Ankle reflexes are absent. Vibration sense is absent at toes and ankles.

Carotid Dopplers show 50–70% stenoses, bilateral.

Diagnosis Transient ischemic attacks.

Neurology consultation is requested regarding:

1. Should carotid angiography be performed?
2. If stenosis is confirmed, should a carotid stent or surgery be performed?
3. Which side should be treated first?

The neurologist's assessment focuses on the history, repeating many of the questions already asked.

1. Are you certain that you did not lose consciousness? "Yes."
2. Did you lose vision? "Yes." For how long? "Less than 1 min."
3. Did everything turn pitch black or just blank, like nothing was there? "Pitch black."
4. You fell twice. What happened the other time? "I just sat down."
5. Why did you sit down? "I was short-winded and felt dizzy."
6. Did you have a spinning sensation, lightheadedness or loss of balance? "Lightheadedness."

7. What were you doing when you fell? "I was walking out of the bathroom once and the other time I had just gotten out of bed and walked outside to get the newspaper."
8. Had you urinated or moved your bowels before walking out of the bathroom? "I had just urinated."
9. How long had you been out of bed when you picked up the newspaper? "2–3 min."

Analysis

1. Visual loss in this context can be due to retinal, optic nerve, optic tract, optic radiation or occipital lobe disease.
2. This is *not* amaurosis fugax which affects only one eye due to retinal ischemia.
3. Transient blackness usually indicates retinal ischemia. Absent vision (blank) suggests occipital lobe disease.
4. Bilateral ischemia implies poor retinal perfusion which occurs with hypotension. Usually brief blindness, described as nothing there, is most common with transient ischemic attacks in the basilar artery-bilateral posterior cerebral artery distributions.
5. Prodromal symptoms of dizziness occur with hypotension. Shortness of breath is probably due to insufficient perfusion of the lung apices.
6. After urination there is commonly a drop in blood pressure associated with a vagal response since bladder contraction is parasympathetic and the latter causes a decreased heart rate. A contributing factor is diminished sympathetic tone associated with inadequate peripheral vasoconstriction.
7. Three episodes in 2 weeks implies a predisposition, an underlying dysfunction of the autonomic nervous system.
8. The neurologic examination is identical but further assessment of blood pressure is indicated.

   Blood pressure supine is 118/75 with a pulse of 80.
   Blood pressure sitting is 115/70 with a pulse of 84.
   Blood pressure standing at 1 min is 110/65 with a pulse of 88.
   Blood pressure after standing for 3 min is 78/50 with a pulse of 100. (The patient feels dizzy.)

9. *Diagnosis*: Diabetic neuropathy and autonomic neuropathy.
10. *Summation*:

    (a) Duration is less than 1 min. The differential diagnosis is near-syncope, TIA and seizure.
    (b) The location is both eyes. The differential diagnosis is near-syncope with retinal ischemia, TIA involving occipital lobe.
    (c) The character is black. The diagnosis is near-syncope as blackness implies retinal hypoperfusion.
    (d) *The source*: Hypotension or cardiac arrhythmia with decreased cardiac output.

(e) *Risk factor*: Diabetes.
(f) Loss of ankle reflexes and impaired vibration perception at the toes and ankles is typical of a neuropathy.

11. *Diagnosis:* Diabetic neuropathy including autonomic neuropathy.

Lessons:

1. A meticulous history discloses a probable diagnosis.
2. The standing blood pressure should be checked over time, at least 3 min in this case since symptoms occurred after 2–3 min of walking.
3. The final diagnosis is established after both history and examination are completed.

Case 2 A 55-year-old woman complains of three episodes of loss of vision affecting the right eye. She says, "They don't last very long," but her vision is blurry and she cannot read. Her past medical history includes diabetes, and she smokes two packs of cigarettes per day. Examination discloses bilateral carotid bruits but is otherwise normal. Laboratory evaluations include an MRI of the brain which reveals moderate subcortical ischemic change. Carotid Dopplers reveal mild carotid stenoses bilaterally. Angiography demonstrates moderate-to-severe bilateral external carotid stenoses and minor atherosclerotic changes at the bifurcation.

A neurologic consultation is requested. The neurologist queries the patient who expresses some annoyance and is oppositional at his insistence of clarifying her comment, "They don't last very long." Eventually she responds to the question, "Do they last seconds, minutes or closer to an hour?" She responds, "Closer to an hour." "Do you have a headache?" "No." "Is your eye or head sore afterwards?" "Of course my eye and forehead are a little sore." "Have you ever had severe headaches?" "I had severe sinus headaches in my 20s during the allergy season." "Were you ever nauseated with them?" "Sometimes, but usually in the sun when my headache was worse." The diagnosis is migraine. Had there been no pain whatsoever, the diagnosis would be ophthalmic migraine.

Lessons:

1. Long duration of visual symptoms, more than 5 min, suggests migraine. A TIA is typically less than 5 min although by definition it may last up to 24 h.
2. Despite an initial refusal to answer a question, giving the patient a few choices may elicit a response.
3. A diagnosis of "sinus headaches" given by a patient should always be suspect. Details are required and, in this case, the presence of nausea and photophobia indicates migraine which is far more common.

A neurologic history is incomplete without questioning the patient about all neurologic symptomatology even if deemed irrelevant. If a 62-year-old patient seeks attention because of a weak right leg, should he be questioned about memory or speech disturbances? A left cerebral lesion may cause elements of aphasia as well

as right leg weakness. If a 40-year-old woman complains of leg weakness associated with stiffness, questions about vision may uncover the diagnosis. For example, she may have blurred vision affecting one eye with poor color perception indicating an optic nerve lesion. Stiff, weak legs point to a myelopathy with spasticity. Widely separated lesions suggest a demyelinating disorder such as multiple sclerosis or, in this case, possibly neuromyelitis optica (Devic's disease).

Consequently, a neurologic history requires questioning all patients about episodes of loss of consciousness, memory loss, sleep patterns, speech or language function, headache, visual disturbances, hearing disorders, difficulty swallowing, dizziness, impairment of balance and gait, strength, numbness and tingling, and fatigue. The presence of neck or back pain may be important. Additional questions regarding bladder, sexual and bowel function may be pertinent.

The past medical history is obviously essential to obtain in depth. Nevertheless, there are numerous pitfalls. Open-ended questions such as, "Do you have any illnesses?" may be answered negatively. For instance, many people do not consider hypertension an illness. Others may deny it when specifically asked because treatment has been successful. If recent blood pressures are normal on medication, then, by their analysis, they no longer have hypertension. Prior surgeries are often forgotten such as a mastectomy for breast cancer. Metastases from carcinoma of the breast 10–15 years after mastectomy is a well-known occurrence. Finally, a review of current medicines, dosages included, is mandatory.

The family history is of interest but seldom yields diagnostic information. A positive family history of tremor is useful if that is the patient's primary complaint. Conversely, if a female patient has a chief complaint of headache, a family history of migraine is of questionable pertinence since close to 20% of the female population has migraine. Certainly a strongly positive family history of malignancy or vascular disease conveys relative risk but does not obviate the need to address each symptom on its own merits.

The social history provides important information. Aside from smoking and alcohol consumption, the patient's sleep history and changes in appetite convey meaningful data. For instance, restless sleep and daytime somnolence may indicate obstructive sleep apnea or periodic leg movements of sleep. Chronic fatigue associated with muscle pain and insomnia with early morning awakening strongly suggests depression with somatic manifestations. Occupational exposures to toxic agents should always be documented. A list of allergies to medications is routine.

Review of systems often contains useful information. Palpitations of the heart may tip the physician off to the possibility of cardioembolism as a cause of stroke. Genitourinary symptomatology is often of clinical importance. Urinary incontinence associated with a vague history of brief altered mentation may indicate a complex partial seizure. Difficulty initiating urination may occur with lumbosacral root lesions. Unawareness of urinary incontinence during an alert state suggests cerebral pathology. For example, difficulty getting out of a chair and a shuffling gait with start hesitation accompanied by unawareness of urine-stained pants suggests normal pressure hydrocephalus. Gastrointestinal disorders such as Crohn's disease can be associated with a stroke. Whipple's disease may be the cause of a brainstem

lesion. Diabetic enteropathies with diarrhea may be a tip off for the etiology of a neuropathy.

There are other special situations which require modification of standard interview methods. The nearly deaf patient can be extraordinarily difficult to evaluate. Many doctors shout loudly at the patient forgetting that speaking directly into the patient's ear from a distance of 1 or 2 inches is much more effective than shouting at a distance. It is also considerably less disturbing to other patients or personnel in the vicinity. If this is also ineffective, short written questions will be necessary. Patience is essential and allotted time must be extended.

Minority patients may require a different interview technique. Many Hispanic patients who have lived in the United States for years and speak English fairly well may still insist on a translator. When the physician can speak a little Spanish, even if not fluent, patients will be exceptionally pleased and may be willing to communicate in faulty English without assistance, very useful if no translator is available.

African-American patients may distrust Caucasian physicians because of preconceived notions or prior disagreeable experiences. This may affect how they present their symptoms which must be taken into consideration for interpretation. The following case illustrates this issue.

Case 3 A 56-year-old African-American woman was leaving a supermarket on a rainy day. She slipped on the wet pavement and landed on her back. She went to a busy local emergency room where an X-ray of her lumbar spine was obtained because of her complaint of severe low back pain. This was normal. The Emergency Room physician suspected she was malingering and planning a lawsuit. The following day she decided to seek a neurologic opinion and, in the waiting room, was screaming in agony. When she was first seen her behavior was hysterical, appearing disproportionate to any conceivable injury. The neurologic examination was normal, but she was explicitly tender in the mid-to-lower thoracic region. Plain films revealed a T9 compression fracture. This patient displayed the cry-for-help syndrome, i.e., "take me seriously." The take-home lesson is never dismiss a complaint despite circumstances implying dishonest behavior.

The nonspecific complaint may be particularly challenging and frustrating. A good example is the patient who says, "I blacked out." This could mean loss of vision, loss of consciousness or a sleep disorder. An intriguing case report is described below.

Case 4 A 26-year-old man complains of numerous "blackouts." While watching TV he reports suddenly losing consciousness and being unarousable by family members for several minutes. No overt seizure phenomena have been described by witnesses. He has taken short-term disability since these "blackouts" are occurring at least a few times a day. He is desperate to return to work. Neurologic examination reveals an alert, athletic-appearing man with normal speech. There are no abnormal neurologic signs. An EEG shows a few suspicious sharp waves in the right temporal region. A tentative diagnosis of complex partial seizures is made and treatment with phenytoin is initiated. Despite good therapeutic levels the patient

continues with these episodes. On the patient's fourth visit his sister accompanies him and adds critical information. When queried about the patient's sleep habits she adds that he snores loudly. Polysomnography discloses severe obstructive sleep apnea, a well-known cause of excessive daytime somnolence.

Lessons:

1. Always obtain the report of witnesses when the history is unclear.
2. Queries about sleep habits should be a routine part of any neurologic history.

Neurologic Symptoms in Psychiatric Disease

Many if not most cultures, including western civilization, consider psychiatric illness a failure of the individual to cope with the normal stresses of everyday life. The eradication of this stigma is in progress throughout the western world but has had limited success. This mind-set facilitates somatization which legitimizes the illness for the patient. Thus every neurologic symptom has the potential of being the physical manifestation of a psychiatric illness. Sometimes considered the bane of a neurologist's practice, somatization must be quickly recognized before extensive, expensive and, especially, invasive tests with an element of risk to the patient are ordered. This requires a confident physician willing to oppose a patient's demand for an unnecessary examination. Conversely, a hasty, reckless diagnosis of a psychiatric disease when confronted with peculiar but nonetheless realistic symptoms is not unusual. Hence the neuropsychiatric illness can be the most challenging and intriguing part of a neurology practice.

Depression can manifest itself in innumerable ways without an acknowledgment of a mood disorder by the patient. There are several symptoms, however, which patients are not reluctant to discuss and can provide the necessary clues for a diagnosis. They often feel free to acknowledge difficulty with concentration and may use the term "brain fog" to explain slowing of thought processes. Not unusual spontaneous complaints are derealization, a feeling of being disconnected from the environment, and depersonalization, a sense of detachment from the body. If only brief, seconds to a few minutes, simple partial seizures must also be considered. A change in sleeping pattern, particularly early morning awakening and an alteration in appetite, most often anorexia, are common. Loss of motivation, fatigue, restriction of interests, loss of libido, and poor performance at work are additional features.

Memory loss is a frequent complaint of the depressed patient and this inevitably raises the question of the pseudodementia of depression versus the mild cognitive impairment of incipient Alzheimer's disease. Slow responses to questions may reflect the bradyphrenia (slowed thinking) of dementia or the psychomotor retardation of depression. In this instance, neuropsychological testing is usually required to differentiate between structural disease and a "functional" disorder although the latter is physiological, possibly structural, and most often precipitated by external events.

Conversion disorders [2] are manifested by motor or sensory symptoms that suggest neurologic or medical disease and are provoked by psychosocial stresses. There is often a secondary gain through this behavior. Some physicians believe they are less common than a century ago since the lay public is exposed, if not deluged, to medical information. Conversely, the presentations may be more sophisticated. There is high comorbidity with other psychiatric disease, especially depression, as well as underlying neurologic conditions which may even be the precipitating factor. Consequently, the examining physician is easily led astray and quick diagnoses can be hazardous. La belle indifference, demeanor inconsistent with the illness, once considered a classical sign of a conversion disorder is not a reliable indicator since many patients with severe disability will be stoic and minimize symptoms. More useful signs include collapsing leg weakness, a sudden drop of an arm when evaluating for arm drift, overactive facial movements such as grimacing or blinking and Hoover's sign. When one symptom is leg weakness the patient is examined supine and requested to lift one leg. The opposite leg should exhibit downward pressure; thus the examiner places his hand under the heel to detect this compensatory movement. The absence of detectable downward pressure, Hoover's sign, supports a diagnosis of a conversion reaction or malingering.

Panic disorders are recurrent attacks of fear, if not terror, which are associated with physical symptomatology. Occasionally, the patient latches onto these physical complaints as the major issue. Palpitations, tremor, faintness, difficulty swallowing due to a "lump" or fullness in the throat, shortness of breath, and paresthesias of the extremities due to hyperventilation are some of the manifestations. Differentiation from simple partial seizures is ordinarily not difficult since the duration of symptoms is usually more than 10 min in patients with a psychological etiology.

Hypochondriasis is a well-known and usually easily recognized disorder because of multiple, frequent visits to a physician with a multiplicity of complaints. Diagnostic studies which refute these worries are rejected as insufficient or unreliable. Other uncommon conditions such as factitious disorders and malingering, which must always be considered, require practical judgment by an alert physician.

Factitious disorders involve a psychological urge to be ill. Self-medication, falsifying test results, and use of artificial methods are utilized to feign illness. Munchausen syndrome, one form of this disorder, is associated with traveling from one physician or hospital to another to seek treatment, even surgical, through lying (pseudologia fantastica), and self-medication. Munchausen by proxy, a horrific disorder, involves a mother or caregiver who produces a disease in a child by medication or other manipulations.

Malingering [2] is seldom seen in most neurology clinics but not unusual in practices which are visited by patients seeking workmen's compensation. The malingerer often arrives with a cane, crutches or even in a wheelchair. He or she tends to be hostile, sullen and exhibits a low pain threshold. There is ordinarily an obvious materialistic gain for being declared disabled. These patients commonly have an antisocial personality disorder.

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Chapter 4
Neurologic Examination

The purpose of this chapter is to review the techniques of observation and examination. As Max Wintrobe, an eminent internist, remarked, "The physical examination must be carried out with a watchful eye, a sensitive touch, discerning ears, and an alert sense of smell. Above all, what is needed is an alert mind free of dogma and routine." Nowhere is this more essential than in the specialty of neurology. *(Please see the in-depth accompanying video on performing a neurologic examination. It can be found on the Springerlink.com page for this book with* Chap. 4 *in the Supplementary Material area.)*

Despite the detailed description of required observations, a thorough neurologic examination is easily completed in an uncomplicated patient within 15 min. Only consistent practice on all history and physicals can this allotted time allowance be achieved. If complicated abnormal signs are elicited, a return to a portion of the examination may be necessary to ensure accuracy and thus entail a more lengthy assessment.

The neurologic examination requires specific instruments. These are:

1. Watch. A watch with a second hand is preferred over fumbling with a cell phone or other device when taking a pulse.
2. Stethoscope.
3. Ophthalmoscope.
4. Penlight.
5. 128 frequency tuning fork.
6. Reflex hammer.
7. Visual acuity card and pinhole.

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8. Two red tipped matches or other small red targets.
9. Pin.
10. Cotton or Q-tip.

Useful specialized equipment:

1. Tape measure.
2. Two-point discriminator.
3. Coins, rubber band, key, or other small objects.
4. Red glass for testing diplopia.
5. 512 frequency tuning fork (to check Weber's and Rinne's tests).
6. Tube of cinnamon or other spice.

Categories of examination:

1. Vital signs, cervical bruits, heart examination if vascular disease is a diagnostic consideration.
2. Mental status.
3. Cranial nerves.
4. Motor function.
5. Gait and station.
6. Reflexes.
7. Sensory testing.
8. Mechanical signs.

Vital Signs

Vital signs can be taken either at the beginning or the end of the examination. If there is any history of impaired cognition the taking of vital signs is often best deferred to the end of the neurologic examination. There is a natural merging from the history to the evaluation of the mental status. Relegation of vital signs to a nurse or other assistant can detract from the patient's perception of the physician's interest. Saving 1 min or less for blood pressure and pulse may not be worthwhile as many patients benefit from the reassurance of the physician's touch.

> Checking the blood pressure and pulse is mandatory for a neurologic examination.

Any history of neurologic symptoms such as faintness, dizziness, nausea, weakness, loss of balance, or impairment of vision with a change of position requires blood pressure evaluation in supine, sitting, and standing positions. The blood pressure standing should be taken every minute for 3 min and, if the blood pressure has not stabilized, up to 5 min. or longer if necessary. The blood pressure should be taken in both arms to assess for the subclavian steal syndrome if TIA's in the vertebrobasilar distribution are a suspected diagnosis. This occurs when there is a

reversal of blood flow in the vertebral artery to compensate for a proximal occlusion or high-grade stenosis of one subclavian artery impairing blood flow to the arm. The systolic pressure difference is usually greater than 30 mm of Hg. A pulse delay when both radial pulses are palpated simultaneously is often detectable.

A history of loss of balance requires checking blood pressure for orthostatic hypotension.

Examination of the neck for cervical bruits is essential even though a direct correlation to stenosis cannot be made. The first decision is to distinguish between an arterial bruit and venous hum. The latter is low pitched and heard through both systole and diastole. The former is usually high-pitched and audible only during systole. Each carotid artery should be auscultated in low, middle, and high cervical regions. If the bruit is very localized it is more likely to be associated with stenosis. Bruits heard high in the neck are more often correlated with stenosis. Supraclavicular bruits are usually transmitted from the chest, but occasionally they indicate a significant subclavian stenosis. The bell is more useful than the diaphragm for cervical bruits. Auscultation of the heart is necessary in any patient who gives a history suggestive of cerebrovascular disease.

Mental Status Examination

A detailed mental status examination is not always required.

This examination done in its entirety is optional if the patient's major complaint is completely unrelated to cerebral function such as low back pain. The decision assumes that the past medical history includes no previous illness affecting cognition. The patient is certain to be annoyed if a full mental status examination is performed unnecessarily.

Preliminary observations begin when the patient is first seen or heard.

Visual Observations

Facial symmetry and expression are key initial observations.

1. Facial asymmetry, spontaneous or with emotion, especially a laugh.
2. Facial expression. For example, is the affect sad or flat? Is the face immobile?

3. Facial features. For example, is there prognathism or proptosis? The former suggests acromegaly. The latter may indicate hyperthyroidism.
4. Eye position. Look for skew deviation (vertical separation of the globes). Is there dysconjugate gaze or forced eye deviation, up or down, right or left?
5. Head position. Is the head tilted or turned to left or right, up or down?
6. Body position. Is the patient stooped, hyperextended, turned to one side, or is there a dystonic (twisted) posture?
7. Arm and leg positions.
8. Note the presence of abnormal involuntary movements of eyes, trunk, or limbs. For example, is there nystagmus, tremor, tic, myoclonus, athetosis, chorea, or hemiballismus? Description of these entities will be located in the sections of cranial nerves and motor function.

Observing the patient for involuntary eye, trunk, and limb movements is essential.

Auditory Observations

Dysarthria (nonlocalizing) must be distinguished from aphasia (localizing).

The most obvious and first element of the mental status examination is the assessment of speech and the first hurdle is to distinguish dysarthria (nonlocalizing) from aphasia (localizing). Ninety to ninety-five percent of the population is left-hemisphere dominant and this includes about one-half of left-handed people. Aphasia affects all language functions, verbal, reading, comprehension, and writing. Dysarthria is an impairment of articulation and pronunciation.

Dysarthria

Typical types of dysarthria include hoarse, nasal, breathy, wavering, and tremulous speech. Disorders of strength, speed, inflection, pitch, and rhythm are additional elements to observe. Commonly used words to test for dysarthria are “Methodist Episcopal” and “baby hippopotamus.” Spontaneous speech provides most, if not all, of the evaluation.

Nasal speech is characteristic of soft palate weakness.

Hoarseness, breathiness, and low pitch occur with weakness of laryngeal muscles and vocal cord paralysis. Nasal speech is characteristic of soft palate weakness. All of these findings may occur with lesions of the brainstem, 10th cranial nerve (vagus), neuromuscular disease, and vocal cord paralysis; the last is commonly due to lesions of the recurrent laryngeal nerve. Wavering, irregular speech with variable loudness suggests scanning speech, characteristic of cerebellar system dysfunction. Fatigue of speech is demonstrated by counting up to 50 or 100 and, if present, suggests myasthenia gravis. Any involvement of labial muscles, especially as occurs with peripheral seventh nerve lesions, will cause difficulty repeating words such as "mama" and "papa." Pseudobulbar speech is a spastic dysarthria which is slow, harsh, strained, and implies bilateral upper motor neuron lesions. Associated findings are forced, uncontrollable crying and laughing. Patients with Parkinson's disease frequently have rapid, mumbled and low volume speech. Spasmodic dysphonia is characterized by involuntary spasms causing intermittent vocal cord abduction or adduction and sometimes tremulous speech. Absence of inflection or monotone speech is called a dysprosody, a common manifestation of nondominant hemisphere lesions. Tremulous speech may be present in patients with essential tremor.

Pseudobulbar speech is a spastic dysarthria associated with forced uncontrollable crying or laughing.

Aphasia [1, 2]

Evaluation of the aphasic patient has been initiated prior to formal testing since spontaneous speech yields much of the needed information.

Detection of paraphasias is the first task when evaluating a patient for aphasia.

Spontaneous speech includes propositional, emotional, and automatic forms. Propositional speech refers to the ability to convey thoughts, ideas and judgments using appropriate words, syntax and rules of conversation. A patient with a nonfluent aphasia may still be able to curse fluently. Patients with global aphasia may repeat the same simple word or neologism to every question. This has been termed monophasia or a verbal automatism. The most important observation is the detection of paraphasias. These may be frequent and obvious, but occasionally barely recognizable. Three types of paraphasias are phonemic, semantic (verbal), and neologisms. A phonemic paraphasia might be to say, for example, "sleet" instead of "street." A semantic (verbal) paraphasia would be substituting an incorrect word

such as “door” for “window.” A neologism is a manufactured word with no meaning such as “flubsum” for “shoe.”

Other errors which may occur include perseveration, circumlocutions, excessive pauses, hesitation, agrammatism, and echolalia. Perseveration is repeating the response to a first question when a new request is given. Circumlocution would be, for example, to say “what you tell time with,” instead of “watch.” Agrammatism (telegraphic speech) is manifested by defective syntax such as words spoken out of sequence as well as the missing of many filler words. Inflection is commonly absent. Completely unintelligible speech is termed jargon aphasia. Echolalia is immediate repetition of what has just been heard.

Comprehension is tested by giving verbal instructions such as “open your mouth” and “put out your tongue.” These are simple commands. A two-step command is “raise your arm and open your mouth.” A three-step command would be adding a third instruction such as “cross your legs.” A four-step command would be to add a fourth instruction. In the absence of right–left confusion, a four-step command could be “touch your right (1) ear (2) with your left (3) hand (4)”. Finally, a statement and question could be, “The dog bit the cat. Which animal is injured?” Occasionally, gestures are understood but not verbal instructions; thus, the patient is able to imitate the examiner.

Naming is impaired in nearly all types of aphasia. This may be for objects or body parts. Testing may elicit paraphasias of any type and circumlocutions. Responsive naming, for example, would be, “What do you do with a glass?,” “What do birds lay in their nest?,” “How does a lemon taste?” These questions test verb, noun, and adjective retrieval, respectively.

Naming is impaired in nearly all types of aphasia.

The ability to repeat simple phrases such as the standard, “no ifs, ands or buts,” may help to localize a lesion to the perisylvian region. Inability to read, alexia, can be congenital or acquired. It may occur with or without agraphia. Alexia without agraphia is a classical disconnection syndrome due to a lesion most often in the dominant medial occipital cortex involving the splenium of the corpus callosum. A right homonymous hemianopsia is usually an associated finding. In this instance, alexia without agraphia, the patient may write a sentence and, after a delay of a few minutes plus two or three intervening questions, may be unable to read it. Alexia with agraphia is more common and is usually associated with a lesion of the angular gyrus or with Wernicke’s aphasia. The latter occurs with a lesion of the superior temporal gyrus.

Alexia without agraphia is a classical disconnection syndrome due to a lesion in the dominant medial occipital cortex involving the splenium of the corpus callosum.

Table 4.1 Aphasia classifications

Aphasia type	Fluency	Repetition	Comprehension	Naming
Global	A	A	A	A
Broca	A	A	NL	A
Transcortical motor	A	NL	NL	A
Transcortical sensory	NL	NL	A	A
Transcortical mixed	A	NL	A	A
Conduction	NL	A	NL	Variable
Wernicke's	NL	A	A	A
Anomic	NL	NL	NL	A
Subcortical	Variable	NL	Variable	A

A abnormal, *NL* normal

Aphasia classifications require specific observations. The precise identification of the aphasia has limited practical value since there are many instances of lesions in approximately the same anatomic location with different manifestations. Nevertheless, important distinctions include fluent vs. nonfluent, good vs. poor repetition, and good vs. poor comprehension. Naming is usually impaired with all types of aphasia. Paraphasias are common in fluent and global aphasias. Anatomic correlations are noted in Table 4.1.

Useful distinctions in aphasia analysis are fluent vs. nonfluent, good vs. poor repetition, and good vs. poor comprehension.

1. Nonfluent. Posterior inferior frontal lobe lesions.
2. Fluent. Posterior temporal and parietal lobe lesions.
3. Poor repetition. Perisylvian.
4. Good repetition. Outside the perisylvian region.
5. Poor comprehension. Posterior temporal and parietal.
6. Good comprehension. Posterior frontal.

Global aphasias are typically due to large perisylvian lesions. Broca's aphasia is associated with lesions of the posterior inferior frontal gyrus and anterior perisylvian region. Wernicke's aphasia is due to a lesion in the superior temporal gyrus. Transcortical aphasias have normal repetition and are due to lesions outside the perisylvian region, transcortical motor is located anteriorly, transcortical sensory posteriorly, and transcortical mixed is a combination. Echolalia, the repetition of the examiner's words or phrase, is not unusual in the transcortical aphasias because of the maintained ability to repeat.

Lesions of the posterior inferior frontal gyrus and the superior temporal gyrus of the dominant hemisphere may cause Broca's aphasia and Wernicke's aphasia, respectively.

Lesions of the arcuate fasciculus, a tract running between the posterior and anterior language areas, may result in conduction aphasia, a fluent aphasia with good comprehension but poor repetition. Subcortical aphasias are those due to lesions of the thalamus, caudate, putamen, and often associated with internal capsule involvement. These are usually of vascular origin and too variable to categorize.

Additional terms to be aware of include:

1. Aphemia. This refers to mutism but with preserved ability to communicate using written language although the latter can be riddled with misspelling or absence of prepositions.
2. Anarthria. This is a disturbance of articulate speech but with no impairment of its intellectual basis.
3. Aphonia. This is a loss of voice.
4. Asymboly for pain (pain asymbolia). This is the absence of a reaction to the threat of a painful stimulus such as no withdrawal or movement of defense when a lit match is moved towards the patient's face.

Agnosias [3]

Agnosia indicates normal reception of a sensory stimulus but inability to identify it.

Agnosia indicates normal reception of a sensory stimulus but inability to identify it. These can be considered disconnection syndromes. They are due to lesions which interfere with information transfer from primary sensory cortical areas to language centers. Consequently, there are descriptions of visual, auditory and tactile agnosia, phonagnosia, autotopagnosia, finger agnosia which is a focal type of autotopagnosia, prosopagnosia, astereognosis, and visual spatial agnosia. The concept of visual agnosia has been questioned since many of these patients have some disorder, often subtle, of visual perception. Tactile agnosia can be considered astereognosis, the inability to recognize a stimulus by touch even though the perception of touch is intact. Additionally, there are patients diagnosed with visual or tactile agnosia who have dysnomia and thus are inaccurately labeled. Visual agnosia implies normal naming by touch of an unrecognizable visual stimulus. Clearly, agnosia must be accompanied by normal naming using a different sensory stimulus.

Agnosia must be accompanied by normal naming using a different sensory stimulus.

Autotopagnosia (body image) is a patient's impaired ability to name or recognize his or her own body parts in the absence of dysnomia for objects, an exceedingly rare phenomenon. A specific type of autotopagnosia, finger agnosia, is one of the four parts of Gerstmann's syndrome which also includes right–left confusion, agraphia, and acalculia. This syndrome is due to a lesion of the dominant angular gyrus (parietal lobe). Phonagnosia is the inability to recognize voices and prosopagnosia, the inability to recognize faces. Prosopagnosia has been popularized by the book, *The Man Who Mistook His Wife For A Hat,* by Oliver Sachs. Lesions, commonly bilateral, in occipitotemporal and nondominant posterior hemisphere locations, are associated with visual agnosia and prosopagnosia.

Apraxias

Apraxia is the inability to perform an act despite intact comprehension, attention, motor, and sensory function. Apraxias are common with any type of dementia which indicates bilateral cerebral disease. Specific types may be caused by unilateral hemisphere disease. The most recognizable are the motor apraxias; they are limb-kinetic, ideomotor and ideational. These apraxias are associated with dementia or dominant hemisphere lesions.

Apraxia is the inability to perform an act despite intact comprehension, attention, motor and sensory function.

Limb-kinetic apraxia is actually clumsiness and thus not a true apraxia but a common initial abnormality of one of the motor systems, corticospinal, extrapyramidal, and cerebellar. Ideomotor apraxia is inability to perform an act such as wave good-bye, brush your teeth, or comb your hair. Occasionally, the patient may be unable to imitate an act demonstrated by the examiner. Ideational apraxia is the inability to plan an act requiring several steps such as "fold a letter, put the letter in an envelope, seal the envelope, stamp it and mail it." Sympathetic apraxia has been identified with left frontal lobe lesions; there is a right hemiparesis and left limb apraxia.

Ideomotor apraxia is inability to perform an act such as wave good-bye or imitate a gesture.

Constructional apraxia is the inability to copy diagrams such as intersecting pentagons or drawing a clock face including the numbers appropriately placed and requesting the patient to add a selected time with the hands drawn correctly.

Constructional apraxia (apractagnosia) is commonly associated with nondominant hemisphere lesions.

Dressing apraxia can be evaluated by turning a shirt sleeve inside-out and asking the patient to put the shirt on. Hemineglect is observed when the patient dresses just one-half of his body. This phenomenon occurs most often with right parietal lesions. More often, the patient is unable to put his shirt on because of a confusional state.

Apraxia of eye opening or eye closure is not an infrequent symptom of nondominant hemisphere lesions.

Apraxia of eye opening or eye closure is not an infrequent symptom of nondominant hemisphere lesions. It becomes obvious when requesting the patient to close his eyes in order to check position sense. The patient does so for 1 or 2 s only, no matter how many requests are given. Checking visual fields will be nearly impossible when the patient maintains eye closure. This latter problem also occurs with blepharospasm from which it must be distinguished. Motor impersistence is a term which is most often used for inability to maintain eye opening or closure. Another example might be to instruct the patient to "raise both arms and maintain that position for 1 minute" which the patient can do for only a few seconds.

Disorders of Attention and Recognition [3, 4]

Under the rubric of disorders of attention and recognition are anosodiaphoria, anosognosia, asomatognosia, autotopagnosia, extinction, inattention, and neglect. Anosodiaphoria refers to recognition of the deficit but an absence of concern, a dismissal of its importance. Patients with neglect pay no attention to the involved limb which is weak, but when given a specific request to move it will do so. Anosognosia is utter denial of any deficit.

Anosognosia refers to denial of illness which is a common finding associated with degenerative brain disease and nondominant hemisphere lesions.

Asomatognosia is loss of awareness of one-half of the body. Autotopagnosia refers to a failure of the patient to recognize his own limb or body part. Finally, a specific and dramatic symptom is denial of blindness, Anton's syndrome. Extinction is a sensory phenomenon whereby the patient perceives a single sensory stimulus whether visual, auditory, or tactile, but when given a competing stimulus on the contralateral side, perceives only the contralateral stimulus. Hemi-inattention is another word employed for this finding. This may be intramodal, e.g., two touch stimuli, or intermodal, e.g., auditory on the right and touch on the left. There is increased

sensitivity of the intramodal stimulus when the touch stimuli are on different parts of the body such as right hand and left leg. All of these perceptual disorders are nearly always due to nondominant hemisphere lesions, particularly the parietal lobe.

To summarize, some of the above-noted terms are often used interchangeably, although incorrectly, such as neglect, anosognosia and anosodiaphoria. Hemi-inattention is another commonly used term for both motor and sensory phenomena. These issues have been discussed and debated by generations of neurologists and differences of opinion persist. Most important is the ability to recognize or elicit these phenomena, particularly in near-isolation, in order to confirm the presence of neurologic pathology.

The Mini-Mental State Examination should be completed if memory loss is a primary or significant element of the present illness (see Table 4.2). If memory loss is a minor or questionable concern, a screening exam is ordinarily sufficient. This assumes that the patient's history as well as any observation made by a family member elicits no information that suggests significant impairment of cognitive function.

The Mini-Mental State Examination should be completed if memory loss is a primary or significant element of the present illness.

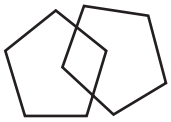
The screening exam may include:

1. Orientation to person, place, and date.
2. Following commands such as:
   (a) Open your mouth (simple or one-step).
   (b) Touch your left ear (two-step).
   (c) With your left hand touch your nose (three-step).
   (d) With your right hand touch your left ear (four-step).
   Should right–left disorientation be present, different commands are necessary such as "raise your hand," "open your mouth," "put out your tongue," and "cross your legs." (four-step command without need for right–left awareness). Additionally, perseveration may be uncovered. This is the repetition of the same response (verbal or motor) despite a new request.
3. Naming objects and body parts.
4. Repetition of simple phrases such as: "No ifs, ands or buts."
5. Calculations. Addition of two-digit numbers, such as 14 + 17, is a reasonable expectation for high school graduates. College graduates might be expected to perform serial 7 s. The educational status of the local community should be assessed before deciding on normal parameters.
6. Spelling and reversing five-letter words such as "table" or "world" and, if the patient fails the test, using four, then three, and finally, two-letter words.
7. Short-term recall. The patient is given three words, nouns, and is asked to repeat them in 1–3 min. To avoid interrupting the examination as well as losing time, it is useful to ask the patient to repeat the words when checking for arm drift or during the reflex examination since neither test requires any active response from the patient. This test is critical since it may be the only abnormal sign in early dementia.

Table 4.2 Mini-mental state examination (MMSE)[a]

Mini-Mental State Examination (MMSE)

This test should be performed after a history is taken which establishes rapport. Inform the patient why the test is being performed in a nonthreatening manner. Ask the questions in the order listed.

Maximum Score	Score	
		ORIENTATION
(5)	( )	1. "What is the (year, season,month, date,day)?"
(5)	( )	2. "What is the (state, county, city, hospital or adjacent street/highway, floor)?"
		REGISTRATION
(3)	( )	Tell the patient "please remember these 3 words." The words should be unrelated nouns and be spoken clearly, about 1 second for each (e.g. "car," "spoon," "flower.") "Now please repeat them." The first repetition determines the score (0-3). Continue asking until he/she can repeat all 3, up to 6 trials.
		ATTENTION AND CALCULATION
(5)	( )	Ask the patient to do serial 7 subtractions from 100. Stop after 5 subtractions (93, 86, 79, 72, 65). Score the number of the correct subtractions by 7. For example, 93, 87, 80, 73, 66 would equal 4. An alternative test is to spell a 5-letter word forwards then backwards such as "TABLE." Only the attempts to spell backwards are scored. The score is the number of letters in the correct order (e.g. ELBAT=5; ELAT=4; ELABT, ELT=3; ELTAB=2; ETABL=1). Ordinarily, individuals who have some education after high school can be expected to be successful performing serial 7s.
		LANGUAGE
(2)	( )	Naming: Show the patient 2 objects to name such as watch and pen.
(1)	( )	Repetition: Ask the patient to repeat the phrase "no ifs, ands, or buts."
		RECALL
(3)	( )	Ask the patient to repeat the 3 words given to him/her earlier.
		LANGUAGE
(3)	( )	3-Stage Command: Give the patient a blank sheet of paper and ask him/her, "take this paper with your left hand, fold it in half and put it on the floor."
(1)	( )	Reading: Print "CLOSE YOUR EYES" in letters large and clear enough to see. Ask him/her to read this and do what it says. Score 1 point only if he/she actually closes his/her eyes.
(1)	( )	Writing: Give the patient a blank sheet of paper and ask him/her to write a sentence. Do not dictate the sentence. It must contain a subject, a verb and be sensible. Correct grammar and punctuation are not required.
(1)	( )	 Copying: Ask the patient to copy a figure of intersecting pentagons. All 10 angles must be present and 2 must intersect to form a 4-sided figure to score 1 point. Tremor and rotation are ignored.

Maximum Total Score	Total Score	*Severity of cognitive impairment:*	
30	(_____)	Mild Cognitive Impairment:	MMSE 25-27
		Mild Dementia:	MMSE 19-24
		Moderate Dementia:	MMSE 10-18
		Severe Dementia:	MMSE 0-9

Interpretations and requirements:

1. At least an 8th grade level of education is required.
2. The individual should be fluent in English.
3. This is a screening device and an abnormal result is not sufficient to diagnose dementia. It is an indication for the need of further neurologic investigation.
4. The result can be used to document changes in the severity of cognitive impairment.
5. Depression and anxiety may interfere with the test result and will require clinical judgment of the examiner to determine its accuracy.

[a]Adapted from Cockrell and Folstein [15]

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Short-term recall deficits are often the first and only abnormal finding in patients with early dementia.

8. Optional. Proverb interpretation. This is primarily useful to elicit concrete responses. For example, when asked, "What does it mean if someone tells you 'you hit the nail on the head'?," the patient may answer, "You took the hammer and hit the nail into a log." Another commonly used test phrase is "don't cry over spilt milk." Abnormalities suggest the presence of frontal lobe disease.
9. Optional. Face-hand test. The patient is given two touch stimuli, one on each side of the body, on different parts. Typically, these are face, chest, hand, and leg. When given two stimuli the patient may extinguish all the stimuli on one side which indicates the presence of a contralateral cerebral lesion. Repeated bilateral errors of extinction may occur if the patient's ability to perceive more than one stimulus is defective. Persistent bilateral extinction phenomena suggest generalized cerebral dysfunction. The least sensitive sign for unilateral extinction is touching both hands, both legs, or both sides of the face. However, the use of sensory hierarchy in descending order of dominance, face, chest, leg and hand, may elicit focal signs not discernable by other means. An example would be touching the patient's right face and left hand and vice versa. If only the left hand is not perceived on repeated testing, a right cerebral lesion would be suspected.
10. Head turn observation. Commonly, patients with dementia will turn to their spouse or significant other for help in answering questions. Although frequently noted when dementia is clearly apparent, it may be an early signal of dementia. The reliability of this sign remains to be confirmed. Psychogenic factors must certainly be taken into consideration.

Neuropsychological Evaluation [6]

Neuropsychological testing is the epitome of investigation for impaired cognition. This is frequently required for a firm diagnosis of organic memory loss as well as quantification of the deficit and characterization of the disorder. Although this testing is not part of the standard neurologic examination it is worth being familiar with some of the terminology, procedures, concepts and neuroanatomic correlations.

Episodic Memory

There are visual and verbal forms. The clinical presentation of the verbal type pertains to the ability of the patient to recall personal experiences such as what

she ate for her last meal or forgetting to turn off the water faucet (completing a task). Examples of the visual type are exemplified by difficulty locating a frequently used store such as a supermarket or remembering the location of a figure in space.

Neuropsychological testing for the verbal form includes recall of an oral narrative and the Wechsler Memory Scale. The California Verbal Learning Test assesses learning new verbal information and retrieval after a delayed interval. Testing for the visual form involves examining for recall of simple figures as well as both immediate and delayed recall of complex figures. The Brief Visual Testing Revised is a good measure of visual memory.

The involved anatomic structures are the medial temporal lobe and the Papez circuit. The latter is comprised of the hippocampus, fornix, mammillary bodies, mammillothalamic tract, anterior and dorsomedial thalamic nuclei, cingulate gyrus and cingulum.

Semantic Memory

This form can also be subdivided into verbal and visual types. Examples of the verbal type may include identifying household objects and stating the months of the year. Semantic paraphasias are common. The visual form might be failure to recognize and identify famous faces.

Neuropsychological testing involves evaluation of the general fund of knowledge for the verbal form and both recognition and identification of famous faces for the visual form.

Deficits are usually due to lesions of the anterior and inferior temporal lobes.

Working Memory

Impaired executive function is incorporated in working memory. This also relates to maintaining information, both verbal and nonverbal, for potential use in goal-directed behavior. Deficits are manifested by impaired ability to think in a flexible manner, generate a plan of action and rejecting irrelevant stimuli which interfere with reaching the set goals. There is a limited capacity to store and consciously manipulate information such as remembering a phone number before dialing it.

Neuropsychological testing includes the use of the Wechsler Adult Intelligence Scale for both digit span and spatial span. Processing speed may be measured by the Trail Making Test and the Symbol Digit Modality Test.

Neuroanatomical correlates are the prefrontal cortex, parietal association cortex, and associated subcortical white matter connections.

Procedural Memory

Examples of deficits include impaired ability to use tools such as how to start and use a lawnmower, using a bow to play a stringed instrument or using a cell phone. One might say that this is an apraxia. Standard neuropsychological testing does not ordinarily include evaluation of procedural memory.

Neuroanatomical correlates are the basal ganglia, supplementary motor area and the cerebellum. The supplementary motor area is located on the midline surface of the cerebral hemisphere anterior to the primary motor cortex leg representation. The body map is not clearly delineated. It becomes activated immediately before a voluntary action.

Cranial Nerve Examination

Olfactory Nerve (I)

Anosmia is an early sign in many patients with Parkinson's and Alzheimer's disease.

The examination of this nerve is not routine, but its function may be impaired with several neurologic disorders. Usually the patient's main complaint is loss of taste as olfaction provides much of the nuance of taste. It is commonly impaired after a serious head injury and may be lost on one or both sides with subfrontal or parasellar neoplasms. Anosmia is an early sign in some patients with Parkinson's and Alzheimer's disease. Diseases of the sinuses and nasal mucosa must be excluded. This sense is easily tested with a small tube of spice such as cinnamon.

Optic Nerve (II) [7]

1. Ophthalmoscopic technique (see Fig. 4.1). A dimly lit room is advantageous. The patient must keep both eyes open and fixed on a distant object, preferably at least 10 ft. away, to prevent a near response with pupillary constriction. The best visualization of the fundus occurs when the examiner is close enough to touch the patient's cheek with a finger while holding the ophthalmoscope. The examiner should approach the patient from the side, adjacent to the shoulder, to prevent obstruction of the patient's central vision. If the pupil is small, less than 3 mm, a small aperture should be selected.

The funduscopic examination should emphasize the optic disk and immediate vicinity.

Fig. 4.1 Ophthalmoscopic examination. The examiner should be close enough to touch the patient's cheek with a finger while holding the ophthalmoscope

2. The funduscopic examination should emphasize the optic disk and immediate vicinity. The normal optic disk has distinct edges, but the nasal margin may occasionally be blurred. There is a physiologic cup in the center which shows a latticework due to the underlying lamina cribrosa. The temporal margin of the disk is often pale; thus, observation of temporal pallor is very subjective and often inaccurate. The temporal portion of the optic disk is located where the papillomacular bundle enters the nerve. If there are any visual symptoms the macula should be inspected by requesting the patient to look directly into the light. The macula is located about 2 disk diameters temporal to the optic disk.
3. Attenuated arteries and arteriovenous nicking imply arteriolar disease in similar-sized intracerebral vessels. Hollenhorst plaques are bright yellow, seen within arterioles especially at branching points, and are composed of cholesterol. This implies embolism originating from atherosclerotic plaques in the carotid artery or aortic arch.

Absence of venous pulsations is expected when intracranial pressure exceeds 200 mm H_2O. Ten percent of the normal population display no venous pulsations.

4. Papilledema. The main features are bilateral blurring of the optic disk margins, especially the temporal side, which are rarely blurred in the normal population. Nasal margins of the disk, often blurred in the normal population, are affected first in the patient with papilledema. Absence of venous pulsations is expected when intracranial pressure exceeds 200 mm H_2O, but they are not seen in approximately 10% of the normal population. Venous pulsations are best visualized in or near the center of the optic disk. Flame and splinter hemorrhages at the disk margins ordinarily secure the diagnosis of papilledema. Hemorrhages only in the

peripheral portion of the fundus are not characteristic of papilledema. Without hemorrhages the diagnosis of papilledema is suspect. There are other features which support the diagnosis, however, such as tortuous veins, angulation of vessels at the disk margins and hyperemia of the disk. Vision is normal in early papilledema with the exception of enlarged blind spots, very difficult to determine at the bedside. Chronic papilledema will cause visual field constriction. Fluorescein angiography with fundus photography can be utilized in questionable cases, specifically to rule out pseudopapilledema. Dye leakage beyond the disk margins is noted in true papilledema. False negative tests rarely occur in early papilledema.

Vision is normal in early papilledema with the exception of enlarged blind spots.

Optic Nerve: Evaluation of Central Vision (See Fig. 4.2) [8, 9]

Impairment of color and light perception is often the earliest sign of optic nerve disease.

Light perception is normal in macular disease.

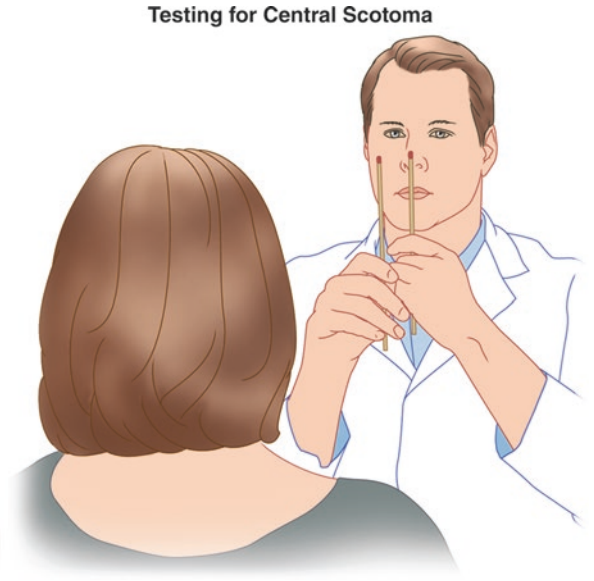

Fig. 4.2 Testing for a central scotoma with a red-tipped match. Each eye is tested alone with the patient focused on a match placed on the examiner's nose. A second match is placed on the examiner's cheek. The match which should be perceived as brightest is on the examiner's nose. If the match on the nose is dull or darker in color, the patient has a relative central scotoma

1. Each eye is evaluated independently by covering the unexamined eye. A comparison is made of light and color perception. A small, bright red match is most often used to evaluate this quality. An abnormal eye sees less light and colors are less bright. The patient may interpret the defective eye perceiving more color as there is a "deeper" red. Thus, clear definitions are essential. Furthermore, in macular disease color perception is impaired, but light perception is normal since the entire retina perceives light.
2. Color comparison of two red matches. One is held on the examiner's nose and one on his cheek. The patient is instructed to fixate on the match placed on the examiner's nose and compare the brightness of the red color. If the match on the cheek appears brighter, then there is a defect in central vision or a relative central scotoma assuming the match is perceived. Obviously, inability to maintain focus invalidates the examination. It is quite easy, however, to see the patient shift focus and two or three attempts may be required to complete the test.
3. The patient is simply requested to look at the examiner's nose and simultaneously instructed to point out features on the examiner's face that appear indistinct. This is often difficult for patients, but when there is a consistent abnormality, a scotoma is easily identified and precisely localized.
4. The patient is requested to focus on the examiner's nose and a red match is moved in a circular fashion around the nose. When the color is lost or the matchstick not even perceived a scotoma can be outlined.
5. Scotomas may be central, paracentral, or cecocentral, the latter extending to the blind spot.
6. Visual acuity. An accurate assessment requires an evaluation with a pinhole to correct for a refraction error. The pinhole should be 2–2.5 mm in diameter. Despite normal visual acuity a central scotoma may still be present, especially for color.

The central scotoma is the hallmark finding of optic nerve disease and a more reliable sign than visual acuity.

7. Ischemic optic nerve disease most often produces altitudinal or quadrantic defects, whereas demyelinating or metabolic optic neuropathies more often produce central scotomas.
8. Central vision and macular disease. A central scotoma is often perceived by the patient as a dark spot (a positive scotoma) when there is macular disease. Optic nerve pathology produces blurry vision (a negative scotoma). Metamorphopsia occurs frequently with macular disease. An example is a distortion of straight lines which appear wavy, crooked, or angulated due to macular edema. Photopsias and micropsia may occur.

9. Relative afferent pupillary defect (RAPD). An older term is Marcus-Gunn pupil. This abnormality defines the presence of optic nerve disease. It is almost never found in macular disease unless there is extensive damage to the entire retina. The patient is best examined in a dimly lit room and is focusing at a distant object. The light should be bright and shined from below the level of the eyes to prevent it from being a near stimulus. The light should be moved quickly from eye to eye several times after holding the light on the pupil for about 2 s. An obviously positive test is present when one pupil dilates. A test is considered positive if there is a reduced amplitude of constriction and a more rapid dilation (escape). It may also be considered positive when the normal eye constricts briskly when the light is moved from the abnormal eye, i.e., the direct response is better than the consensual response. It may remain as the sole residual sign of a prior optic neuropathy.

A relative afferent pupillary defect (RAPD) is present with optic nerve disease but almost never with macular disease. It may remain as the sole residual sign of a prior optic neuropathy.

10. Photostress test. This test is performed to distinguish between macular and optic nerve disease. A light is shined directly into one eye for 10 s with the other eye covered. Visual acuity is then tested and timed. When the visual acuity returns to the next larger line the time is recorded. For instance, if visual acuity is 20/20, the time recorded to achieve a visual acuity of 20/25 is noted. The same is done with the other eye. With optic nerve disease the time to return to pretest visual acuity is the same as a normal eye. With macular disease light causes bleaching of the visual pigments and significantly lengthens the recovery time.
11. Flight of colors. A light is shined directly into one eye for 10 s. The patient closes his eyes and reports the observed colors. Patients with optic nerve disease perceive few colors. A definite asymmetry between eyes supports a diagnosis of optic nerve disease. This test has been found to be more sensitive than visual-evoked potentials.

Visual Field Examination (See Fig. 4.3) [8, 9]

Detecting motion is the least sensitive method of evaluating visual fields.

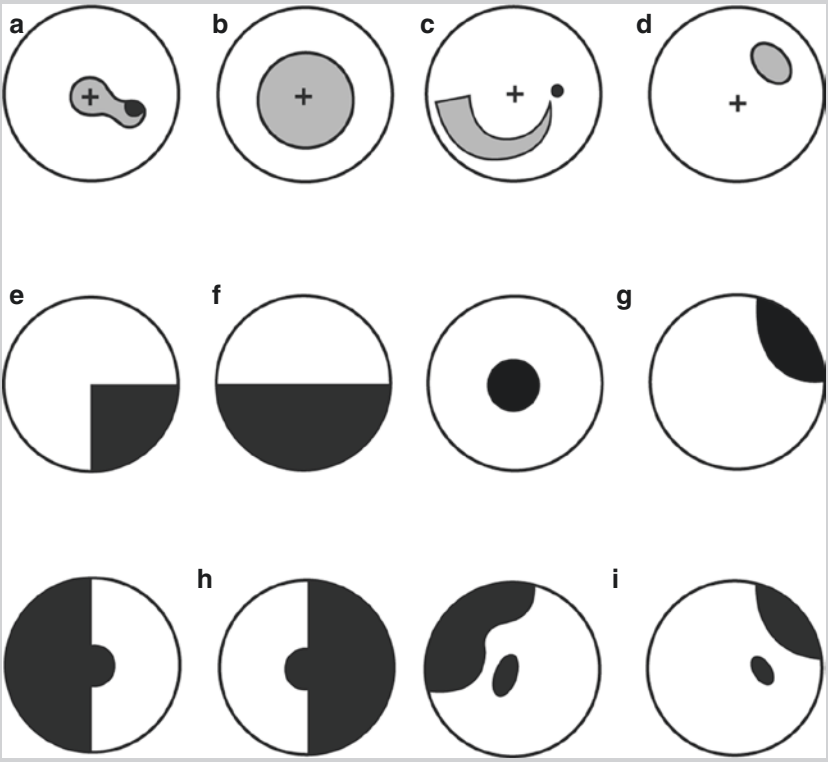

Fig. 4.3 (**a–f**). Retinal or optic nerve lesions. (**a**) Cecocentral scotoma. (**b**) Central scotoma. (**c**) Arcuate scotoma (nerve fiber bundle defect), O.D. (**d**) Paracentral scotoma. (**e**) Inferonasal quadrant defect. (**f**) Altitudinal defect. (**g**) Optic chiasm lesion (a junctional defect). An optic nerve lesion on the left side just anterior to the chiasm affecting crossing nasal fibers which receive visual information from the right temporal field. (**h**) Bitemporal hemianopsia and central scotomas. Optic chiasm lesion. (**i**) Bitemporal hemianopsia and bilateral paracentral scotomas. Optic chiasm lesion. (**j**) Incongruous homonymous hemianopsia. Left optic tract lesion. (**k**) Homonymous scotomata, right side, due to a left occipital or optic tract lesion. (**l**) Homonymous superior quadrantanopsia, right side. Left temporal or occipital lobe lesion. Occipital pathology is much more common. (**m**) Homonymous inferior quadrantanopsia, *right side*. Left parietal or occipital lobe lesion. Occipital pathology is much more common. (**n**) Homonymous macular sparing hemianopsia, *left side*. Optic radiation or occipital lobe lesion, *right side*. (**o**) Bilateral inferior altitudinal hemianopsia. Bilateral occipital (superior), bilateral optic nerve and, least common, optic chiasm mass lesions. (**p**) Bilateral superior altitudinal hemianopsia. Bilateral occipital (inferior), bilateral optic nerve and, least common, optic chiasm mass lesions. (**q**) Homonymous hemianopsia, splitting of fixation, *right side*. Optic radiation lesions, *left side*. (**r**) Temporal crescent defect, *right side*. Occipital lobe lesion, left anterior calcarine cortex lesion. (**s**) Homonymous hemianopsia, *right side*, with sparing of the temporal crescent. Left occipital lobe lesion with sparing of the anterior calcarine cortex

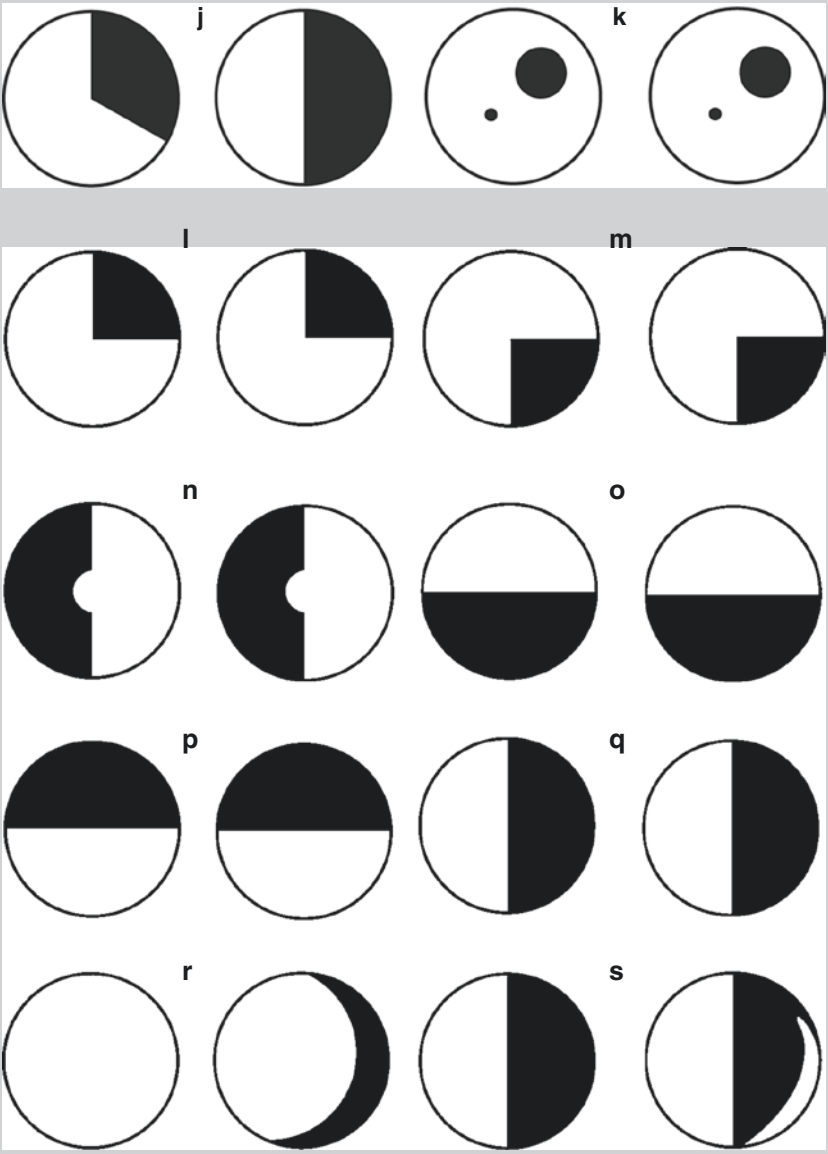

Fig. 4.3 (continued)

1. In the asymptomatic patient the visual field examination remains an essential part of a routine neurologic examination. It would be both tragic and embarrassing if the patient has an asymptomatic brain tumor, usually benign, or a stroke that affected the visual pathway despite a primary complaint, for instance, of arm pain. A quick screen with double simultaneous motion is the least sensitive first step. Adding rapid finger-counting in four quadrants with both eyes open is sufficient in an asymptomatic patient when there is no history or evidence of cerebral disease.

Visual fields at the bedside can be examined by motion, rapid finger-counting, object identification and color, e.g. red matches.

2. The symptomatic patient. Each eye is examined individually with both double simultaneous stimulation using motion and rapid finger-counting in two quadrants such as inferior nasal and superior temporal. The total finger count should be an odd number to thwart the completion phenomenon. Many patients will see only one side moving but assume that the other side also moves. The patient may respond to two fingers in one quadrant and one finger in the contralateral quadrant as four fingers when one side is not clearly seen. It should also be understood that even the functionally blind person can pick up motion but not form. This is called Riddoch's phenomenon and thus the additional test of finger-counting is necessary.

Riddoch's phenomenon, perception of movement in the hemianopic field, requires finger count or object recognition when visual impairment is suspected.

Optional tests include using different objects, e.g., a coin in the superior temporal quadrant O.S. and a key in the superior nasal quadrant O.D. This test has the advantage of eliminating the completion phenomenon as a confounding factor. Rapid double simultaneous exposure to two bright red matches flashed in one nasal and one temporal quadrant of one eye may elicit an extinction phenomenon, perception of only one red-tipped match. A third and perhaps most useful subtle test is color comparison. For example, the examiner can hold one hand in each field or quadrant and request the patient to state which hand is brighter (i.e., the normal side).

Finally, the time of the stimulus exposure can be critical in eliciting a visual field defect. Extinction, the obliteration of a percept, may occur when the stimulus is held up in a flash fashion. The longer the stimulus is kept in view the less likely the possibility of discovering a visual field defect. The exception, of course, is color comparison.

Lesions of the optic chiasm are most often associated with neoplasm, especially of pituitary origin. The earliest sign is ordinarily a central scotoma. Macular fibers are most dense in the central and posterior region of the chiasm and constitute the

great majority of fibers in that structure, thus explaining this early sign. A typical pattern of visual loss is the junctional scotoma, a central, paracentral or cecocentral scotoma in one eye and a superior temporal field defect in the other eye. This is due to a lesion, ordinarily a neoplasm, which involves one optic nerve close to the chiasm and the inferonasal fibers from the contralateral eye as they loop a short distance anteriorly (Wilbrand's knee) before they enter the chiasm. The classic bitemporal hemianopsia is typically a later development. Inferior fibers of the chiasm serve the superior fields. Thus, bitemporal superior homonymous quadrantanopsias usually precede a complete bitemporal hemianopsia if caused by a pituitary neoplasm. The reverse is the case, for example, with a craniopharyngioma which compresses the chiasm from above.

The earliest sign of an optic chiasm lesion is commonly a central scotoma. Macular fibers constitute the great majority of axons in that structure. The classic bitemporal hemianopsia is typically a later development with optic chiasm lesions.

Homonymous, which means both eyes involved, hemianopsias are caused by lesions affecting the visual pathways behind the chiasm. For instance, a left optic tract, lateral geniculate, optic radiation or occipital lobe lesion will produce a partial or complete right homonymous hemianopsia.

Homonymous hemianopsias are due to retrochiasmal lesions.

There are two types of homonymous hemianopsias, congruous and incongruous. Congruous hemianopsias have the same defect in both eyes whereas incongruous hemianopsias are different in each eye. Examples are noted in the figures. Lesions of the optic tract are often incongruous. Thus, the presence of an incongruous homonymous hemianopsia raises the serious question of a mass lesion, neoplasm or aneurysm, which are often located adjacent to the optic tract. Ischemic stroke and multiple sclerosis are uncommon etiologies. Lesions of the lateral geniculate nucleus are rare but may also cause incongruous homonymous hemianopsias.

Congruous hemianopsias have the same defect in both eyes whereas incongruous hemianopsias are different in each eye.

The principle of unilateral visual loss being caused only by retinal, optic nerve and, infrequently, optic chiasm disease is violated by the temporal crescent defect which may occur with occipital lobe lesions.

Patients with postchiasmal lesions usually complain of loss of vision rather than darkness. The defect is often perceived in only one eye, ordinarily the eye with the temporal defect which is nearly always larger than the nasal defect. Careful examination can usually uncover the nasal defect. The principle of unilateral visual loss being caused only by retinal, optic nerve and, infrequently, optic chiasm disease is violated by the temporal crescent defect. This is due to an anterior, medial occipital lobe lesion as the visual fields of both eyes overlap except for the temporal crescent which extends from 60° to 90° on the horizontal meridian. This location explains why the temporal field is larger than the nasal field. Homonymous hemianopsias with sparing of the temporal crescent occur when the anterior medial occipital lobe is spared.

Homonymous hemianopsias or quadrantanopsias with or without macular sparing occur with lesions behind the optic chiasm. Lesions of the optic radiations in the temporal lobe produce "pie-in-the-sky," superior homonymous contralateral quadrantanopsias. Lesions of the optic radiations in the parietal lobe produce "pie-on-the-floor," inferior homonymous contralateral quadrantanopsias.

Occipital lobe lesions produce a large variety of visual field defects.

Occipital lobe lesions produce a large variety of visual field defects. These are listed in Table 4.3. When there is an abrupt onset of bilateral superior or inferior altitudinal hemianopsia, vascular disease in the basilar artery distribution producing infarctions of the inferior or superior banks of the calcarine fissure, respectively, is the usual etiology. Naturally, if the visual loss is staggered, one eye alone at first followed by the second eye, bilateral optic neuropathies often of ischemic origin may be present. An infrequent etiology would be a large prechiasmal mass lesion. Cortical blindness and Anton's syndrome (denial of blindness) may occur when there are bilateral occipital lobe lesions. Macular sparing is most often present with occipital lobe lesions. Explanations include dual vascular supply to the occipital pole by branches of either middle or posterior cerebral arteries as well as the intermixture of fibers from retinal ganglion cells projecting to both ipsilateral and contralateral occipital poles.

Ophthalmoscopic Findings and Visual Field Defects with Lesions of the Visual System

Effective use of an ophthalmoscope is a declining art. But it should be a routine part of any neurologic consultation even if there is a low yield of diagnostic information. The case described below is an example of its potential diagnostic role in an unexpected clinical scenario.

Case 1: A 52-year-old man is brought to the Emergency Department after a cardiorespiratory arrest in a supermarket. He receives prompt cardiopulmonary resuscitation by a physician who happened to be shopping in the next aisle. In the Emergency

Table 4.3 Ophthalmoscopic findings, visual field defects and pupils with lesions of the visual system

Anatomic location	Funduscopic findings	Character of visual impairment	Pupils
Retinal/ macular disease	Retinal/macular hemorrhage or edema	Central scotomas, paracentral, cecocentral and arcuate scotomas (nerve fiber bundle defects), ring scotomas (fusion of superior and inferior arcuate defects), altitudinal defects and wedge-shaped defects with the point of origin at the blind spot	Normal
Optic nerve disease	Normal appearance or there may be disk edema, disk atrophy, flame or splinter hemorrhage at disk margins	Central, paracentral, cecocentral scotomas, arcuate scotomas (nerve fiber bundle defects), ring scotomas (fusion of superior and inferior arcuate defects), altitudinal and quadrantic defects	Relative afferent pupillary defect (RAPD)
Optic chiasm	Normal appearance or nerve fiber layer atrophy	Junctional scotomas, bitemporal hemianopsias or quadrantanopsias with or without macular splitting, central scotomas, bitemporal scotomas with intact peripheral fields	Normal except RAPD when one optic nerve is preferentially involved
Optic tract	Normal appearance or bilateral segmental atrophy	Contralateral homonymous hemianopsia, particularly incongruous, often macular splitting. Homonymous scotomata	RAPD may occur
Lateral geniculate nucleus	Normal or bilateral atrophy (bow tie pallor)	Homonymous hemianopsia, especially incongruous and often with macular splitting	Normal
Optic radiations			
Parietal	Normal	Contralateral homonymous hemianopsia, contralateral homonymous inferior quadrantanopsia (pie-on-the-floor), macular sparing or splitting	Normal
Temporal	Normal	Contralateral homonymous hemianopsia, contralateral homonymous superior quadrantanopsia (pie-in-the-sky), macular sparing or splitting	Normal
Occipital lobe	Normal	Contralateral homonymous hemianopsia or quadrantanopsia usually congruous and with macular sparing or macular splitting, temporal crescent defect (monocular), bilateral visual field defects such as checkerboard vision, bilateral altitudinal hemianopsias, homonymous scotomas, cortical blindness, denial of cortical blindness (Anton's syndrome)	Normal

Department an EKG disclosed ST wave abnormalities and he was admitted to the Coronary Care Unit with a diagnosis of an acute myocardial infarction and hypoxic-ischemic encephalopathy. A stat CT (head) scan was normal. The neurologic consultant found an intermittently agitated patient who responded to painful stimuli by pushing the examiner's hand away. He had a positive Brudzinski sign and bilateral Babinski signs. A funduscopic examination revealed bilateral blurring of the optic

disk margins, splinter hemorrhages at the margins and a subhyaloid hemorrhage O.D. (see Fig. 4.8). A lumbar puncture yielded bloody spinal fluid. The patient steadily improved over 4 days returning to a normal mental status. Angiography demonstrated a posterior communicating artery aneurysm which was coiled successfully.

Lessons:

1. Electrocardiograms may show abnormal ST segments after a subarachnoid hemorrhage. This is probably due to an outpouring of norepinephrine which causes contraction band necrosis of cardiac muscle.
2. This patient had papilledema and a subhyaloid hemorrhage, the latter finding virtually diagnostic of a subarachnoid hemorrhage.
3. In this case only a thorough neurologic examination unmasked the diagnosis.

See Figs. 4.4, 4.5, 4.6, 4.7 and 4.8 for a look at a few important funduscopic abnormalities.

See Tables 4.3, 4.4, 4.5 and 4.6 for reviews of retinal, macular and optic nerve diseases (Table 4.4).

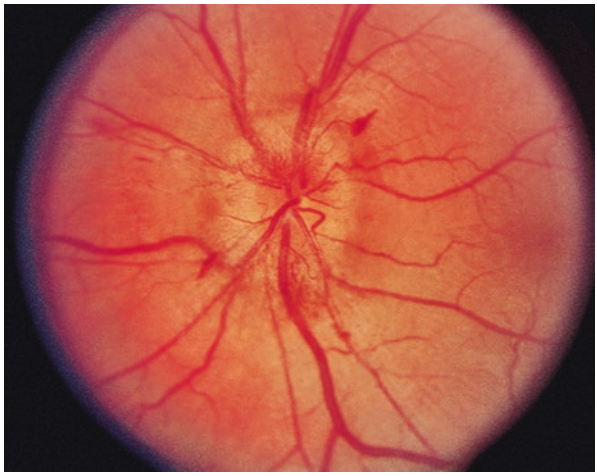

Fig. 4.4 Papilledema. There are blurred disk margins and hemorrhages adjacent to the disk

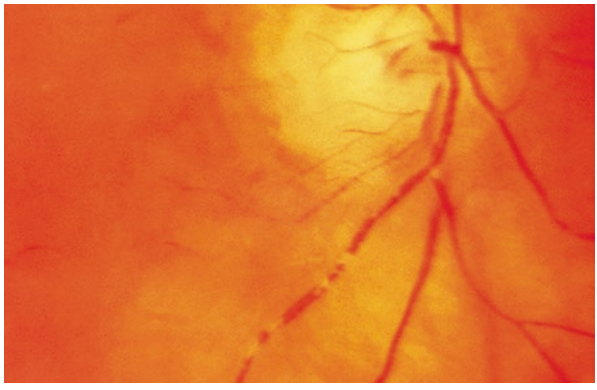

Fig. 4.5 Central retinal artery occlusion and boxcarring of blood column in an inferior retinal artery

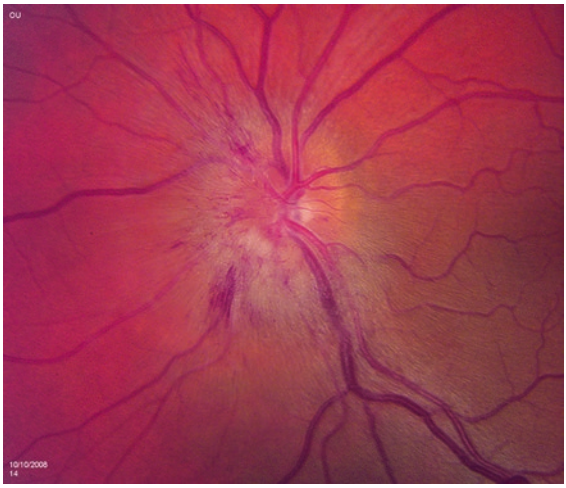

Fig. 4.6 Optic neuritis. *Blurred disk margins* and hemorrhage adjacent to the inferior portion of one optic disk

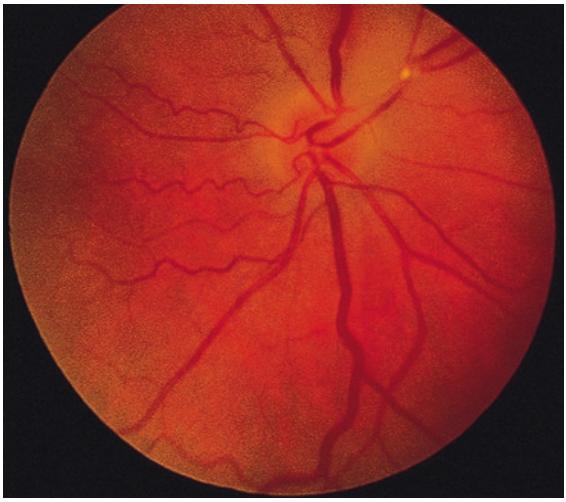

Fig. 4.7 Hollenhorst plaque. *Bright yellow* cholesterol embolus lodged at a bifurcation of the superior retinal artery

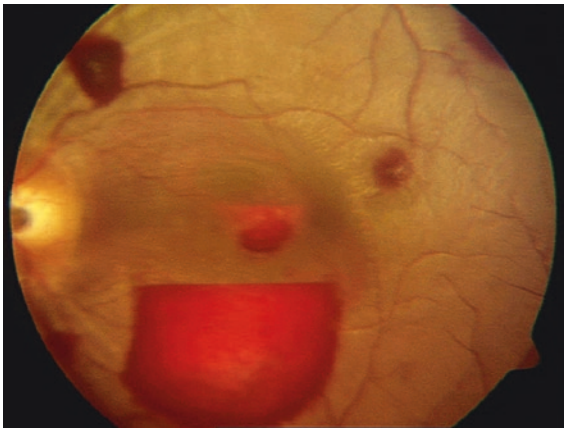

Fig. 4.8 Subhyaloid (preretinal) hemorrhage. This is located under the preretinal membrane and above the nerve fiber layer. This is a good marker for a subarachnoid hemorrhage in the appropriate clinical setting

Table 4.4 Differential diagnosis of optic nerve pathology

Pathology	Fundus	Laterality	Vision	Pupil	Miscellaneous
Papilledema	Blurred disk margins, absent venous pulsations, frequent splinter or flame hemorrhages at disk margins, disk hyperemia	Bilateral	Normal except enlarged blind spots	Normal	History of transient visual obscurations, unilateral or bilateral, lasting seconds
Papilledema, chronic	Same as above, ± optic atrophy, and central cup is obliterated	Bilateral	Constricted visual fields, enlarged blind spots	Normal unless there is secondary optic atrophy	Transient visual obscurations as described above
Retrobulbar neuritis	Normal appearance. Infrequent optic disk pallor with a preference for the temporal side	Unilateral, rarely bilateral	Central, paracentral or cecocentral scotoma. Less frequently arcuate, altitudinal and quadrantic defects	Relative afferent pupillary defect (RAPD)	History of impaired color and light perception
Optic neuritis	Blurred disk margins, absent venous pulsations, ± splinter or flame hemorrhages at disk margins	Unilateral, rarely bilateral	Central, paracentral or cecocentral scotomas. Less frequently arcuate, altitudinal and quadrantic defects	RAPD	History of impaired color and light perception
Pseudopapilledema	Blurred disk margins, absent venous pulsations, and no hemorrhage	Bilateral	Hyperopia common, normal vision with refraction	Normal	Fluorescein angiography used to differentiate from papilledema

Table 4.5 Distinguishing optic nerve from macular disease

Lesion location	Fundus	Laterality	Vision	Pupil	Miscellaneous
Macula	Edema, hemorrhage or other pathology in the macula	Unilateral or bilateral	Central scotomas, often positive (dark), decreased visual acuity, arcuate and ring scotomas, altitudinal and quadrantic defects.	Normal	Abnormal photostress test, metamorphopsia, micropsia and photopsia
Optic nerve	Optic nerve pallor, edema and hemorrhage at disk margins or normal	Unilateral, rarely bilateral	Central, paracentral or cecocentral scotomas, arcuate and ring scotomas, altitudinal and quadrantic defects. Decreased visual acuity	Relative afferent pupillary defect (RAPD)	Normal photostress test. Abnormal flight of colors

Table 4.6 Differential diagnosis of optic nerve and retinal pathology of vascular origin

Pathology	Fundus	Laterality	Vision	Pupil	Miscellaneous
Central retinal artery disease	Optic disk pallor, arteriolar attenuation, segmented appearance of blood in arterioles (boxcar effect)	Unilateral	Monocular, altitudinal and quadrantic defects, blindness, decreased visual acuity	Usually normal unless there is an extensive infarction which rarely results in the relative afferent pupillary defect (RAPD)	Commonly of embolic origin, occasionally associated with temporal arteritis or other vasculitides
Anterior ischemic optic neuropathy	Pallid edema with hemorrhages at disk margins	Unilateral	The most common findings are altitudinal and quadrantic visual field loss. Decreased visual acuity, central, paracentral or cecocentral scotomas may occur	RAPD	Small cup-to-disk ratio (less than 0.2). Painless, sudden loss of vision
Posterior ischemic optic neuropathy	Normal	Unilateral	Same as above	RAPD	Same as above
Central retinal vein occlusion	Engorged veins, numerous hemorrhages distal to occlusion, ± disk edema	Unilateral	Variable loss, more often mild and with peripheral scotomas	Normal	Good prognosis
Venous stasis retinopathy	Small dot and blot hemorrhages in the middle portion of the retina and microaneurysms	Unilateral	Normal but frequently associated with episodes of amaurosis fugax	Normal	Associated with severe occlusive internal carotid artery disease

3rd, 4th, and 6th Cranial Nerves (Oculomotor, Trochlear, Abducens)

Eyelids: A Critical Initial Observation [10]

> When pure ophthalmologic disease is absent obvious asymmetric palpebral fissures have just four etiologies.

Are there asymmetric palpebral fissures, i.e., the distance between the upper and lower lids? Assuming the absence of normal variation (a judgment call), sagging eyelids (blepharoptosis) in the elderly and ophthalmologic diseases or prior eye surgery which affect the eyelids, there are primarily four neurologic conditions that cause asymmetric palpebral fissures. These are diagnosed by anatomic criteria.

1. Ptosis due to a Horner's syndrome associated with sympathetic nervous system pathology causing weakness of Müller's muscle in the upper eyelid. This may also result in lower lid elevation due to paresis of smooth muscle attached to the inferior tarsal plate resulting in weak eyelid retraction. This explains the original observation of enophthalmos.
2. Ptosis due to a third nucleus or nerve lesion which causes weakness of levator palpebrae superioris (LPS)
3. Ptosis due to LPS weakness associated with pathology affecting the neuromuscular junction (myasthenia gravis) or muscle (ocular myopathy).
4. Widened palpebral fissure due to weakness of orbicularis oculi. This is most often secondary to neurogenic pathology, central or peripheral, affecting facial muscles.

The diagnosis of Horner's syndrome is secured by the simultaneous presence of miosis with or without anhidrosis. Patients with a suspected Horner's syndrome should be examined in a darkened room to augment the pupillary asymmetry. The normal pupil dilates more quickly and this increases the asymmetry if the eyes are examined between 5 and 15 s after the lights are turned off. The diagnosis of a third nerve or nucleus lesion is supported by a larger, ipsilateral, poorly reactive or non-reactive pupil and/or extraocular muscle weakness involving only third nerve innervated muscles. It is best appreciated in a brightly lit room. Weakness of orbicularis oculi is discerned at distance by observing a slower eye blink on the involved side. Lesions may be located in the contralateral cerebral hemisphere, corticobulbar pathway and brainstem. This pathway descends down the contralateral internal capsule, contralateral midbrain until the fibers cross in the upper pons to synapse in the ipsilateral facial nucleus and thence to the ipsilateral facial nerve.

Ptosis may occur as a late sequela after Bell's palsy due to aberrant reinnervation. An extremely rare finding is supranuclear ptosis due to lesions of the contralateral cerebral hemisphere. Bilateral supranuclear ptosis has been observed with unilateral or bilateral hemispheric disease. The majority of patients with cerebral ptosis have right cerebral hemisphere lesions.

Additional uncommon causes of ptosis or lid asymmetries:

1. Unilateral ptosis associated with contralateral eyelid retraction (Hering's Law of Equal Innervation). An attempt to lift the ptotic lid causes the opposite eyelid to retract.
2. Ptosis on the side of adduction in patients with Duane's syndrome. (See Chap. 13 under Syndromes).
3. Inverse Marcus-Gunn phenomenon. Mouth opening causes transient lid retraction due to synkinesias between oculomotor and trigeminal nerves.
4. Congenital ptosis due to abnormal development of levator palpebrae superioris which is sometimes associated with superior rectus weakness since they both originate from the same embryonic mass.
5. Pseudoptosis due to mechanical factors of inflammation as seen in orbital pseudotumor or neoplasm.

Ptosis may occur after Bell's palsy due to aberrant reinnervation.

Eyelid retraction is present when sclera is seen between the cornea (located over the iris) and the lid margin. Eyelid retraction and lid lag on downgaze suggest thyroid eye disease due to pathologic shortening of the LPS muscle associated with inflammation and fibrosis. Dorsal supranuclear mesencephalic lesions involving the nucleus of the posterior commissure cause eyelid retraction on direct forward gaze and upgaze but not downgaze (Collier's sign). Lastly, transient eyelid retraction may occur with aberrant third nerve regeneration. For instance, recovery from a third nerve paresis due to extirpation of a compressing neoplasm may result in fibers which ordinarily innervate adduction but are rerouted to the levator palpebrae superioris. Thus eye movement using the medial rectus will cause eyelid retraction, activation of levator palpebrae superioris.

Apraxias of eyelid opening and closing may occur especially with nondominant hemisphere lesions and extrapyramidal disorders.

Apraxias of eyelid opening and closing may occur especially with nondominant hemisphere lesions, less often with Parkinson's disease and Parkinson-plus syndromes. For instance, the patient may be requested to close his eyes and keep them closed, but does so only for 1 or 2 s in extreme cases. This has also been termed motor impersistence in which case it should be evident on other requests such as "raise your arm and maintain the position" which the patient will not do.

Blepharospasm is an involuntary, symmetrical and strong contraction of the orbicularis oculi. It is most often seen as an isolated phenomenon and considered a focal dystonia. Otherwise, it may accompany other extrapyramidal diseases, particularly Parkinson's disease.

Proptosis is often difficult to assess at the bedside and criteria relate to gender and race. Thus, if minor or debatable, an ophthalmologic consultation is required for precise measurements with an exophthalmometer. Upper limits in millimeters for white females is 20.1, white males 21.7, black females 23.0, and black males 24.7. Etiologies include thyroid eye disease, orbital pseudotumor, carotid-cavernous fistula, cavernous sinus thrombosis, orbital neoplasm.

Extraocular Muscles *(See Fig. 4.9)*

A brief review of pertinent anatomy should be helpful. The organization of the nuclei, oculomotor, trochlear, and abducens is complex, the nerves less so.

Actions of Extraocular Muscles with the Eye in Primary Position *(See Table 4.7) [11]*

One oculomotor nucleus supplies the innervation of the ipsilateral inferior rectus (IR), medial rectus (MR), inferior oblique (IO), and the contralateral superior rectus (SR) muscle. The nerve fibers destined to supply the SR decussate at the level of the nucleus. There is a single midline nucleus that supplies both levator palpebrae superioris (LPS) muscles. The oculomotor nucleus is in the midbrain and lies ventral to the Sylvian aqueduct. The axons cross the red nuclei and exit the midbrain just medial to the cerebral peduncle.

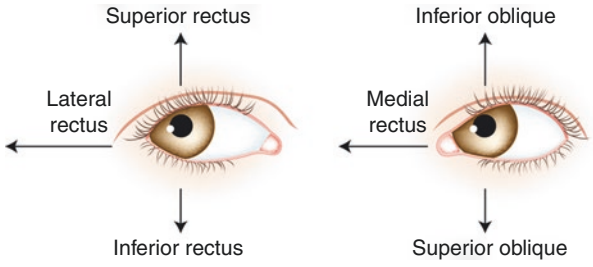

Fig. 4.9 Eye muscle function

Table 4.7 Actions of extraocular muscles with the eye in primary position

Muscle	Primary action	Secondary action
Lateral rectus	Abduction	–
Medial rectus	Adduction	–
Superior rectus	Elevation	Intorsion
Inferior rectus	Depression	Extorsion
Superior oblique	Intorsion	Depression
Inferior oblique	Extorsion	Elevation

One oculomotor nucleus supplies the innervation of the ipsilateral inferior rectus, medial rectus, inferior oblique, and the contralateral superior rectus muscles. There is bilateral innervation of LPS.

The oculomotor nerve passes between the superior cerebellar and posterior cerebral arteries, runs near the medial aspect of the uncus of the temporal lobe and enters the cavernous sinus. The nerve separates into the superior division and inferior division in the anterior portion of the cavernous sinus as each passes through the superior orbital fissure. The superior division supplies the LPS and the SR muscles. The inferior division innervates the IR, MR, IO muscles and the sphincter pupillae.

The trochlear nucleus provides fibers for the contralateral fourth nerve as the fibers completely decussate in the anterior medullary velum located in the dorsal region of the midbrain. The fourth nerve is the only completely crossed cranial nerve. The fibers emerge from the dorsal midbrain near the midline, travel through the adjacent cisterns, enter the cavernous sinus, pass through the superior orbital fissure and innervate the superior oblique (SO) muscle.

The fourth nerve is the only completely crossed cranial nerve.

The sixth nucleus supplies fibers for the ipsilateral sixth nerve which innervates the lateral rectus. The sixth nerve also travels through the cavernous sinus and enters the orbit through the superior orbital fissure. There are interneurons in the sixth nucleus which supply fibers for the contralateral medial longitudinal fasciculus (MLF).

The examination begins with asking the patient to look up, down, right and left. This is followed by a request to look up and down when the eyes are deviated right and left. When the eye is adducted the oblique muscles elevate (IO) and lower (SO) the eye. When the eye is abducted the SR and IR are active. Therefore, on left upward gaze, the IO and MR are active O.D. and the SR and LR are the prime movers O.S.

Fourth nerve function depends on the position of the eye in the orbit.

Isolated fourth nerve palsies are not rare. Hence, the SO muscles may be the only extraocular muscle involved when a patient complains of diplopia. Its function depends on the position of the eye in the orbit. When there is a total third nerve palsy the involved eye is deviated laterally and usually down. When the patient is asked to look down the eye intorts. If this does not occur the patient has a combined

third and fourth nerve lesion indicating pathology in the cavernous sinus where the nerves are adjacent to each other. When the eyes are in midposition fourth nerve function is a mixture of intorsion and lowering. When the eye is adducted the SO lowers the eye without any rotation. A lesion of the fourth nerve usually results in an upward deviation (hypertropia) in primary position presumably due to unopposed action of the IO muscle. The head tilts away from the side of the fourth nerve lesion to reduce the diplopia. The Bielschowsky head-tilt test involves tilting the head toward the side of the weak SO which increases the separation of the images (see Fig. 4.10).

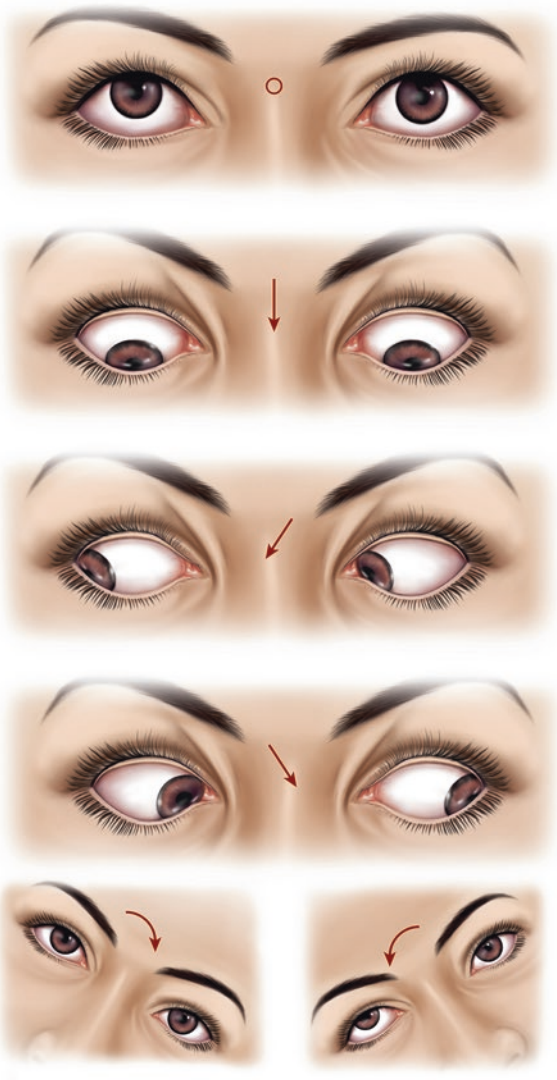

Fig. 4.10 Bielschowsky test for a right trochlear (4th) nerve lesion. Right hypertropia is seen in the top image and with gaze down and to the left. With head tilt left the deficit is erased and with head tilt right the deficit increases

A mass lesion compressing the third nerve usually affects pupillary fibers because they are superficial and on the dorsal surface of the nerve.

An isolated lesion of one third nerve nucleus, although rare, provides a unique opportunity to understand the anatomic organization. The consequences are a complete ipsilateral third nerve palsy and contralateral SR weakness and ptosis. A mass lesion compressing the third nerve usually affects pupillary fibers first since they are superficial and on the dorsal surface of the nerve. A third nerve lesion sparing the pupil is most common with an ischemic infarction affecting the central portion of the nerve such as occurs with the small vessel disease of diabetes. Rarely, an internal carotid artery aneurysm within the cavernous sinus is the etiology.

A lesion of the sixth nucleus affects both the neurons of the sixth nerve and interneurons which send fibers to the contralateral MLF. There are a few case reports which describe conjugate gaze paresis with such lesions. For the most part, however, gaze palsies due to brainstem pathology are caused by lesions of the paramedian pontine reticular formation (PPRF).

Horizontal gaze palsies due to brainstem pathology are usually caused by lesions of the paramedian pontine reticular formation (PPRF) and rarely isolated sixth nucleus lesions.

A sixth nerve lesion which results in ipsilateral lateral rectus weakness is often accompanied by a head turn to the side of the lesion. Additionally, horizontal diplopia at distance is a common symptom and sign of sixth nerve palsies since the eyes must diverge at distance. Lateral rectus weakness caused by a sixth nerve lesion, a common early sign of increased intracranial pressure, is due to its ascending path along the clivus which makes it vulnerable to any movement of the brainstem resulting from mass or pressure effect.

Convergence spasm (spasm of the near reflex) has the appearance of bilateral sixth nerve palsies. It is provoked by near fixation on an object followed by persistence of near fixation despite removal of the object. Pupillary miosis, not present with sixth nerve palsies, uncovers the physiology which is ordinarily psychogenic. The miosis resolves when one eye is occluded. Rare organic etiologies include the pretectal syndrome, Wernicke's encephalopathy, phenytoin toxicity, head injuries, during tonic-clonic seizures, thalamic hemorrhage, cyclic oculomotor spasm and any lesion at the diencephalic – mesencephalic junction.

Red Glass Test for Diplopia

When the patient complains of diplopia or there appears to be an ocular paresis, the red glass test can identify the weak muscle. A translucent red filter is placed over one eye. The light is directed at the pupil and the patient focuses on the light. If, for

example, the patient has diplopia on upgaze, the color of the light coming from the uppermost image arises from the weak muscle. Specifically, if there is a left superior rectus muscle weakness and the left eye is covered by the red filter, the red light is higher on upgaze. If the patient has a left lateral rectus weakness, diplopia is elicited on left lateral gaze. For instance, if the red filter is placed over the right eye (MR function), the farthest image to the left is white which arises from the left eye indicating a left lateral rectus paresis.

With the red glass test the distal image with ocular deviation comes from the weak muscle.

To summarize, on right lateral gaze the color of the image (white or red) farthest to the right designates the weak muscle. On downgaze, the color of the lowest image (white or red) designates the weak muscle. Thus, the test can be applied to assess any muscle by requesting the patient to look in the direction of the function of that eye muscle.

Saccades and Pursuit [10]

Testing both saccades and pursuit may seem onerous or excessive, but it can be easily accomplished in 10–20 s. Testing saccades is commonly omitted, but useful information is often obtained in patients with central nervous system (CNS) pathology.

Saccades are examined by requesting the patient to look quickly from one stationary point to another.

Saccades are examined by requesting the patient to look quickly from one stationary point to another. The test may elicit evidence of a specific ocular muscle paresis. For example, from central fixation to far right lateral fixation, the test may uncover a right LR or left MR weakness. Weakness of only the left MR muscle may indicate pathology involving the muscle, neuromuscular junction, third nerve, third nucleus or MLF. Weakness of only the right LR may indicate pathology involving the muscle, neuromuscular junction, sixth nerve or sixth nucleus.

Saccades from either a lateral or vertical fixation point to central fixation may be inaccurate and disclose significant pathology.

Saccades from either a lateral or vertical fixation point to central fixation may be inaccurate. This is often an undershoot, a hypometric saccade, followed by a small corrective saccade in the same direction. This is a normal phenomenon. The eyes may overshoot, a hypermetric saccade, then slide back, a "glissade," to the central point of fixation. This is called ocular dysmetria. The eyes may also return to central fixation with another saccade. Both phenomena, ocular dysmetria and a corrective saccade in the opposite direction to reach the target, are indicative of cerebellar system pathology.

The saccade velocity to right vs. left and up vs. down should be roughly compared. If, for instance, saccades are slower or incomplete to the right, there must be a lesion in the oculomotor pathway that generates eye movements to the right. This would be the left frontoparietal eye fields, left anterior limb of internal capsule or thalamus, left mesencephalic reticular formation, and right PPRF. This is the most clinically applicable of several pathways which also involve basal ganglia and superior colliculus.

Pursuit is examined by requesting the patient to follow the examiner's slowly moving finger in all directions of gaze. This is the usual method of examination and uncovers any obvious ocular paresis. Nystagmus may be elicited at the termination point. If there is a defect of the pursuit system, the patient's eyes may not be able to keep up with a moving target and saccades may be substituted to catch up with it. This "saccadic pursuit" is especially common in patients with extrapyramidal disorders such as Parkinson's disease, but has no precise localizing significance. It is not unusual in the normal elderly population.

Saccadic pursuit occurs when the patient is unable to keep up with a moving target using the pursuit system and saccades are substituted.

Dysconjugate Gaze and Abnormal Eye Positions [10]

The MLF is primarily a quick system pathway; thus, it is best examined using the saccadic system.

The essential element of an internuclear ophthalmoplegia (INO) is an ipsilateral adduction defect.

1. Horizontal dysconjugate gaze. This is typified by the syndrome of the MLF or internuclear ophthalmoplegia (INO). As previously outlined the pathway connects the PPRF with the contralateral oculomotor nucleus via intervening synapses in the ipsilateral abducens nucleus before crossing the midline. It is primarily a quick system pathway and thus best elicited by testing with saccades. The main finding is ipsilateral paresis of adduction or an adductor lag, a slow saccade of the medial rectus as compared to the lateral rectus. A second element

is nystagmus in the contralateral abducting eye. The etiology of this component is speculative but it depends on the detectable presence of ipsilateral MR paresis. A third and variable feature is preservation of convergence. When absent it implies a lesion in the midbrain near the termination of the MLF.

2. Bilateral INO. This is associated with abnormalities in the vertical plane, especially downbeat and/or upbeat nystagmus. Occasionally, this is unilateral with contralateral rotatory nystagmus. See-saw nystagmus may occur. Vestibular fibers in the MLF originating from the posterior semicircular canal may explain the torsional elements. Skew deviation, a vertical separation of the eyes, secondary to acquired supranuclear or vestibulo-ocular disruptions can be present with the higher eye ipsilateral to the lesion. The WEBINO syndrome, wall-eyed bilateral internuclear ophthalmoplegia, is self-explanatory and has been well described. The "one-and-a-half" syndrome indicates involvement of the PPRF and MLF on the same side. For example, a left-sided lesion results in an ipsilateral gaze paresis (PPRF) and ipsilateral MR paresis (MLF). Thus the ipsilateral eye has no horizontal movement. The only remaining horizontal movement is abduction of the contralateral eye which typically exhibits right-beating nystagmus in abduction. A common associated finding is an ipsilateral facial weakness.

The "one-and-a-half" syndrome indicates involvement of both PPRF and MLF on the same side.

3. Vertical dysconjugate eye movements are infrequent. The vertical one-and-a-half syndrome is manifested by upgaze paresis and monocular paresis of downgaze on the side of the lesion. This occurs with thalamo-mesencephalic lesions. Monocular elevation paresis (double elevator palsy) occurs with contralateral or ipsilateral pretectal lesions which interrupt efferent pathways from the rostral interstitial nucleus of the MLF (riMLF) to the SR and IO subnuclei.

Skew deviation is a vertical misalignment of the eyes due to disruption of pathways from the utricle to the rostral mesencephalon.

4. Skew deviation (see Fig. 4.11), a vertical misalignment of the eyes, is primarily due to central nervous system lesions which are supranuclear and disrupt pathways from the otolith organs (utricle and saccule) to vertical oculomotor nuclei and the interstitial nucleus of Cajal. Lesions are in the brainstem, cerebellum or projections from the otolith organs. It may be difficult to distinguish skew deviation from fourth nerve lesions. A trochlear neuropathy results in ipsilateral hypertropia in primary

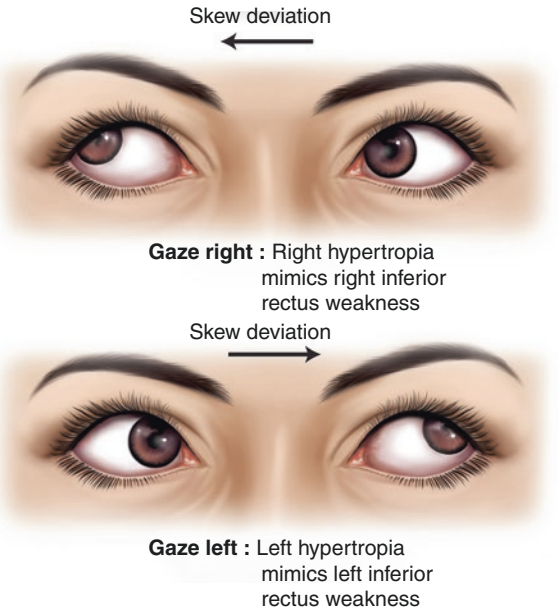

Fig. 4.11 Skew deviation. Gaze to right mimics right inferior rectus weakness (hypertropia O.D.). Gaze to the left mimics left inferior rectus weakness (hypertropia O.S.)

position, head tilt away from the side of the lesion and a positive Bielschowsky head-tilt test. This has already been discussed under 4th nerve function.

5. The ocular tilt reaction is manifested by skew deviation, cycloversion (eyes rotate in direction of the lower eye), and ipsilateral head tilt toward the side of hypotropia. Pendular nystagmus and lid retraction may be associated features. Lesions producing this triad have been discovered in the ipsilateral labyrinth, 8th nerve, vestibular nucleus and contralateral meso-diencephalon involving the interstitial nucleus of Cajal. Involvement of the labyrinth and 8th nerve are sufficiently rare such that an ocular tilt reaction indicates a brainstem lesion for practical purposes. This reaction may be persistent (tonic) or intermittent (phasic). Patients may complain of a tilt of the environment.

Gaze Paresis [12]

Horizontal gaze paresis occurs with lesions of the oculomotor pathway for horizontal gaze.

1. Horizontal gaze paresis occurs with lesions of the oculomotor pathway for horizontal gaze. Briefly, gaze paresis to the right (gaze preference left) indicates a lesion above the oculomotor decussation on the left or below it in the right PPRF. The oculomotor decussation is located at the pontomesencephalic junction.

Upgaze paresis is usually due to a lesion of the posterior commissure. Downgaze paresis is associated with riMLF lesions.

2. Upgaze paresis is usually due to a lesion of the posterior commissure.
3. Downgaze paresis is usually due to a lesion of the rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF). This is a structure separate from the MLF.

Pretectal Syndrome [12]

Eponyms include dorsal midbrain, Parinaud's, Sylvian aqueduct and posterior commissure syndrome. Pretectal is preferred by some neurologists since it is a reminder of pupillary involvement.

Features include:

1. large, round nonreactive or poorly reactive pupils with light-near dissociation. (Argyll-Robertson pupils are small.)
2. upgaze paresis with saccades involved first followed by ocular pursuit, vestibulo-ocular reflexes and Bell's phenomenon.
3. lid retraction (Collier's sign) and lid lag.
4. convergence – retraction nystagmus on attempted upgaze but best evoked by an optokinetic stimulus moving downward.

Hydrocephalus and pineal tumors are the most common etiologies of the pretectal syndrome.

Eye Deviations

1. Eye deviation left, for example, indicates a lesion on the left side above the oculomotor decussation, which is at the midbrain-pontine junction, or below this decussation, usually a right PPRF lesion.

Downward eye deviation occurs with thalamic hemorrhage, metabolic, and hypoxic-ischemic encephalopathies.

2. Downward eye deviation is less specific. It occurs with thalamic hemorrhage, metabolic, and hypoxic-ischemic encephalopathies.
3. Upward eye deviation, if persistent, occurs almost always with hypoxic-ischemic encephalopathy. Oculogyric crises associated with neuroleptics are rarely the etiology.

Ocular Oscillations: Nystagmus

Nystagmus is best observed by looking at the blood vessels on the sclera since rotatory (torsional) elements are often otherwise missed.

1. Nystagmus is usually of the "jerk" type. There is a quick phase analogous to a saccade and a slow phase analogous to pursuit. The quick phase determines its direction. Nystagmus is best observed by looking at the blood vessels on the sclera since rotatory (torsional) elements are often otherwise missed. A comment such as "There is nystagmus on upgaze" has no meaning without a notation of the quick phase. Lesions of the central or peripheral nervous system (PNS) can provoke some form of nystagmus in any direction of gaze. Conversely, a note which states "There is upward beating nystagmus on upgaze" indicates brainstem pathology or toxic effect of drugs. Infrequently, low amplitude nystagmus is discovered only on funduscopic examination and not merely visually. The retinal movement is opposite to the movement of the globes and thus upbeat retinal nystagmus is observed as downbeat nystagmus. Only an astute examiner identifies this phenomenon which can be dismissed as poor cooperation. Pendular nystagmus is manifested by rapid horizontal eye movements of equal velocity in both directions. Occasionally, there is a mixed jerk and pendular nystagmus. This type of nystagmus is most often congenital in origin. Acquired forms have been described such as in patients with the ocular tilt reaction, previously discussed under Dysconjugate Gaze and Abnormal Eye Positions.
2. Horizontal nystagmus of vestibular origin. This is due to lesions of the peripheral vestibular apparatus, 8th nerve, or vestibular nuclei in the brainstem. The nystagmus is usually present on direct forward gaze and increases in intensity when the eyes are deviated in the direction of the quick phase (Alexander's law). It is horizontal or combined horizontal rotatory. The rotation is clockwise when the quick phase is to the left and counterclockwise when it is to the right. When the nystagmus is direction-fixed such as always to the right, whether the eyes are deviated right, up, down, or left, peripheral vestibular origin is suspected. Clearly, the

absence of brainstem/cerebellar system symptoms and signs is required before a peripheral etiology can be diagnosed. The physiology of the vestibular system will be discussed under the section on the "8th Cranial Nerve."

Direction-fixed nystagmus to the contralateral side in all eye positions is a common finding with peripheral vestibular disease.

Since visual fixation inhibits nystagmus of vestibular origin vertigo may be present without visible abnormalities, an indication for electronystagmography.

Visual fixation suppresses nystagmus of peripheral origin. Consequently, with eyes closed, the patient is often more symptomatic. Nystagmus may sometimes be perceived as eye rolling behind lightly closed lids. Proof of nystagmus behind closed lids can be obtained through electronystagmography which uses the corneo-retinal potential to record eye movements, or at the bedside using Frenzel glasses. These are glasses with thick lenses which prevent visual fixation and magnify the eyes allowing for more accurate observation by the examiner.

Horizontal gaze-evoked nystagmus indicates drug effect or a brainstem/cerebellar lesion.

3. Gaze-evoked nystagmus. This is nystagmus provoked by looking up, down, right, or left. Horizontal gaze-evoked nystagmus means nystagmus to the right on right lateral gaze and nystagmus to the left on left lateral gaze. It is the most common form of nystagmus encountered. The most likely etiology is drug effect, sedatives, and especially some anticonvulsants. Brainstem/cerebellar lesions may cause gaze-evoked nystagmus. This is not seen with peripheral vestibular disease. Gaze-evoked nystagmus may be upbeat which is either due to toxic effect of drugs or brainstem/cerebellar system pathology. Downbeat gaze-evoked nystagmus is rare and usually associated with lesions affecting the cerebellar flocculus at the cervical-medullary junction. It is often more prominent on lateral gaze. This is probably most commonly seen with a Chiari I malformation or spinocerebellar degeneration. Periodic alternating nystagmus may be an associated finding and is discussed below.
4. Specific types of nystagmus.

- Endpoint nystagmus. This is a physiological form of nystagmus if the eyes are deviated more than 30° to either side. It is occasionally sustained when the eyes are deviated more than 40° to either side.

- Torsional (pure rotatory) nystagmus. This is seen with brainstem disease, especially the medulla and has been described with Wallenberg's syndrome. This syndrome is most commonly seen with vertebral artery disease resulting in ischemia in the posterior inferior cerebellar artery distribution.

An INO commonly causes dissociated nystagmus which is observed in the abducting eye.

- Dissociated nystagmus. Internuclear ophthalmoplegia is the best representative of this form of nystagmus. A lesion of the left MLF, for instance, commonly results in an ipsilateral paresis of adduction (left medial rectus weakness) and horizontal jerk nystagmus to the right of the contralateral eye on attempted right lateral gaze. Between ages 15 and 50 it nearly always points to multiple sclerosis. In childhood, ages 4 to 8 a pontine astrocytoma, and over age 50, a brainstem infarction due to basilar artery disease are primary diagnostic considerations.
- Periodic alternating nystagmus. This is horizontal jerk nystagmus that changes directions every 90 s after about a 10 s interlude of stability. Thus, for example, on direct forward gaze there is horizontal nystagmus to the right for 90 s, then 10 s of stability, and then 90 s of horizontal nystagmus to the left. The pattern persists indefinitely. This form of nystagmus is commonly unrecognized since it requires prolonged observation to diagnose. The location of the lesion is at the cervical-medullary junction and specific etiologies to consider include Chiari I malformation and multiple sclerosis.

Periodic alternating nystagmus is due to lesions at the cervical-medullary junction.

- Convergence-retractory nystagmus. This nystagmus is provoked by upgaze or sliding an optokinetic tape downwards. It is manifested by adducting saccades and retraction of the eyes into the orbit due to simultaneous activation of all extraocular muscles. Lesions are in the dorsal midbrain. Etiologies include pineal neoplasm, hydrocephalus, multiple sclerosis and stroke.

Convergence-retractory nystagmus is found in patients with dorsal midbrain lesions.

- Downbeat nystagmus. The quick phase beats downward in primary position, but it is usually more prominent on lateral gaze. The lesion is most common at the

cervical-medullary junction and often involves the cerebellar nodulus and flocculus. The most common causes are Chiari I malformation, multiple sclerosis and spinocerebellar degeneration.

Downbeat nystagmus is associated with lesions of the cerebellar nodulus and flocculus, located near the cervical-medullary junction.

- Upbeat nystagmus. This is a primary position nystagmus with quick phase beating upward and more intense on upgaze. Brainstem lesions, especially involving the perihypoglossal nuclei in the medulla, have been discovered in some of these patients. Stroke, multiple sclerosis, and toxic effect of drugs are the most common etiologies.
- See-saw nystagmus. This is characterized by an intorsion of the elevating eye and extorsion of the opposite descending eye. It is most often pendular and has been described with parasellar neoplasms and thalamic-midbrain lesions. There are congenital forms which have distinctive features; the intorting eye falls and the extorting eye rises, just opposite to the pathologic form described above.
- Bruns' nystagmus. This type of nystagmus is often associated with neoplasm, especially schwannomas of the 8th nerve which compress the brainstem. There is rapid contralateral nystagmus of small amplitude and slower, larger amplitude ipsilateral nystagmus due to brainstem compression.

Seizures produce horizontal nystagmus with quick phase directed contralateral to the epileptic focus.

- Seizures. Seizures produce horizontal nystagmus with quick phase directed contralateral to the epileptic focus. The nystagmus is ordinarily brief, seconds to 2 or 3 min, the usual duration of seizures.
- Positional nystagmus. Direction-changing positional nystagmus (DCPN) has two forms, geotropic and ageotropic. Geotropic indicates that, when lying supine with head turned to the right, the quick phase beats right and with head turned to the left the quick phase beats left. In other words, nystagmus is always directed towards the ground when the head is turned. Ageotropic is quick phase to the left when the patient is supine with head right and vice versa when the head is turned left. Both are most often observed with peripheral vestibular disease. Rarely, the ageotropic type has been described with brainstem/cerebellar system pathology. There remains some controversy about the localizing value of these forms of nystagmus.

Benign paroxysmal positional vertigo (BPPV) will be discussed later under special tests.

Congenital nystagmus is usually binocular, pendular, decreased by convergence, increased by visual fixation and has a null point.

- Congenital nystagmus. This is typically a pendular nystagmus although there may be jerk elements. It is binocular, ordinarily horizontal, decreased by convergence and increased by visual fixation. There is often a null point, a specific eye position where the patient has no nystagmus. It is associated with albinism and achromatopsia (absence of color perception).

Latent nystagmus is binocular nystagmus present only when one eye is covered. It is most often discovered during the funduscopic examination. Hence, it is commonly dismissed as inability to focus or noncooperation.

- Voluntary nystagmus. This is actually rapid back-to-back saccadic eye movements which can be induced at will and is likely to be of genetic origin. It is important to recognize as nonpathologic since it may be employed by malingerers.

Myasthenic nystagmus occurs because paretic muscles fatigue and the eye drifts back to central gaze.

- Myasthenic nystagmus. Paretic muscles fatigue easily and hence there is a slow drift back to central gaze. Usually, the eye movements are asymmetric due to different degrees of weakness in the contracting muscles. Pseudointernuclear ophthalmoplegia is a well-known feature of myasthenia gravis.

5. Guidelines.

The direction of nystagmus is specified by the direction of the quick phase.

- Always designate the direction of nystagmus by the direction of the quick phase and focus on the sclera for both detection of torsional elements and accuracy.
- Evaluate all directions of gaze.
- Nystagmus which has more than one direction is of either central origin or due to drug effect. A rare exception is DCPN, just described.
- Pure torsional (rotatory) nystagmus indicates brainstem/cerebellar system pathology.
- Horizontal direction-fixed nystagmus which may be present in some or all directions of gaze is commonly of peripheral vestibular origin. This includes lesions of the 8th nerve and semicircular canals.
- Purely positional nystagmus is usually of peripheral origin, but there are important exceptions especially if there is no fatigability. Posterior fossa mass lesions have rarely presented in this fashion.

Special Tests

The Dix-Hallpike test is mandatory when there is a complaint of dizziness or vertigo associated with a change of position.

1. The Dix-Hallpike test for benign paroxysmal positional vertigo (BPPV).

This test is mandatory when there is a complaint of dizziness or vertigo associated with a change of position, sitting up, lying down or turning over in bed. Rarely, elderly patients complain of only a sense of instability and thus warrant testing if there is no other obvious pathology. The seated patient's head is turned to the examiner and the patient is moved rapidly to the supine position with the head extended backwards as shown in Fig. 4.15. Involvement of the posterior semicircular canal is most common. This results in rotatory, upbeat, vertical nystagmus directed to the undermost ear after a latency of up to 20 s. The nystagmus usually dissipates within 30 s. Habituation occurs with repeat testing as the nystagmus becomes more difficult to elicit. Mechanical treatment with the canalith repositioning maneuver is usually curative (see Fig. 11.1). Medical treatment is useless.

Induced nystagmus, optokinetic or caloric, may uncover a focal lesion.

2. Induced nystagmus. Optokinetic nystagmus. Using a striped or dotted cloth, the patient is requested to focus on the stripes or dots as the cloth is moved slowly from the patient's left to right and vice versa. When the patient's eyes follow the cloth movement to the right, a saccade to the left is elicited to return the eyes to central fixation. This is compared with the opposite direction of movement. Significant asymmetries are noted and correlated with other neurologic findings. Poor quick phases to the right might imply a lesion involving the left oculomotor pathway above the oculomotor decussation, which is located at the pontomesencephalic junction, or an ipsilateral lesion below this level in the pons (right PPRF).

Caloric nystagmus requires raising the head 30° which brings the horizontal canal vertical, enabling a maximum response with cold water irrigation.

3. Caloric nystagmus. The head is raised 30° to bring the horizontal canal vertical which elicits a maximum response with cold water irrigation. After an inspection shows an intact tympanic membrane the ear is irrigated with cold water. This should elicit contralateral quick phases. Warm water irrigation produces ipsilateral quick phases but the temperature of warm water must be precise and, therefore, for practical purposes, only cold water is used. This is a useful test for patients in the Intensive Care Unit with altered levels of consciousness and will be discussed in Chap. 5, Evaluation of the Poorly Responsive Patient.

The most important ocular dyskinesias are ocular dysmetria, ocular flutter and opsoclonus. These are associated with cerebellar system pathology.

Ocular Oscillations: Dyskinesias

These are saccadic system abnormalities associated with cerebellar system dysfunction, less often brainstem.

1. Ocular dysmetria, discussed earlier, is the most common dyskinesia. It is examined by asking the patient to look from a lateral or vertical point of fixation to a central point. There is an overshoot with slow return (glissade) which defines ocular dysmetria.
2. Ocular flutter is several back-to-back saccades without an intersaccadic interval in the horizontal plane when the eyes are following a moving target.
3. Opsoclonus is defined by chaotic saccades without an intersaccadic interval in all planes. Some etiologies are brainstem encephalitis, drug toxicity, hyperosmolar nonketotic coma, post infectious syndrome, multiple sclerosis and paraneoplastic syndromes, especially neuroblastoma and visceral carcinomas.
4. Square wave jerks, macrosquare wave jerks and macrosaccadic oscillations are additional ocular dyskinesias. Further discussion of these disorders is beyond the scope of this book.

The most common causes of opsoclonus are encephalitis, paraneoplastic syndromes and multiple sclerosis.

5. Ocular-palatal myoclonus. These are rhythmic oscillations of the eyes combined with simultaneous oscillations of one or more of the following structures, soft palate, tongue, mouth, larynx and diaphragm. The frequency is 1–3 Hz. The lesion location is in the Guillain-Mollaret triangle. This triangle includes the red nucleus, inferior olivary nucleus and the dentate nucleus plus their connections. The latter are the central tegmental tract, superior and inferior cerebellar peduncles. The abnormal neuronal discharge is located in the inferior olivary nucleus. Stroke is the most common cause.

Pupils: Observations

1. Pupillary size. The normal pupil is usually between 2 and 7 mm. In infants, the pupils are small and gradually increase to normal adult size by about the age of 8. Otherwise, pupils are larger in youth and smaller in the elderly. Fluctuation of pupillary size is common and is called “pupillary play.” Large fluctuations are called “hippus.” And, although quite noticeable on inspection, it has no definite pathologic association. Pupils constrict in sleep and with forced eye closure.

2. Pupillary shape and position should be noted. The pupils may be oval, irregular and, in rare instances, eccentric in position. Although abnormalities are usually of ophthalmic origin, oval and eccentric pupils (corectopia) can be associated with midbrain pathology.

The pupillary reaction to both light and near are graded 1+ (slow) to 4+ (brisk).

3. The pupillary reaction to both light and near are graded 1+ (slow) to 4+ (brisk). A slower reaction on one side could be due to impaired constriction of the sphincter pupillae (3rd nerve) or partial interruption of the afferent pathway (optic nerve). Assuming there is a brisk reaction to light in the opposite eye, a persistent sluggish consensual response indicates an impaired efferent pathway or 3rd nerve lesion. A brisk consensual reaction in the involved eye means a poor afferent pathway, thus an optic nerve lesion.
4. Relative afferent pupillary defect (RAPD) was formerly called the Marcus-Gunn pupil. This test is designed to diagnose optic nerve disease. It may occur with optic chiasm lesions since some involvement of the optic nerve is common; it is a rare phenomenon with optic tract disease. Even though vision may be seriously impaired due to a dense cataract, amblyopia ex anopsia and macular disease, the test remains valid since these disorders do not impair pupillary reactions to light. Macular disease almost never produces an afferent pupillary defect. If so, it would require simultaneously obliteration of most of the retina. Optic nerve disease with a visual acuity of 20/25 in one eye and a cataract with 20/400 in the other eye may nevertheless produce an afferent pupillary defect in the eye with 20/25 vision. Furthermore, an optic nerve lesion causing poor color perception yet having 20/20 visual acuity may still yield an afferent pupillary defect.

As long as light is perceived, cataracts, amblyopia ex anopsia and macular disease do not impair pupillary reactions to light.

When the pupils are tested the patient must fixate on a distant point at least 6 ft. away.

Technique is critical. The test is best performed in a dimly lit room. The patient must fixate on a distant point at least 6 ft. away. It is best to shine the light from below the horizontal meridian which should prevent contamination with a near response. Firstly, each eye is tested individually to grade the pupillary response, 1+ to 4+, and whether it fatigues. Assuming a questionable difference or a possible optic nerve lesion, a bright light is shined into the good eye for 3–5 s and quickly switched to the suspected involved eye. This may be repeated a few times. The first well-defined movement of the pupil is key to the diagnosis as there is often a small fluctuation in pupillary size in normal individuals. The abnormal side will dilate.

When an RAPD is suspected the primary question is: Which response is better, direct or consensual?

The primary question to answer is: Which response is better, direct or consensual? A reverse afferent pupillary defect is another approach. If one focuses on the suspected abnormal eye a consensual response may provoke an obvious constriction when the light is switched to the other eye, thus securing the diagnosis of optic nerve disease.

5. Light-near dissociation. The near synkinesis is composed of three elements – convergence, accommodation and miosis. If the pupillary light reflexes are 4+ bilaterally, there is no need to check the near response since the only known dissociation is a poor light response with a good near reaction. The most reliable method for checking the near response is to ask the patient to follow his own finger as it moves towards his nose. Guiding the patient's arm may be necessary. Severe visual loss or even blindness does not obviate the test since patients can imagine the location of their finger.

Argyll-Robertson pupils are bilateral and miotic, whereas Adie's pupils are usually unilateral and large.

- Argyll-Robertson pupils. Features include minimal-to-absent light response and intact near response. There does not need to be a totally absent response to light. The pupils are bilateral, miotic, irregular, and often asymmetric. Vision should be grossly normal to make this diagnosis.
- Adie's syndrome (tonic pupil). These pupils are unilateral and large in bright light. They do become bilateral at a slow rate of 4% per year. There is a poor-to-absent light reaction, slow constriction to prolonged near response and slow redilation. Segmental vermiform movements of the iris are observed on slit-lamp examination. There is denervation hypersensitivity as only the involved pupil reacts to dilute pilocarpine 0.125%. Ankle reflexes are decreased or absent. The lesion is in the ciliary ganglion or short ciliary nerves.
- Midbrain pupils. These are midposition, irregular, nonreactive to light and may have a good reaction to near. Corectopia, eccentric displacement of the pupil, and oval pupils may be present.
- Pretectal pupils. These are large round, nonreactive or poorly reactive with light-near dissociation.
- Bilateral optic nerve or chiasm disease. When the afferent loop of the pupillary reflex has a prominent lesion the near reflex usually exceeds that of the light response.

6. Asymmetric pupillary size. What is significant in the absence of eye disease or prior eye surgery which could affect the response?

If there is no local ophthalmic pathology, asymmetric pupils are due to a parasympathetic or sympathetic lesion when there is a difference in pupillary size of greater than 0.5 mm.

- Parasympathetic involvement. This is clearly present when the larger pupil reacts sluggishly to both direct and consensual light or not at all. The asymmetry is best noted in a well-lit room since the sphincter pupillae is then preferentially stimulated and the normal side responds well.
- Sympathetic involvement. The pupils are briskly reactive. After the room is darkened the patient should be examined between 5 to 15 s later. The asymmetry increases since the dilator pupillae is maximally stimulated but the involved side initially functions poorly for several seconds. Horner's syndrome is an example.
- Central anisocoria. This is usually less than 0.5 mm. Both pupils react normally and the asymmetry is the same in light and dark.

Pupils are equal when there is amaurosis due to optic nerve disease.

7. Amaurotic pupil. Unilateral amaurosis due to optic nerve disease results in equal pupillary size because of an intact consensual response from light stimulation of the normal eye. A light stimulus to the amaurotic eye due to optic nerve disease yields no response in the normal eye. An afferent pupillary defect is obvious. Bilateral amaurosis due to optic nerve or chiasm involvement will produce light-near dissociation, as described above.

Trigeminal Nerve

1. Background anatomy.

The trigeminal nerve has sensory and motor components. The motor nucleus is located in the midpons and receives fibers from both cerebral hemispheres. The decussation is in the pons, just above the nucleus. The motor root (portio minor) joins the mandibular division (V_3). This root supplies the muscles of mastication; these are the masseter, temporalis, medial and lateral pterygoids.

The motor root of the trigeminal nerve joins the mandibular division (V_3) which supplies the muscles of mastication.

The sensory portion arises from three nuclear complexes, the nucleus of the spinal tract of V, the main sensory nucleus and the mesencephalic nucleus. The spinal tract of V, which mediates pain and temperature, descends from the pons down to C3–C4 of the cervical cord. Axons from the tract terminate in the adjacent nucleus of the spinal tract of V. The nucleus divides into the pars oralis which travels from midpons to the inferior olivary nucleus, the pars interpolaris from the inferior olive to the obex of the fourth ventricle and pars caudalis which extends down to the dor-

sal horn gray matter of the cervical spinal cord. Fibers of the ophthalmic division extend most caudally and those of the mandibular division terminate in the most rostral level of the spinal nucleus of V. The fibers cross and ascend to the ventral posteromedial nucleus of the thalamus (VPM).

The main sensory nucleus is located in the rostral part of the pons just lateral to the motor nucleus. It mediates touch and proprioception. It sends crossed and uncrossed fibers to the VPM via the quintothalamic and trigeminothalamic pathways, respectively.

The mesencephalic nucleus is located in the caudal midbrain and mediates proprioception from the muscles of mastication.

The sensory root and motor root expand to form the gasserian ganglion which sits in Meckel's cave. The ganglion gives rise to the V_1 (ophthalmic), V_2 (maxillary) and V_3 (mandibular) divisions.

The trigeminal nerve passes through the cerebellopontine angle. The ophthalmic and maxillary divisions travel through the cavernous sinus along with cranial nerves 3, 4, 6 and the internal carotid artery which carries sympathetic fibers in its sheath. The sympathetic fibers merge with the ophthalmic division as it passes through the superior orbital fissure. The maxillary division travels a short distance in the inferolateral portion of the cavernous sinus before it exits the skull via the foramen rotundum. The mandibular division joints the motor root and passes through the foramen ovale.

The ophthalmic division receives sensory information from the upper lid, forehead, anterior scalp, upper half of cornea and iris, top and side of nose, frontal sinus and carries sympathetic fibers to the dilator pupillae via the long ciliary nerves. The

The trigeminal nerve passes through the cerebellopontine angle. The ophthalmic and maxillary divisions (V_1 and V_2) travel through the cavernous sinus along with cranial nerves 3, 4, 6 and the internal carotid artery.

maxillary division is purely sensory and supplies the lower eyelid, lateral nose, lower cornea, hard and soft palate, upper gums and teeth, maxillary sinus and nasal mucus membrane. The mandibular division mediates sensory information from the anterior two thirds of the tongue (except taste), lower gums and teeth, chin, lower lip, tympanic membrane, upper ear and auditory meatus. It contains the motor root which innervates the muscles of mastication. The muscles which close and clench the jaw are the temporalis, masseter, and medial pterygoids. The lateral pterygoids protrude and move the jaws laterally. Additionally, the trigeminal nerve innervates the meninges and the arteries of the circle of Willis. Thus, it mediates pain due to meningitis, subarachnoid hemorrhage and migraine.

The trigeminal nerve innervates the meninges and the arteries of the circle of Willis.

2. Examination of the trigeminal nerve:

> The corneal reflex is tested by using a wisp of cotton to touch the cornea which is over the iris, not the sclera.

Pinprick sensibility is checked in all three divisions. Additional testing of gums, buccal mucosa and tongue can be added if clinically relevant. Sensory loss may occasionally be in an "onion-skin" pattern since there is an extensive longitudinal distribution of the spinal tract of V. Midline structures, nose and mouth are represented in the rostral part of the nucleus and lateral fibers in the caudal part.

The corneal reflex (see Fig. 4.12) can be considered an optional test depending on the history. A wisp of cotton can be used to touch the cornea over the iris. The sclera is insensitive. An absent reflex with good sensation indicates a weak orbicularis oculi. A good contralateral blink is expected with a unilateral seventh nerve lesion. This is a useful test in an unresponsive patient.

Bulk and pallor of the masseters and pterygoids can be assessed by palpating the muscles when the patient's jaws are clenched. With nuclear or infranuclear lesions unilateral weakness causes the jaw to deviate to the weak side. Deviation can sometimes be observed on jaw opening. Although there is bilateral innervation of these muscles the masseters are primarily controlled by the contralateral hemisphere and thus deviation of the jaw away from the lesion may occur.

Jaw jerk (see Fig. 4.13) (masseter reflex): When the lower jaw is tapped there is contraction of the masseter and temporalis muscles. The afferent and efferent limb run through the mandibular branch (V_3). Bilateral supranuclear lesions cause an increased reflex which can be a useful finding. The jaw reflex is often absent in normal individuals.

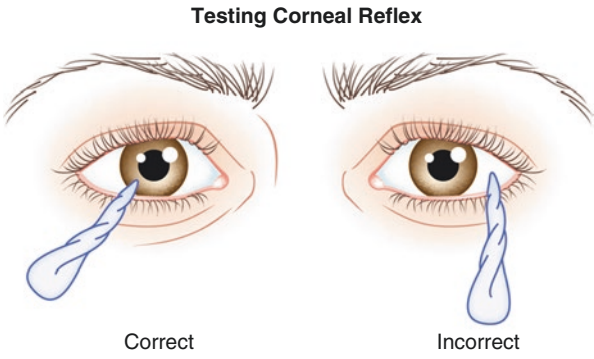

Fig. 4.12 Jaw reflex. Method of obtaining a jaw reflex

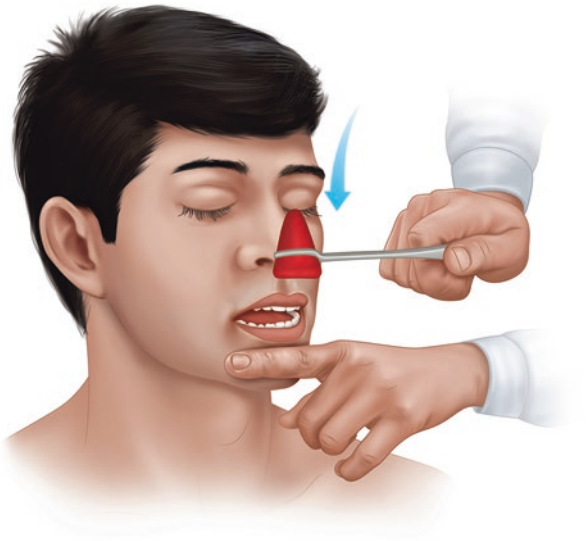

Fig. 4.13 Corneal reflex. The correct method for testing the corneal reflex is performed O.D. There is no response when the sclera is touched, O.S., since it has minimal innervation

Seventh Cranial Nerve (Facial)

1. Background anatomy.

The 7th nerve nucleus is located in the caudal pontine tegmentum. It receives corticobulbar fibers which originate from the lower third of the precentral gyrus; these fibers decussate in the upper pons. There are both ipsilateral and contralateral fibers which supply the upper facial muscles, mainly frontalis, but primarily contralateral fibers which innervate the lower facial muscles. Contralateral orbicularis oculi weakness is a common finding with supranuclear lesions (wider palpebral fissure). The seventh nerve roots loop around the sixth nucleus, then exit the ventrolateral portion of the pons, pass through the cerebellopontine angle adjacent to the fifth and 8th nerves, and then enter the internal auditory meatus. The nervus intermedius lies between the seventh and 8th nerves and mediates both parasympathetic and sensory function (taste). The facial nerve motor fibers innervate frontalis, orbicularis oculi, orbicularis oris, buccinators, stapedius, and platysma musculature.

Frontalis musculature is innervated by both ipsilateral and contralateral fibers. Sparing of frontalis musculature occurs with most supranuclear lesions. Contralateral orbicularis oculi weakness is common with supranuclear lesions (wider palpebral fissure).

Parasympathetic and sensory function is mediated by the nervus intermedius. The parasympathetic origin is in the superior salivatory nucleus in the pontine tegmentum. The adjacent lacrimal nucleus supplies nerve fibers to the lacrimal gland via the greater superficial petrosal nerve. Thus, a facial nerve lesion proximal to this nerve may cause a dry eye. Excessive tearing (epiphora) is associated with orbicularis oculi weakness. Parasympathetic fibers in the nervus intermedius also supply the submaxillary, submandibular, and sublingual glands via the chorda tympani.

The most important sensory function of the facial nerve is taste which is mediated by the chorda tympani which supplies the anterior two thirds of the tongue.

The most important sensory function of the facial nerve is taste which is mediated by the chorda tympani which supplies the anterior two thirds of the tongue. These nerve fibers travel through the nervus intermedius and terminate in the nucleus of the solitary tract in the medulla. Other sensory fibers in the seventh nerve supply the mucosa of the nose, pharynx, palate, pinna, mastoid and skin of the external auditory meatus.

2. Examination of the facial nerve:

   (a) Observations.

Asymmetry of palpebral fissures, the distance between the upper and lower eyelids, is quite common with a central facial nerve paresis.

Because of the anatomy, discussed above, a central seventh paresis may involve only the lower facial muscles, whereas a peripheral seventh lesion usually involves all facial muscles. However, the well-trained neurologist is quite aware that asymmetry of the palpebral fissures, the distance between the upper and lower eyelids, is quite common with a central seventh nerve paresis. The wider palpebral fissure indicates orbicularis oculi weakness. Beginners mistakenly believe that the opposite eye is ptotic. A flattened nasolabial fold may be evident on the weak side, but note should be made that older individuals often have asymmetries without indicating pathology. The frontalis muscle is rarely affected with facial weakness due to a supranuclear lesion. Ultimately, one has to depend on clinical judgment as to whether the asymmetry is abnormal.

Facial asymmetry may be evident only with spontaneous expressions, especially smiling, and is called “mimetic” facial weakness.

Facial asymmetry may be evident only with spontaneous expressions, especially smiling, and is called “mimetic” facial weakness. This may be associated with frontal lobe lesions as a separate pathway probably mediates this response. Frontalis asymmetry, fewer wrinkles on one side, can be discerned on upward gaze. Asymmetric eye blinks, slower on the weak side, are a good clue for a seventh nerve paresis.

(b) Voluntary movements.

Forced eye closure may be incomplete, evident by seeing the eyelashes on the weak side, whereas they are "buried" on the normal side. When weakness is suspected the examiner should compare eyelid strength by attempting to pull the lids open with his or her fingers on both sides, simultaneously. A facial grimace or a request to "show me your teeth" will assess strength of orbicularis oris. Retracting the lower jaw with a strong grimace tests platysma function. Puffing out the cheek tests the buccinator muscle. Bell's phenomenon may occur on forced eye closure as the eye moves up and laterally. This is a normal response which is visible if the orbicularis oculi is weak on this side. Only 10% of normal patients will not have this movement. Consequently, an asymmetry may possibly have clinical significance by indicating a unilateral upgaze paresis.

(c) Abnormal involuntary movements.

Facial synkinesias are movements that occur after Bell's palsy when there is aberrant reinnervation.

- Facial synkinesias. These are movements that occur after Bell's palsy when there is aberrant reinnervation. For example, nerve fibers that were to be directed to the orbicularis oris innervate the orbicularis oculi instead. Thus, movement of the lips results in closure of the ipsilateral eye. The opposite may occur such that eye closure causes movements of orbicularis oris and platysma. "Crocodile tears" are a form of synkinesia due to aberrant reinnervation of the lacrimal gland when the patient is using ipsilateral facial muscles.

"Crocodile tears" are a form of synkinesia due to aberrant reinnervation of the lacrimal gland when the patient is using ipsilateral facial muscles.

- Dyskinesias and dystonia. These include an array of especially lower facial movements such as pouting and pursing of the lips as well as grimacing and grinning. They are commonly associated with involuntary tongue movements. Tardive dyskinesias are a prototypical example; these occur as a complication of long-term treatment with neuroleptic drugs.
- Facial myokymia. These are worm-like movements associated with lesions of the pons probably involving the facial nucleus. This must be differentiated from fasciculations which are twitches of individual muscle fibers.

Hemifacial spasms are gross spasmodic movements believed to be caused by compression of the facial nerve by an arterial loop.

- Hemifacial spasm. These are gross spasmodic movements of a few or all of the facial muscles on one side. They occur spontaneously and are believed to be caused by compression of the facial nerve by an arterial loop, typically the anterior inferior cerebellar artery, which is the artery located in the cerebellopontine angle.
- Focal seizures. Simple partial focal motor seizures may affect only the face with gross jerky movements ordinarily of relatively short duration such as 2 min or less. They occur in a regular cadence whereas hemifacial spasm is irregular and spasmodic with no reprieve throughout the day.
- Tics. These are sudden contractions of a group of muscles which may occur in a focal fashion or be part of a generalized syndrome, Tourette's disease.

Apraxia of eyelid opening or closing may occur with lesions of the nondominant hemisphere as well as extrapyramidal disorders.

- Apraxia of eyelid opening or closing. Apraxia of eyelid closing is often called "motor impersistence." When the patient with this disorder is asked to close his eyes he often does so momentarily. Maintenance of eye closure is impossible. The opposite occurs with apraxia of eyelid opening. True motor impersistence must affect other motor functions and commonly occurs with lesions of the nondominant hemisphere.

(d) Sensory function

The primary test of sensory function of the facial nerve is taste which is lost only with peripheral facial nerve involvement.

- The primary test of sensory function of the facial nerve is taste. Although not every patient with Bell's palsy loses taste perception, its loss confirms a peripheral etiology. Central facial weakness never causes impairment of gustation. The chorda tympani which arises from the nervus intermedius mediates this function. Taste is tested by placing a supersaturated sugar solution on the anterior two thirds of the protruded tongue, sequentially. Usually, a Q-tip is used to brush on the solution, first on the suspected abnormal side and then on the normal side. The patient is requested to nod his or her head when taste is perceived since the tongue must remain protruded for the duration of the test to prevent moving the solution to the posterior portion of the tongue which is innervated by the glossopharyngeal (9th) cranial nerve.
- Stapedius muscle. A branch of the facial nerve innervates the stapedius muscle which, if nonfunctional, results in magnification of sound, hyperacusis. This can be a major complaint in some patients with Bell's palsy. The stapedius muscle tightens the ossicular chain which protects the cochlea from excessively loud sound.

The corneal reflex assesses facial nerve as well as the trigeminal nerve function.

(e) Reflexes

- Facial nerve reflexes are tested through the corneal reflex. A delayed or slow eye blink with good sensation supports the presence of facial nerve involvement. A corneomandibular reflex is present when the jaw deviates away from the side of corneal stimulation. In unresponsive patients it is more likely to occur with structural disease involving the upper brainstem rather than metabolic encephalopathy. Glabellar and snout reflexes also test facial muscles and will be described under the section on reflexes.

Vestibulocochlear Nerve (8th Cranial Nerve)

Cochlear Nerve: Background Anatomy

The auditory pathway begins in the hair cells of the organ of Corti in the cochlea. The cell bodies are in the spiral ganglion. The nerve fibers which emanate from these first order neurons make up the cochlear portion of the 8th nerve which terminates in the dorsal and ventral cochlear nuclei located near the pontomedullary junction. There are ipsilateral and commissural pathways. The latter include the trapezoid body and pathways connecting both inferior colliculi before they ascend to the medial geniculate nucleus and then to the auditory cortex in the superior temporal gyrus. The primary clinical significance of this anatomy is the sparing of hearing when there is a unilateral lesion which destroys one superior temporal gyrus.

> There is no clinically significant hearing loss when one superior temporal gyrus (auditory cortex) is destroyed because of both ipsilateral and commissural pathways.

Cochlear Nerve: Clinical Evaluation

Hearing loss is either conductive or sensorineural. Conductive hearing loss occurs when there is a lesion between the environment and the organ of Corti. Sensorineural hearing loss occurs with lesions of the cochlea, 8th nerve and central auditory pathways. Testing is done with a 512 Hz tuning fork.

> Conductive hearing loss is diagnosed with Weber's test lateralizing to the abnormal ear associated with a negative Rinne's test.

Rinne's test is performed by placing the stem of the tuning fork on the mastoid process. When the vibration is no longer heard, the tines of the tuning fork are moved to within 1–2 in. from the external auditory meatus. A normal Rinne's test equals continued perception of vibration and is called positive. An abnormal Rinne's test means no perception of vibration and is designated negative.

Weber's test is performed by placing the stem of the tuning fork on the midline of the skull or forehead. When the vibration is perceived equally in both ears the test is normal. With conductive hearing loss the vibration is heard louder in the deaf ear. With sensorineural hearing loss the sound is heard louder in the normal ear.

Sensorineural hearing loss is diagnosed by Weber's test lateralizing to the normal ear and Rinne's test which is positive.

In summary, conductive hearing loss is associated with Weber's test lateralizing to the abnormal ear accompanied by a negative Rinne's test. Sensorineural hearing loss is manifested by Weber's test lateralizing to the normal ear and a Rinne's test which is positive (normal).

Vestibular Nerve: Background Anatomy

The vestibular system begins in the labyrinth which is composed of the otolith organs (utricle and saccule) and the semicircular canals (posterior, anterior and horizontal). Linear acceleration is mediated by the utricle and saccule, angular acceleration by the semicircular canals. Stimulation of either unit results in a volley of afferent impulses which terminate in the neurons within Scarpa's ganglion which is located in the internal auditory meatus. Nerve fibers emanating from this ganglion comprise the vestibular portion of the 8th nerve which enters the medulla and terminates in one of the four vestibular nuclei on each side, the superior, medial, inferior and lateral. These are situated in the rostral medulla and caudal pons. Additional pathways project via the inferior cerebellar peduncle to the vestibulocerebellum. The latter structures are the flocculonodular lobe, uvula and fastigial nuclei. Projections from the vestibular nuclei form part of the MLF which plays a role in eye, head and neck movements. The medial and lateral vestibulospinal tracts contain fibers which affect muscular tone. Decerebrate posturing, for example, requires an intact vestibulospinal system.

Vestibular Nerve: History

The vestibular triad is manifested by vertigo, nausea and diaphoresis.

The vestibular triad is a useful term denoting the symptoms of vertigo, nausea and diaphoresis. This triad occurs with a focal unilateral 8th nerve lesion or semicircular canal pathology. Additional common complaints include increased vertigo with eyes closed, staggering, a sense of rotation opposite to the side of the lesion

and oscillopsia. The latter symptom is simply a perceived oscillation of the environment simultaneous with the observed nystagmus. Additional auditory manifestations may occur depending on the underlying pathology.

Vestibular Nerve: Physiology [13]

> The vestibular portion of the 8th nerve governs slow phase movement of the eyes.

The vestibular portion of the 8th nerve governs slow phase eye movements. In other words, stimulation (function) of the left 8th nerve results in contralateral slow phases. This is followed by an ipsilateral quick phase mediated by the PPRF. Thus, if there is a left 8th nerve lesion, for example, the unopposed function of the normal right 8th nerve generates slow eye movements to the left (side of the lesion) with a quick return to the right. Consequently, a left 8th nerve lesion will cause nystagmus to the right (opposite to the side of the lesion). This contralateral nystagmus is present on right lateral gaze, direct forward gaze, upgaze, downgaze and is much smaller on left lateral gaze, if present at all. One can explain the absence or near-absence of contralateral nystagmus with ipsilateral gaze by the inability to generate an ipsilateral slow phase since the eyes are already fully deviated to the left side. This is the basis of Alexander's Law; the amplitude of nystagmus is greatest when the eyes are deviated in the direction of the quick phase. It is important to note that there is no persistent eye deviation with 8th nerve lesions as visual fixation overrides the slow phase imbalance.

> The amplitude of nystagmus is greatest when the eyes are deviated in the direction of the quick phase (Alexander's Law).

Vestibular Nerve: Examination [13]

Direction-fixed contralateral nystagmus is the hallmark of an 8th nerve lesion although it may also occur with CNS disease. Direction-fixed nystagmus indicates contralateral nystagmus in all directions of gaze. There is a slight rotatory element which is the summation of the vectors resulting from involvement of all three semicircular canals. When the nystagmus is directed to the left side there is a clockwise element and, when directed to the right, the rotatory part is counterclockwise. The nystagmus conforms to Alexander's Law. When the observed nystagmus is anything but direction-fixed, CNS disease or drug toxicity are the primary diagnostic considerations.

Contralateral nystagmus is the hallmark of an 8th nerve lesion but it is not a pathognomonic sign.

The head thrust test also known as the head impulse test, if abnormal, is virtually diagnostic of a peripheral vestibular lesion (see Fig. 4.14). The patient is instructed to look straight ahead at the examiner's nose. Then, for example, the patient's head is turned to the left while maintaining fixation on the examiner's nose. This requires the patient to maintain right lateral gaze. With a rapid head turn to a central position, the patient must keep his eyes straight ahead. Consequently, the eyes must move from a right lateral to a central position. This movement which is part of the vestibu-

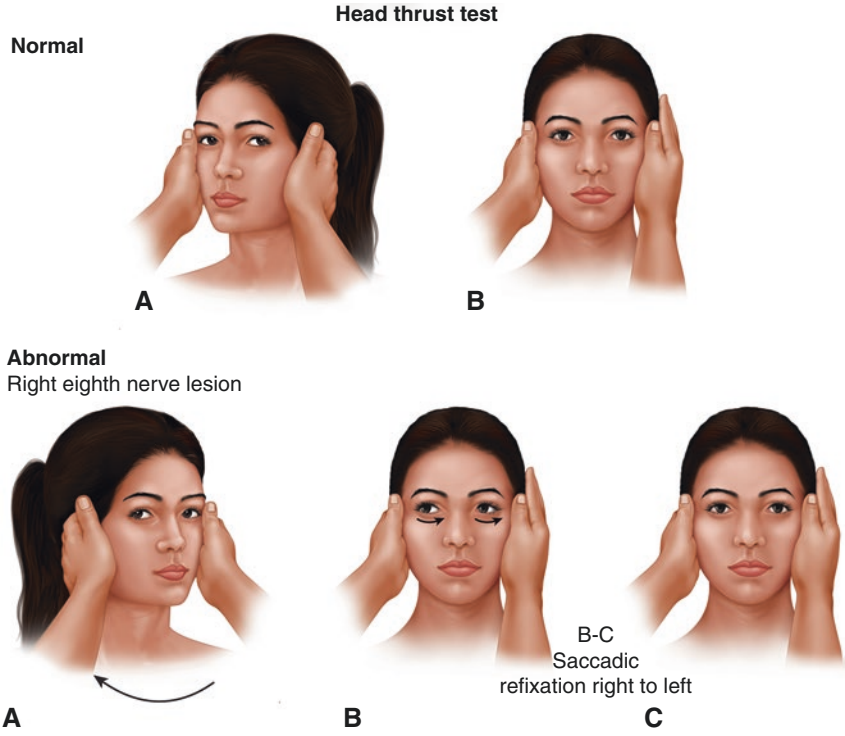

Fig. 4.14 Head thrust test. Normal response. (**a**) The patient's head is turned to the right about 20° with her eyes fixed on the nose of the examiner who is standing directly in front of her. (**b**) The patient's head is then rapidly turned from right to left while she is maintaining focus on the examiner's nose. The patient's eyes have moved from left to right at the same speed as the head movement right to left as there is no adjustment of eye position. Abnormal response (right 8th nerve lesion). (**a**) The patient's head is turned to the left about 20° with her eyes fixed on the nose of the examiner who is standing directly in front of her. (**b**) The patient's head is quickly turned from left to right but her eyes cannot move with sufficient velocity from right to left to maintain fixation on the examiner's nose. Thus there is a refixation saccade from the patient's right to left (shown by arrows). (**c**) The refixation saccade, right to left, has restored fixation on the examiner's nose

lar reflex arc requires the function of the right 8th nerve to generate the requisite eye movement from the right lateral position to the central position. If the patient has a right 8th nerve lesion, slow movements to the left are impaired and, as the patient's head stops, there is a corrective saccadic refixation from right to left. Thus, the head thrust test indicates a right peripheral 8th nerve lesion.

The head thrust (impulse) test, if abnormal, is virtually diagnostic of a peripheral vestibular lesion.

Normal response

A. The patient's head is turned to the right about 20° with her eyes fixed on the nose of the examiner who is standing directly in front of her.
B. The patient's head is then rapidly turned from right to left while she is maintaining focus on the examiner's nose. The patient's eyes have moved from left to right at the same speed as the head movement right to left as there is no adjustment of eye position.

Abnormal response (right 8th nerve lesion)

A. The patient's head is turned to the left about 20° with her eyes fixed on the nose of the examiner who is standing directly in front of her.
B. The patient's head is quickly turned from left to right but her eyes cannot move with sufficient velocity from right to left to maintain fixation on the examiner's nose. Thus there is a refixation saccade from the patient's right to left (shown by arrows).
C. The refixation saccade, right to left, has restored fixation on the examiner's nose.

The dynamic visual acuity test is performed by first instructing the patient to read a visual acuity card with or without his glasses. The visual acuity is noted. He is then asked to read the same card while shaking his head at 2 Hz, usually aided by the examiner. The visual acuity is again noted. If there is a decline of visual acuity by more than two lines of the acuity card, there is vestibular dysfunction as the patient is not able to generate the required slow phases to maintain central fixation.

The dynamic visual acuity test is a simple, useful method of evaluating vestibular function.

Past-pointing is a test performed with the patient's eyes closed. The patient is instructed to fully extend his arm in a vertical direction and make repeated movements through a downward arc to touch the examiner's arm. When this test is abnormal the patient gradually moves his arm towards the side of the lesion when the latter is a peripheral vestibular lesion. If there is CNS disease past-pointing is nonlocalizing.

Other tests that are particularly useful to diagnose vestibular disorders are the Romberg test and the stepping test. These tests are commonly abnormal with

vestibular disorders. They will be discussed under the section of "Gait and Station Examination."

The Romberg and stepping tests are useful for evaluation of vestibular disorders.

Vestibular testing in the comatose patient is particularly important. This includes the vestibuloocular reflexes also known as the oculocephalic maneuver and caloric testing. The oculocephalic maneuver was called the Doll's eye test which is an older, less acceptable term. Caloric testing is seldom done in the clinic. It can be performed with either air or water and is part of the electronystagmogram. This neurophysiologic test is critically important to perform when the patient has recurrent vertigo and a normal examination. Since visual fixation frequently eliminates visible nystagmus with peripheral vestibular disease, examination of the patient with eyes closed is necessary. This is done using electronystagmography which records eye movements using the corneoretinal potential. Frenzel glasses can be employed. These are high diopter lenses which eliminate visual fixation and magnify the eyes to improve visualization for the examiner.

The Dix-Hallpike test is best explained by the diagram (Fig. 4.15). While sitting, the patient's head is turned 45° to one side. The patient is then moved to a supine

The electronystagmogram is a neurophysiologic test which is mandatory in a patient with vertigo and a normal neurologic examination.

position with her head extended below the level of the table. Patients who have benign paroxysmal positional vertigo (BPPV) exhibit nystagmus almost immediately, although there may be a latency of up to 20 s, rarely 40 s. The nystagmus usually lasts from a few seconds up to 20 s, rarely 30, and is directed to the undermost ear which is the pathologic side. The most common type of nystagmus is torsional, upbeating nystagmus with a counterclockwise rotation if the head is turned right and a clockwise rotation if the head is turned left. Ordinarily nystagmus is generated on one side only. The etiology is dislodgment of otoconia which are calcium carbonate crystals from the tips of the hair cells located on the macula of the utricle. These most often fall into the posterior semicircular canals and cause this form of nystagmus through deformation of the cupula. Additional features of this nystagmus include rebound nystagmus on sitting up; this is torsional nystagmus in the reverse direction which is usually very brief, if present. There is habituation with repeat testing as the nystagmus gradually subsides. Otoconia particles may less often be deposited in the horizontal semicircular canal (10%) and rarely in the anterior canal (2%). Nystagmus resulting from these occurrences is quite different.

The Dix-Hallpike test elicits torsional nystagmus in the patient with benign paroxysmal positional vertigo (BPPV).

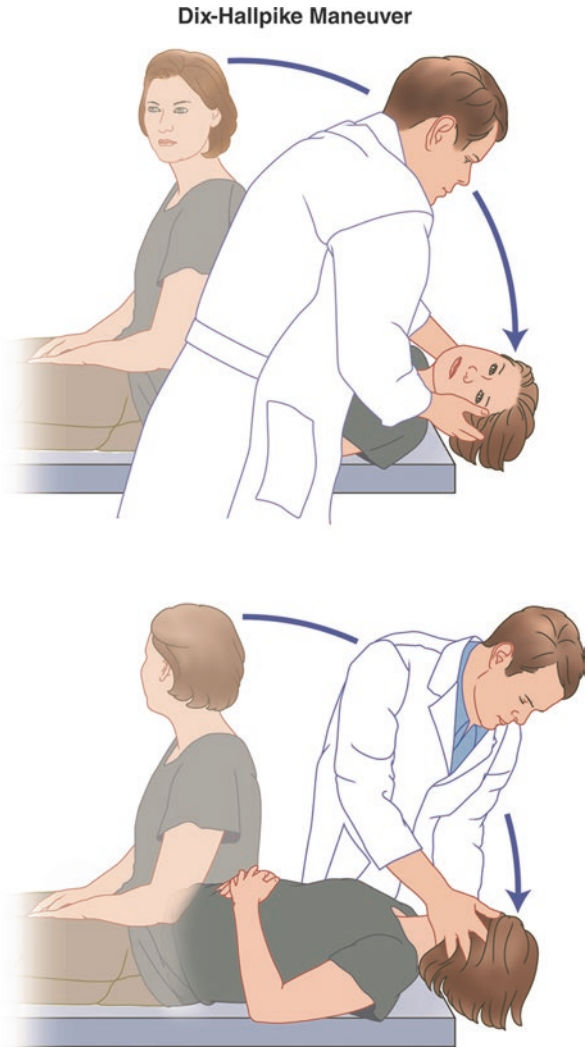

Fig. 4.15 Dix-Hallpike maneuver. The patient sits up straight on the examining table with her legs on the table in front of her and her hands in her lap. The hand position prevents her from holding onto the table edges which would inhibit rapid movement to the supine position. The examiner stands at the patient's left side. The patient is then instructed to turn her head to the left, approximately 45°, and keep her eyes open throughout the maneuver. She is then quickly moved but not jerked to the supine position with her head extended below the level of the table. The patient may look in any direction while her eyes are inspected for up to 45 s or until the nystagmus has abated. She is then brought up quickly to the sitting position and observed briefly for rebound nystagmus, a reversal of the rotation noted in the previous position. This is an inconsistent finding. The procedure is then repeated for the right side in the same manner

Horizontal canal BPPV produces direction changing positional nystagmus (DCPN). The geotropic form is present when nystagmus beats towards the ground. With the patient supine, head turned to the left, nystagmus beats left, and with the patient supine, head turned to the right, nystagmus beats right. Ageotropic nystagmus is the converse. With the patient supine, head right, nystagmus beats left, and with the patient supine, head left, the nystagmus beats to the right.

Geotropic nystagmus occurs with canalolithiasis, free-floating otoconia debris and the ageotropic form occurs with cupulolithiasis when otoconia adheres to the cupula. Rarely, ageotropic DCPN results from brainstem or cerebellar system pathology. Nystagmus from anterior canal BPPV is downbeat and torsional.

Glossopharyngeal Nerve (9th Cranial Nerve)

1. Background anatomy.

> The nucleus ambiguus in the medulla contains the cells of origin of the 9th, 10th, and bulbar portion of the 11th cranial nerves.

The cells of origin of the 9th, 10th, and bulbar portion of the 11th cranial nerves are located in the nucleus ambiguus in the medulla. The nerve fibers emerge close together from the medulla and exit through the jugular foramen. The motor component innervates pharyngeal constrictors and the stylopharyngeus muscle which elevates the pharynx. The sensory portion receives afferents from the posterior one third of the tongue, tonsils, soft palate, tympanic membrane (Jacobson's nerve) and carries chemoreceptor and baroreceptor afferents from the carotid body and carotid sinus, respectively. The central connection is the solitary tract.

> The sensory portion of the 9th nerve receives afferents from the posterior one third of the tongue, tonsils, soft palate, tympanic membrane (Jacobson's nerve) and carries chemoreceptor and baroreceptor afferents from the carotid body and carotid sinus, respectively.

2. Examination.
   (a) The soft palate is observed for asymmetry. Sagging on one side may indicate weakness, but paresis is negligible with pure 9th nerve lesions.
   (b) Check the gag reflex on both sides when there is a history of dysphagia or a suspicion of multiple cranial neuropathies.
   (c) Check perception of touch on the soft palate, uvula, pharynx, and posterior third of the tongue.
3. Clinical correlations.
   (a) Dysphagia.
   (b) Transient hypertension after carotid endarterectomy because of denervation of the carotid sinus. The contralateral carotid sinus assumes control either immediately or within several hours.

> Transient hypertension after carotid endarterectomy may occur if there is denervation of the carotid sinus.

(c) Glossopharyngeal neuralgia. Sharp ear pain (via Jacobson's nerve) and sharp throat pain are often provoked by swallowing.
(d) Jugular foramen syndrome. Paresis of 9th, 10th, and 11th cranial nerves usually due to neoplasm at the foramen.
(e) Decrease or increase in salivary secretions as the nerve innervates the otic ganglion which provides parasympathetic innervation to the parotid gland.

Vagus Nerve (10th Cranial Nerve)

1. Background anatomy.

Motor function arises from the nucleus ambiguus in the medulla. The nerve leaves the skull via the jugular foramen, forms the pharyngeal plexus with the glossopharyngeal nerve and provides motor fibers to the pharynx and soft palate. Branches of the vagus nerve in the neck include the cardiac rami which follow the carotid arteries down to the aorta and eventually to the cardiac plexus. At the base of the neck the recurrent laryngeal nerves supply all the muscles of the larynx. A lesion of this nerve is often a complication of surgery and results in paralysis of the vocal cord on that side. This causes a hoarse, raspy voice.

> The vagus nerve forms the pharyngeal plexus with the glossopharyngeal nerve and mediates motor function of the soft palate.

The parasympathetic fibers arise from the dorsal motor nucleus of the vagus which is located lateral to the hypoglossal nucleus. These parasympathetic branches innervate the pharynx, esophagus, trachea, bronchi, lungs, heart, intestines, liver and pancreas.

> The parasympathetic branches of the dorsal motor nucleus of the vagus nerve innervate the pharynx, esophagus, trachea, bronchi, lungs, heart, intestines, liver and pancreas.

Sensory fibers carry taste from the epiglottis, hard and soft palate and pharynx. These taste fibers run in the solitary tract along with afferent glossopharyngeal fibers. Visceral sensations from the pharynx, chest and abdomen also project through the nucleus of the solitary tract.

2. Examination.

The palate and uvula are examined at rest and with phonation. Sagging of one side of the palate at rest may indicate weakness. With phonation the palate should

elevate in a symmetrical fashion with no deviation of the uvula. With unilateral lesions there is ipsilateral flattening of the soft palate and phonation will not elevate the soft palate. The uvula is deviated to the normal side. With bilateral lesions of the vagus nerve the palate does not move and dysphagia occurs, particularly with liquids.

Spinal Accessory Nerve (11th Cranial Nerve)

1. Background anatomy.

> The 11th cranial nerve has both cranial and spinal contributions. The spinal contribution is located in the first through fifth cervical cord segments.

The cranial portion originates in the nucleus ambiguus in the medulla. The spinal part is located in the first through fifth cervical cord segments. C1–C2 innervate the ipsilateral sternocleidomastoid muscles and C3–C4 innervate the ipsilateral trapezius muscles. The cranial and spinal roots unite and the entire 11th cranial nerve exits through the jugular foramen with the 9th and 10th cranial nerves. Supranuclear innervation of the sternocleidomastoid and trapezius musculature is still debatable. Briefly, the right cerebral hemisphere initiates movements of the head to the opposite side. This view is corroborated by observations of focal seizure activity manifested by head jerk to the left due to a right cerebral epileptic focus. Consequently, the ipsilateral sternocleidomastoid muscle is innervated mainly by the ipsilateral cerebral hemisphere.

> The sternocleidomastoid muscle flexes the head and the trapezius muscle retracts the head and scapula when both sides are activated simultaneously.

The sternocleidomastoid muscle flexes the head when both sides are activated simultaneously. If the right sternocleidomastoid muscle is activated, the head is drawn down to the ipsilateral shoulder and the occiput is pulled down on the same side. This rotates the head to the left. The trapezius muscle retracts the head and the scapula as well as raising the abducted arm above the horizontal plane.

2. Examination.

The right sternocleidomastoid muscle is examined by having the patient turn his head to the left against resistance with simultaneous palpation of its musculature and vice versa. Flexing the head against resistance evaluates both sternocleidomastoid muscles. The trapezius muscle retracts the head and the scapula. It assists the

abducting arm to elevate above the horizontal plane. It is examined by having the patient shrug his shoulders against resistance.

3. Clinical-anatomic correlation.

> Weakness of head flexion occurs in many patients with myopathy, myasthenia gravis and chronic inflammatory demyelinating polyneuropathy (CIDP).

Weakness of head flexion, bilateral sternocleidomastoid weakness, occurs in many patients with myopathy, myasthenia gravis, and chronic inflammatory demyelinating polyneuropathy (CIDP). Less often, the same diseases weaken trapezius muscles and, consequently, head extension. The main muscles for head extension, however, are the splenius capitis, splenius cervicis and the semispinalis capitis which are innervated by middle and lower cervical nerves. Neck surgery in the posterior cervical triangle region can easily injure the C3–C4 roots as they are located superficially. This results in a unilateral drooping shoulder and may affect muscles in the thoracic outlet.

Hypoglossal Nerve (12th Cranial Nerve)

1. Background anatomy.

> The corticolingual fibers from each cerebral hemisphere supply both sides of the tongue with the exception of the genioglossus muscle. The genioglossus muscle, which receives only crossed corticolingual fibers, pushes the tongue to the opposite side and thus may deviate to the hemiparetic side.

The 12th cranial nerve has purely motor function. The nerve fibers arise from the hypoglossal nucleus which is a column of cells extending from the pontomedullary junction down to the cervical medullary junction. The nerve roots are medial to the 9th, 10th and 11th cranial nerves as they pass through the hypoglossal canal. The nerve fibers descend through the neck to the angle of the mandible near the internal carotid artery and the internal jugular vein. They supply the intrinsic and extrinsic muscles of the tongue. The supranuclear control of the tongue is mediated by corticobulbar fibers. They originate in the lower part of the precentral gyrus. The corticolingual fibers from each cerebral hemisphere supply both sides of the tongue with the exception of the genioglossus muscle which receives only contralateral innervation. The pontomedullary junction is the location of the crossing fibers.

2. Examination.

The tongue should be observed for symmetry, atrophy, and abnormal involuntary movements. The latter includes dyskinesias, fasciculations, myoclonus, and tremor.

The patient is then requested to protrude his tongue and move it to either side. The tongue may deviate to the hemiparetic side if the lesion is above the level of the decussation of fibers at the pontomedullary junction. The normal, ipsilateral genioglossus pushes the tongue to the opposite side. Differentiating central from peripheral 12th nerve lesions is often difficult and requires a careful history and neurologic examination.

Motor Examination

There are three motor systems, corticospinal, extrapyramidal, and cerebellar. A practical approach is to assess all of them together, in one category, particularly since there are overlapping functions. The motor examination can be broken down into five categories.

1. General observations.

There are three motor systems, corticospinal, extrapyramidal, and cerebellar.

2. Close inspection.
3. Coordination.
4. Strength.
5. Tone.

General Observations

Among the first observations made on entering the examining room are those of the patient's posture and movements. Is the head in a neutral position, turned to either side, flexed, or extended? Are the arms and hands resting comfortably in the patient's lap or are they in a forced abnormal position? Are the legs extended, flexed, or turned inward? Is the trunk flexed, extended, or twisted? These abnormal findings commonly have more than one interpretation and must be evaluated in the context of the entire neurologic examination.

Abnormal movements are divided into hypokinetic or hyperkinetic.

Bradykinesia is often mistakenly attributed to age.

Abnormal movements are divided into hypokinetic or hyperkinetic. The prototype of a hypokinetic movement disorder is Parkinson's disease. Bradykinesia is the hallmark, a slowing of all spontaneous movements. It is easily spied with any movement such as when the patient takes off or puts on his glasses. In elderly patients bradykinesia is often mistakenly attributed to age. Getting out of a chair, turning in bed, or even sitting down can be challenging tasks. The patient with Parkinson's disease often misjudges the location of the seat and may sit on the armrest. Hypomimia or masked facies, a loss of facial mobility, is common. There may be diminished eye blinks and, quite often, apraxia of eye opening and closing. The latter has been called the "reptilian stare." Blepharospasm commonly prevents reading or watching television. Writing becomes laborious and micrographia is common.

Tremor is the most common hyperkinetic movement disorder. When pathologic it can be divided most simply into three types, postural, action and resting. To evaluate postural tremor the patient is asked to extend his arms and spread his fingers. Essential tremor, if present, is usually bilateral, rapid (6–11 Hz) and of small amplitude. It may be more prominent on one side. As the severity increases the amplitude becomes larger. An action tremor occurs when making a voluntary movement. It is most often perpendicular to the direction of movement and is thus best appreciated on finger-to-nose test. It is the most disabling form since it interferes with using eating utensils or drinking from a cup. Action and postural tremors are virtually always present together, although one may be much more prominent. Having the patient draw a spiral at each visit is a practical way of evaluating the success of treatment. The most common cause of action/postural tremor is essential tremor which is familial in two thirds of cases. Infrequently, a resting tremor can be present which may baffle the examiner. Head and voice tremor are common associated features. Pathological changes have been found in the cerebellum including loss of Purkinje cells and gliosis in the cerebellar cortex.

Physiological tremor, typically 8–12 Hz, has characteristics similar to essential tremor. It affects hands and fingers and is provoked by anxiety, fear and fatigue. Hyperthyroidism, caffeine and adverse effects of other drugs may produce the same type of tremor.

Action and postural tremors are virtually always present together.

Akathisia is a severe form of motor restlessness that affects the legs.

Akathisia is a severe form of motor restlessness that affects the legs. Patients have an inner sense of restlessness and are often pacing the floor or marching in place. This is nearly always due to the use of neuroleptic medication (dopamine blockers). It begins at the onset of treatment or with an increased dose of medication. It resolves when treatment is discontinued.

Resting tremor is the hallmark of Parkinson's disease.

Resting tremor is of lower frequency, about 3–7 Hz, is commonly unilateral and a prototypical sign of Parkinson's disease. It is frequently intermittent and may, if infrequent, only be observed by family members. Thus it may be absent during a brief examination. It can be more obvious when the patient walks at which time there is a "pill-rolling" character. Pill-rolling refers to movement of the thumb on the first two fingers. Resting tremor may affect the lips, tongue, chin, jaw, hands and legs, but not the head. Likewise, it increases with excitement. Tremor with sustained posture may also be present but to a much lesser extent and ordinarily is eliminated with movement. A resting tremor may begin in a single digit. It also increases with excitement and is absent during sleep.

Patients with Parkinson's disease often exhibit a pill-rolling tremor when walking.

Cerebellar tremor is slow (3 Hz), affects proximal muscles and may have a "Wing-beating" appearance. It is usually associated with other cerebellar signs.

Dystonic tremor, usually 4–8 Hz, is a special, unique disorder. It is focal and affects the same body part as the dystonia. An example is head tremor associated with cervical dystonia. It may be responsive to sensory tricks (gestes antagonistiques) such as simply touching or putting light pressure on the neck. Task-specific tremor such as tremor when writing is considered a form of dystonic tremor.

Rubral tremor (Holmes, midbrain) is a rare entity found in patients with lesions of the superior cerebellar peduncle, midbrain tegmentum and posterior thalamus. Despite the name, lesions of the red nucleus have not been clearly associated with this tremor. Most often it affects the arms after a delay of 1–24 months subsequent to the initial injury. It is irregular, slow (4–5 Hz), large amplitude, occurs at rest, but is aggravated by sustained posture and intention.

Psychogenic tremor has a sudden onset, spontaneous remissions and large variations in amplitude and frequency. It may disappear with distraction such as requesting the patient to do serial 7 subtractions. The frequency is quite variable.

Primary orthostatic tremor affects the legs of patients who stand erect. The rate is 12–18 Hz and one may hear the contractions with a stethoscope applied to the calf or thigh musculature. The tremor commences several seconds after standing and gradually increases in amplitude forcing the patient to sit. It has been considered a form of essential tremor by some or a unique category of tremor related to dysfunction in the maintenance of body posture.

Chorea is manifested by almost continuous quick, jerky or fluid movements with a predilection for distal musculature. The movements disappear in sleep, are present at rest but increase with stress and activity. Patients often find it impossible to maintain a fixed position. Hence, the term "milkmaid's grip" as the patient repeatedly grips and releases the doctor's fingers. Additionally, the patient may be unable to maintain tongue protrusion ("trombone tongue"). Hypotonia may be detected. Some etiologies include Huntington's chorea, chorea gravidarum of pregnancy, Sydenham's chorea, systemic lupus erythematosus, hyperthyroidism and adverse effects of levodopa.

Chorea is manifested by quick, jerky or fluid movements with a predilection for distal musculature.

Athetosis is manifested by much slower, larger and almost constant writhing movements with a predilection for distal musculature. The movements may also affect facial and truncal muscles as well as the extremities. Voluntary movements are severely impaired as attempts to move usually increase athetotic movements. Common etiologies are cerebral palsy with injury to the basal ganglia and side effects of levodopa. Other causes are degenerative diseases such as Wilson's disease and kernicterus. Sleep eliminates athetotic movements.

Athetosis is manifested by slow, writhing movements with a predilection for distal musculature.

Dystonia presents with a myriad of characteristics. Agonist and antagonist muscles contract simultaneously. The movements can be generalized or focal. The speed varies greatly. When the contractions last <1 sec they are called dystonic spasms or myoclonus. If they last several seconds they are called movements. An example is athetotic dystonia. Dystonic postures usually last minutes to hours, when postures last days or weeks contractures may develop. Some examples are torticollis (cervical dystonia), tortipelvis (scoliosis), lordosis and inversion of feet and hands.

Dystonic movements can be generalized or focal and tend to occur in the same location. The duration varies widely, from seconds to weeks, and when prolonged can induce contractures.

There are primary dystonias of childhood onset, some of which are probably of genetic origin (autosomal dominant). Dopa-responsive dystonia of childhood should be recognized since it is treatable. There are dystonic forms of Parkinson's disease such as Lubag's disease, a genetic form which occurs in the Philippine islands.

Focal dystonias include cervical dystonia, oromandibular dystonia with blepharospasm (Meige syndrome), blepharospasm alone, musician's cramp, writer's cramp and spasmodic dysphonia. There are two types of the latter, adductor (80–90%) or abductor, the former causes the vocal cords to close and the latter to stay open. Speech abnormalities include a tremor-like quality, breathiness, low volume and breakup of words. Oculogyric crisis, forced upward/lateral eye deviation, is probably dystonia of eye muscles that occurs with encephalitis lethargica and is now rarely observed in patients with the neuroleptic malignant syndrome, Wilson's disease, and those taking neuroleptics.

Cervical dystonia is the most common form of focal dystonia.

Cervical dystonia is the most common form of focal dystonia and has a few manifestations including torticollis (twisting to one side usually with head tilt), anterocollis (forced flexion) and retrocollis (forced extension). Patients may sometimes be able to resume a normal posture using a sensory stimulus (trick), a light pressure to counteract the abnormal contraction. Tremor may be an associated feature.

Hemiballismus is a unilateral, flinging movement of an arm or leg generated at a proximal joint. Hemichorea is a common associated feature with the same anatomic pathology and thus a newer term for this syndrome is hemichorea-hemiballismus. Ischemic or hemorrhagic stroke involving the vertebrobasilar-posterior cerebral artery distribution is nearly always the underlying pathology. Classical clinical anatomic correlation has pinpointed the subthalamic nucleus of Luys as the pathologic site, but the estimate of involvement of this structure is just 10–30%. Other anatomic sites of infarcts or hemorrhage include caudate, putamen, thalamus and brainstem. Disruption of a motor network with connectivity to the posterolateral putamen appears to be the source of this movement disorder.

Hemiballismus is a unilateral, flinging movement of an arm or leg generated at a proximal joint.

Tardive dyskinesias are relatively common and are most often involuntary oral, buccal and lingual movements. These are manifested by chewing and/or lip movements and writhing of the tongue when protruded or even at rest. Less often, there may be respiratory dyskinesias noted as sporadic chest excursions as well as truncal and pelvic movements. Tardive dyskinesia is often accompanied by akathisia, an inner restlessness that may provoke the patient to stand and continually move his legs. Tardive dyskinesias are commonly associated with neuroleptics (dopamine-blocking agents) usually after 3 months of treatment or after at least 3 months of treatment has been discontinued. Metoclopramide, a common medicine used for

Tardive dyskinesias are relatively common and are most often oral, buccal and lingual movements.

gastroparesis, is often the culprit.

Orofacial dyskinesias may occur as a common complication of treatment with levodopa for Parkinson's disease. The movements are similar to tardive dyskinesias. Other etiologies are Wilson's disease, Huntington's and Sydenham's chorea.

Tardive dystonia is manifested by more sustained movements, particularly with facial grimacing, jaw deviation and protrusion. The etiology is the same as with tardive dyskinesias, namely neuroleptics and metoclopramide. These dystonic movements may occur during treatment or shortly after treatment has been discontinued.

Tardive dystonia is manifested by more sustained movements, particularly with facial grimacing, jaw deviation and protrusion.

Myoclonus is a sudden, rapid muscular jerk which may be focal, unilateral or generalized. It has numerous etiologies, metabolic, epileptic, paraneoplastic, hypoxic and infectious, the latter being typically an encephalitis. Other etiologies include a prion disease (Creutzfeldt-Jakob) and degenerative diseases such as Lewy body and Alzheimer's disease. Paraneoplastic sources include neuroblastoma, small cell lung carcinoma, ovarian and breast cancer. Multifocal myoclonus is typical of metabolic encephalopathy. It is often prominent in epileptic syndromes such as juvenile myoclonic epilepsy.

There are additional disorders of myoclonus. Opsoclonus refers to similar movements selectively involving the eyes manifested by chaotic saccades in all planes due to cerebellar or brainstem dysfunction. Palatal myoclonus is a unique rhythmic form accompanied by the patient's complaint of hearing a clicking sound which probably emanates from the eustachian tube. This complaint should prompt careful inspection of the soft palate which contracts at 60–180 times per minute. Synchronous movements of ocular, diaphragmatic or head and neck musculature may occur. Lesions which affect the Guillain-Mollaret triangle which is composed of the red, dentate and inferior olivary nuclei and their connections are the source of this myoclonus. Pathology of the central tegmental tract which connects the red nucleus with the inferior olivary nucleus probably causes hypertrophy of the inferior olivary nucleus which is likely to be the generator of this myoclonus.

Asterixis, a sudden dropping movement of the hands, may occur with any metabolic encephalopathy.

Asterixis refers to sudden dropping movements of the hands when the arms are extended and the hands dorsiflexed at the wrists. There is a sudden loss of muscular tone which has been referred to as negative myoclonus. It is almost always a manifestation of a metabolic encephalopathy unless it is unilateral, a rare phenomenon after stroke involving corticospinal pathways. It is best known as an associated finding with hepatic encephalopathy, but perhaps it is more common in acute hypercapnia. Any metabolic derangement can cause asterixis.

Tics are motor and vocal. Each type can be divided into simple and complex.

Tics are motor and vocal. Each type can be divided into simple and complex. A simple motor tic is a sudden jerky, involuntary movement often similar to a myoclonic jerk or chorea. Simple tics, however, are more likely to be repetitive. Complex motor tics are a series of simple tics often in the same sequence. Sometimes there is

a coordinated pattern of movement. Simple vocal tics are characteristically a sniff, grunt, cough or clearing of the throat. Complex vocal tics would be verbalization such as coprolalia (obscene language). When both motor and vocal tics are present in childhood the diagnosis is Tourette's syndrome. Motor tics alone may be simply a transient habit spasm.

Close Inspection

Atrophy is a result of diseases affecting the anterior horn cells, roots and nerves.

Observations should be made regarding muscular atrophy or hypertrophy, muscle bulk, spasms, fasciculations and myokymia. To assess bulk it is useful to inspect the arms in the pronated and supinated position to evaluate extensors and flexors of the forearm, respectively. Measuring the circumference of a limb is best done at its greatest apparent girth. The normal dominant limb may be 1 cm larger in the thigh or calf and 0.5 cm larger at the forearm and upper arm. Atrophy is a result of diseases affecting the anterior horn cell, roots and nerves. Disuse atrophy and wasting of muscles are noted in patients who are cachectic, deconditioned due to prolonged inactivity or with chronic myopathies. Hypertrophied muscles or pseudohypertrophy typically involve calf musculature and are noted rarely in myopathies such as Duchenne's muscular dystrophy or Thomsen's disease (myotonia congenita).

Spasms or cramps are muscular or neurogenic in origin and often referred to by patients as "charleyhorses." These are sudden tonic contractions of muscles due to a sensory stimulus. Nocturnal cramps are quite common and may provoke the patient to get out of bed and walk around. Should this be the case a presumptive diagnosis of restless legs syndrome can be made and treatment initiated, often with excellent results.

Fasciculations are quick twitches due to contraction of muscle fibers and are not strong enough to move a limb.

Fasciculations are quick twitches due to contraction of muscle fibers. They are never strong enough to produce movement of a limb. Fasciculations are the hallmark findings in diseases affecting the anterior horn cell such as amyotrophic lateral sclerosis. The most common cause of localized fasciculations, however, is a radiculopathy due most often to a herniated cervical or lumbar disk. Fasciculations do not occur with neuromuscular junction or muscle diseases and rarely with peripheral nerve disease. When amyotrophic lateral sclerosis is suspected, the chest and back

of the patient should be carefully inspected under good illumination for fasciculations. Fasciculations persist during sleep.

Fasciculations are primarily due to anterior horn cell disease and radiculopathy; the latter is most common.

Myokymia is an unusual phenomenon characterized by prolonged vermiform movements which are most often seen on the face, especially involving the orbicularis oculi muscles. They have been observed in patients who have lesions of the facial nucleus. Myokymia of limb muscles has been reported after radiation damage to the brachial or lumbosacral plexuses.

Coordination

Testing of coordination often yields more diagnostic information than other parts of the motor examination. The earliest deficit of lesions of the three motor systems, whether corticospinal, extrapyramidal or cerebellar, are first detected by these examinations.

Testing of coordination often yields more diagnostic information than other parts of the motor examination. Impaired rapid alternating movements occur with cerebellar, corticospinal and extrapyramidal disorders.

The most useful is impairment of rapid alternating movements. Abnormalities, called dysdiadochokinesis – a convoluted term – have been defined as a purely cerebellar disorder in the past. Although it is quite characteristic of cerebellar system pathology, it is not pathognomonic, a critical distinction. It is often the earliest sign of a corticospinal tract lesion and certainly a common abnormality found in patients with extrapyramidal disorders such as Parkinson's disease. One difference with cerebellar dysfunction may be the latter's irregular rhythm and rate. This can be difficult to ascertain. The test may be performed in different ways. Alternating pronation and supination of the hands as rapidly as possible on the leg is the most common method. Having the patient do the same movements simultaneously with both hands and with partially extended arms may be the quickest and most sensitive. Rapid finger and foot tapping are equally sensitive and are often abnormal before physical weakness becomes apparent. It is often the last to recover from a corticospinal tract lesion.

More specific signs of cerebellar system dysfunction include the finger-to-nose and heel-to-shin tests.

More specific signs of cerebellar system dysfunction include the finger-to-nose and heel-to-shin tests. The former is performed such that the patient's arm is fully extended when touching the examiner's finger. This is more likely to elicit ataxia or tremor. Heel-to-shin testing is commonly difficult for the obese patient. Testing the patient in the supine position is usually easier for them. Many patients place the heel to the side of the shin which damps the oscillations that might occur if the heel is placed precisely on the edge of the shin. The initial placement of the heel on the knee or the edge of the shin without any movement may elicit the side-to-side oscillations. The movement downwards may be jerky, decomposition of movement, since fluid, coordinated movements are interrupted. It is important to be aware of the fact that severe position sense loss may give rise to similar abnormal signs.

Failure of check, the rebound phenomenon, is a useful sign of cerebellar dysfunction.

Failure of check, the rebound phenomenon, is a useful sign of cerebellar dysfunction.

Failure of check, the rebound phenomenon, is a useful sign of cerebellar dysfunction. The patient is requested to adduct his arm at the shoulder and flex his arm about 90° at the elbow using his biceps muscle. The examiner pulls strongly at the wrist while simultaneously placing his forearm close to the patient's cheek between his fist and face. When the examiner suddenly lets go, the patient must check the flexion movement or his arm will strike the examiner's forearm. Failure to check the movement is a distinctly cerebellar system sign.

Titubation is a slow (3–4 Hz) usually anterior-posterior oscillation of the head and trunk. The frequent presence of other cerebellar signs supports a cerebellar origin of this movement disorder. Lesions of the cerebellar vermis have been correlated with this sign.

Strength [14]

There are different methods of evaluating strength. One method is to have the patient hold a position and resist the examiner's attempt to move the limb. The opposing technique is the reverse. The examiner resists the patient's attempt to move. When the examiner attempts to move the limb from a fixed position, it can be done with a sudden exertion of force or steadily increasing strength. The latter method is more precise, especially when assessing distal musculature.

There are numerous confounding factors when evaluating strength such as fatigue, somnolence, conversion reaction and malingering.

There are numerous confounding factors when evaluating strength. These include fatigue and somnolence which result in a wide variability of effort. Conversion reactions and malingering often produce a ratchety, "give-way" weakness rather than smooth steady weakening. A positive Hoover sign is an additional finding to support either of these diagnoses. This sign is a useful finding when leg weakness is claimed. In the supine position the weak leg is evaluated for strength of hip flexion while the examiner's hand is placed underneath the heel of the good leg. Normally, there is downward pressure exerted by the normal leg. The absence of this pressure suggests unsatisfactory effort. Impaired comprehension also obviates an adequate assessment and persistent efforts to explain the requested movement are often fruitless and are best abandoned after three or four attempts. The syndrome of motor impersistence, the inability to maintain a fixed position despite adequate strength, is a well-known although uncommon manifestation of nondominant hemisphere lesions which impedes the examination.

Examination of strength begins with the assessment of arm drift.

Examination of strength begins with the assessment of arm drift. The patient is instructed to fully extend both arms with the palms facing upwards. A downward drift with pronation is a typical early sign of a corticospinal tract lesion, cerebral, brainstem or spinal cord. A drift upward is noted with proprioceptive deficits and thus is called a "parietal drift." Clearly, position sense loss of any anatomic origin, CNS or PNS, may cause the identical finding. An unusual drift is the one that moves the arm laterally and this may occur with cerebellar system lesions. It is essential to exclude the presence of shoulder pathology which often causes downward drift with pronation.

A general survey of arm and leg strength must include proximal and distal musculature. A standard method of evaluation is noted in the adjacent table (Table 4.8).

Pluses and minuses can be added to the numbers on the scale to provide more options. Selected muscles in the arms usually include interossei, extensor carpi

Table 4.8 The Medical Research Council rating of muscle strength

Scale	Muscle strength
0	No contraction
1	Flicker or trace of contraction
2	Active movement with gravity eliminated
3	Active movement against gravity
4	Active movement against gravity and resistance
5	Normal power

From Medical Research Council: Aids to the Examination of the Peripheral Nervous System. Memorandum No. 45. London: Crown; 1976

radialis, biceps, triceps and deltoids. Leg muscles usually examined are the iliopsoas, quadriceps, hamstrings, anterior tibialis and gastrocnemius. Depending on the patient's symptoms and suspected diagnosis, additional muscles may be added. For example, a history of back pain or possible radicular pain requires evaluation of the extensor hallucis longus, a commonly affected muscle with lumbar radiculopathy.

If myopathy or myasthenia gravis are suspected, proximal muscles should be the focus of the examination, especially head flexion and extension.

If myopathy or myasthenia gravis are suspected, proximal muscles should be the focus of the examination, especially head flexion and extension. Repeated checking of deltoid strength, usually 15 attempts, evaluates for fatigue and is an especially useful evaluation for myasthenia gravis. Climbing up one or two flights of stairs is a good method of eliciting fatigue.

Neuropathies require a more detailed assessment of distal musculature. Suspected radiculopathies and plexopathies require careful assessment of all muscles that could be affected, virtually all muscles of an affected limb.

In summary, examination of muscular strength will vary from patient to patient depending on the history and the suspected diagnosis. What must always be kept in mind is to compare manual strength with functional strength. A patient with weak iliopsoas muscles should not be able to get up quickly from a chair. A patient who has severe weakness of ankle dorsiflexion should not be able to perform heel-walking. A major principle, therefore, is that functional strength nearly always takes precedence over the results of manual strength testing.

Functional strength nearly always takes precedence over the results of manual strength testing.

Tone

There are three common types of abnormal muscular tone, spasticity, cogwheel rigidity and paratonic rigidity (Gegenhalten).

There are three common types of abnormal muscular tone, spasticity, cogwheel rigidity and paratonic rigidity (Gegenhalten). Spasticity of the arm can be most easily evaluated by extremely quick supination movements (biceps) of the patient's relaxed arm such that the spastic catch is visible as well as detected by sensing

resistance. Flexor tone is particularly increased in the arm. There is a free unopposed interval followed by variable resistance (a spastic catch) and then a sudden giving-way (clasp-knife reaction). In the legs, spasticity is most prominent in extensor muscles and is best evaluated at the knees. Rapid flexor movement with the patient sitting and the legs swinging freely may elicit increased tone; but perhaps even better is to evaluate the patient when supine. When a relaxed leg is abruptly and momentarily elevated at the knee, there is a delayed return to a fully extended position. The leg "hangs up," exhibiting a "spastic catch." Adductor tone is also especially increased. This causes a "scissoring," a tendency to adduct the paretic leg which crosses over the normal leg. It is easiest to detect when the patient walks.

Cogwheel rigidity is a characteristic sign of diseases affecting the extrapyramidal system, but it is not pathognomonic of Parkinson's disease.

Cogwheel rigidity is a characteristic sign of diseases affecting the extrapyramidal system. It is a typical feature of Parkinson's disease, Parkinson-plus syndromes such as multiple system atrophy, progressive supranuclear palsy, cortical basal ganglionic degeneration, striatonigral degeneration, Creutzfeldt-Jacob disease, Lewy body disease and adverse effects of neuroleptic drugs which are dopamine blockers, especially the phenothiazines. It is commonly detected in patients with essential tremor which diminishes its diagnostic significance. The combination of cogwheel rigidity with bradykinesia or resting tremor, however, strongly supports a diagnosis of Parkinson's disease. There is a ratchety movement when the examiner very slowly moves the arm, typically rotating at the wrist or flexing and extending the arm at the elbow. Agonist and antagonist muscles have similar tone.

Paratonia is the active resistance to any movement by the patient.

Paratonia (Gegenhalten) is the patient's active resistance to any movement of his limbs by the examiner. Despite clear requests by the examiner to relax, the patient actively resists the examiner's attempt to flex or extend the limb, especially at the elbow and knee. When the physician increases the speed of movement the patient's resistance is often augmented. A common misinterpretation of this sign is "the patient is poorly cooperative" or actively "obstructs" the examination. Paratonia indicates bilateral cerebral dysfunction, whether metabolic, toxic, vascular, degenerative or of infectious origin. Dementing diseases and metabolic encephalopathy are probably the most frequent etiologies.

Myotonia is characterized by impaired relaxation of muscle.

Myotonia is characterized by impaired relaxation of muscle. A tap on the thenar eminence, for instance, induces a muscle contraction which adducts the thumb. This often persists for several seconds. The patient may complain of inability to release a firm grasp quickly even when shaking hands with someone. The edge of a tongue blade can be placed on the midline of the tongue followed by lightly tapping the upper edge with a reflex hammer. This often produces curling of the tongue muscles. The two most common causes of myotonia are myotonic dystrophy and Thomsen's disease.

Other less common abnormalities are hypotonia and flaccidity. Hypotonia is most easily and commonly recognized in infants, especially the neonate. It occurs with both central and peripheral diseases. Cerebellar pathology is an etiology of hypotonia, but it can be difficult to recognize. A sudden attack of decreased tone occurs in cataplexy, a component of narcolepsy which will be discussed in a subsequent section. Momentary loss of tone also occurs with akinetic seizures and asterixis. Flaccidity is prominent with acute spinal cord injuries causing paraplegia.

Finally, there is a rare disorder called stiff-person (stiff-man) syndrome characterized by paroxysmal, often painful muscular rigidity, and spasms of axial and limb musculature. The spasms, which can be provoked by excitement, sudden noise or anxiety are sometimes sufficiently severe to cause fractures. Muscular tone is normal between these paroxysms which have a predilection for axial muscles and can result in abrupt falls. The etiology is antibodies to glutamic acid decarboxylase, an enzyme which breaks down glutamic acid to gamma-aminobutyric acid (GABA), an inhibitory transmitter. This disorder can be a paraneoplastic syndrome.

Three Motor Systems and Neurologic Signs

A. Corticospinal system

1. Weakness.
2. Spasticity.
3. Impaired rapid alternating movements (dysdiadochokinesis).
4. Slower movements, decreased speed of finger and foot tap.
5. Increased reflexes, Babinski signs.
6. No eye movement signs.

B. Extrapyramidal system

1. Bradykinesia.
2. Cogwheel rigidity.
3. Tremor.
4. Postural instability.
5. Impaired rapid alternating movements (dysdiadochokinesis).
6. Chorea, Athetosis, Dystonia, Hemiballism.

7. Reflexes are unchanged. No Babinski signs.
8. No weakness or new reflexes other than Myerson's sign, to be discussed under reflexes.
9. Eye signs. Saccadic ocular pursuit.

C. Cerebellar system (in brainstem and cerebellum)

1. Limb ataxia.
2. Truncal ataxia, titubation.
3. Impaired rapid alternating movements (dysdiadochokinesis).
4. Failure of check ("rebound").
5. No weakness.
6. Reflexes usually unchanged. Rarely they are pendular, slower in rise and fall. No Babinski signs.
7. Romberg test: Rarely positive when vestibulocerebellar fibers are involved.
8. Eye signs. Nystagmus, especially downbeat with lesions affecting the flocculus. Ocular dyskinesias: ocular dysmetria, ocular flutter, opsoclonus.

Gait and Station Examination [14]

Gait can be affected by abnormalities arising from all anatomic sites. The abnormal walk, however, is not always pathognomonic for a specific anatomic locus of disease. There are overlapping findings.

Observations should include:

1. Initiation.
2. Base.
3. Stride.
4. Turning.
5. Arm movements.
6. Speed.
7. Center of gravity.
8. Involuntary movements.
9. Body posture.
10. Balance.

Common Gait Disorders [14]

1. Apraxic gait.

> An apraxic gait is manifested by inability to take that first step followed by shuffling.

An apraxic gait is manifested by inability to take that first step. Initiation of movement is markedly impaired. This is typically followed by shuffling or a very short stride and taking several steps when turning. The base may be wide or narrow. The feet seem stuck to the floor and there is often freezing of movements, especially when going through narrow spaces such as a doorway. "Freezing" in doorways is typical of Parkinson's disease. While seated, however, the patient can move his legs well to imitate stepping or bicycling. Retropulsion is common and may inhibit these movements.

Common causes of an apraxic gait include Parkinson's disease, normal pressure hydrocephalus and bilateral frontal lobe pathology.

Common causes of an apraxic gait include Parkinson's disease, normal pressure hydrocephalus and bilateral frontal lobe pathology.

2. Parkinson gait.

The patient with Parkinson's disease has a gait similar, if not sometimes identical, to an apraxic gait. Initiation of the first step is delayed and hesitant, may be followed by shuffling and then turning en bloc while taking a few extra steps. Turning en bloc is manifested by a rigid posture and an absence of truncal or head movements. The patient may have camptocormia, a flexed spine, is usually stooped and has a diminished arm swing. In addition to the flexed spine the knees may be flexed. The gait may be festinating. This is an uncontrollable acceleration of gait. The patient usually hesitates or "freezes" when going through doorways. Retropulsion when attempting to stand and misjudging both distances and the turning circle in the process of sitting down are common. Patients often stop too soon before sitting. Verbal cues may be helpful when the patient freezes such as, "Now lift your left leg."

3. Sensory ataxia.

Sensory ataxia is due to impaired proprioception.

Sensory ataxia is due to impaired proprioception. The gait tends to be slower, associated with a wide base and may be "slapping." There is gross ataxia with a tendency to fall to either side. The patient focuses on the floor since the absence of visual cues will aggravate the ataxia. Neuropathy is the most likely etiology. Myelopathies, such as subacute combined degeneration which is associated with posterior column demyelination due to vitamin B_{12} deficiency, are much less common.

4. Steppage gait.

This gait is wide-based, slow and often associated with a sensory ataxia. The patient often takes high steps and throws his foot out. It is frequently an audible gait

because of the "slapping" sound due to weakness of ankle dorsiflexion (anterior tibialis). The etiology is usually a neuropathy.

5. Cerebellar system dysfunction.

> Cerebellar diseases may cause a lurching, staggering gait associated with a wide base.

This patient has a lurching, staggering gait. The base is wide and foot placement is irregular. There may be titubation, severe rhythmic truncal and head tremor associated with lesions of the cerebellar vermis. With a unilateral lesion there is usually a drift to that side. When a patient is instructed to walk a few steps forwards then backwards several times with the eyes closed, deviation to the side of a lesion occurs. This is likely to lead to a pattern of movement which is "star-shaped." When the brainstem is involved there may be drop attacks due to a sudden loss of tone, "negative myoclonus."

6. Hemiparetic gait.

> The hemiparetic gait is manifested by a wide base, extension of the knee, circumduction of the leg and a tendency to drag the foot.

The hemiparetic gait is manifested by a wide base, extension of the knee, circumduction of the leg and a tendency to drag the foot. The arm is adducted, flexed at the elbow, pronated and flexed at the wrist.

Ipsilateral loss of arm swing is occasionally the only finding in the arm when the patient has a spastic leg. The etiology is a contralateral cerebral or brainstem lesion or an ipsilateral spinal cord lesion which involves the corticospinal tract.

7. Paraparetic gait.

> The paraparetic gait is associated with a slow walk, narrow base, adducted legs and dragging of the feet.

This gait disorder usually implies a spastic paraparesis. The patient walks slowly with a narrow base, adducted legs and drags his feet. The legs are stiff and extended at the knees. The legs tend to cross over each other or "scissor." A myelopathy is almost always the anatomic basis if there are no other neurologic signs. Other very unlikely considerations would include a parasagittal neoplasm, bilateral infarctions involving the internal capsules and, least likely, brainstem pathology.

The most common etiologies, assuming a myelopathy, would be multiple sclerosis, cervical cord compression due to spinal stenosis or a herniated disk and, lastly, neoplasm.

Uncommon Gait Disorders

1. Vestibular gait.

> A vestibular gait is typified by a wide base and a drift to the side of the lesion.

The patient walks with a wide base and drifts to the side of the lesion. There may be a rigid head position to reduce oscillopsia, the perception that the environment is oscillating, that occurs due to an impaired vestibuloocular reflex. This is associated with an abnormal stepping test which will be described below.

2. Cautious gait.

This is a gait that may occur in elderly individuals who have previously injured themselves in a fall and are fearful of repeated injury. The patient walks slowly with a wide base, short stride and often reaches out for support. The arms are frequently abducted and the turning is en bloc as the patient keeps a rigid posture without head or trunk turning motions.

3. Gait associated with choreoathetosis and dystonia.

The patient with choreoathetosis often has a "dancing" gait which is wide-based and manifested by irregular steps. There are associated abnormal involuntary movements in the upper extremities. Occasionally, there is a spastic element with circumduction of the legs. In the patient who has dystonia there is a sustained abnormal posture.

4. Waddling Gait.

This is due to proximal leg weakness. The patients may walk on their toes and often have a wide base. A lumbar lordosis is common.

5. Antalgic Gait.

This is an abnormal gait provoked by pain. The patient avoids weightbearing, for example, on an injured leg or diseased, painful joint. Occasionally, the appearance simulates a gait due to a neurologic disorder rather than a simple limp. Thus, referrals to a neurologist for an antalgic gait are not rare and care must be taken to avoid unnecessary investigations.

6. Astasia–Abasia.

> Astasia-abasia is typically found in the patient with a conversion reaction who makes lurching irregular steps.

This is typically a patient who has a conversion reaction and makes lurching irregular steps. The patient appears to be on the verge of a near-collapse. An associ-

ated symptom is often a give-way weakness. The patient may manifest a Hoover sign when supine.

7. Tandem Gait.

The patient attempts to walk a straight line with his or her heel touching the tip of the big toe. Impairment is common with any of the above-noted gait disorders. Its significance is particularly relevant when it is the only abnormal finding and thus would suggest either cerebellar system disease or a vestibular disorder. Normal elderly patients, over 70 years, may be unable to perform tandem gait.

8. Heel and Toe-Walking.

Normal elderly patients, over 70 years, may be unable to perform tandem gait.

An inability to get up on heels and take a few steps without a slight footdrop is an excellent functional test. A patient who has give-way weakness of ankle dorsiflexion and a good heel-walk certainly has psychogenic factors which play a significant role in his neurologic presentation. The same comparison can be made with a toe-walk as compared to weakness of gastrocnemius muscles. Lastly, this test may pick up weakness that is not detectable by manual testing. An abnormal functional test trumps assessment of manual strength.

9. Romberg Test

The Romberg test is an assessment for abnormal position sense and vestibular dysfunction.

The Romberg test compares standing with feet together, eyes open followed by eyes closed. When the patient is stable with eyes open and eye closure causes a major sway or an extra step to maintain balance, the test is positive. This is a test for abnormal position sense and vestibular dysfunction. Interpretation of abnormal sway is often controversial and hence an abnormal test often depends on the examiner's judgment. A minimal sway is clearly negative. Unsteadiness with eyes open and closed is also a negative test.

The most common cause of a positive test is a sensory neuropathy. Myelopathies involving the posterior column will cause the same finding but are quite uncommon. Major diagnostic considerations in that instance would be multiple sclerosis, subacute combined degeneration due to vitamin B_{12} deficiency and neoplasm. Cervical spinal stenosis with cord compression due to a herniated disk usually causes motor dysfunction as it first affects the anterior portion of the spinal cord. A positive Romberg is consequently a rare associated finding.

Vestibular dysfunction, especially vestibular neuritis, is manifested by falling toward the side of the involved 8th nerve. Semicircular canal pathology due to drug

toxicity or Ménière's disease are additional etiologies. Eighth nerve damage due to drug toxicity is another distinct cause. Whether a positive Romberg can be caused by cerebellar system dysfunction is controversial. This does occur infrequently, in my opinion, and is probably due to involvement of vestibulocerebellar pathways.

10. Stepping test (Fukuda test).

> The stepping test is useful for evaluating vestibular function.

This is a good test for evaluating vestibular function. The patient is requested to take 60 steps while standing in place with the arms outstretched directly in front of him. Turning more than 45° to one side indicates vestibular dysfunction; usually the turn is towards the side of a peripheral lesion.

11. Pull test.

The examiner stands behind the patient and pulls the patient's shoulders back quickly with moderate force. The patient with Parkinson's disease commonly takes a few steps backwards or may even fall into the examiner's arms.

Reflex Examination [14]

The major purpose of the reflex examination is to distinguish between CNS and PNS pathology. If CNS disease is present, the reflex examination can help to determine the presence or absence of unilateral disease. If there is PNS disease, localized hyporeflexia may help to differentiate plexus, focal root and nerve pathology. For many neurologists minor asymmetries can be of great diagnostic value or simply insignificant. Furthermore, the technique used to elicit reflexes may vary between examiners. Consequently, this section of the examination is quite susceptible to misinterpretation which makes reflex findings often less valuable than functional testing. The latter includes rapid alternating movements, finger and foot tapping, finger-to-nose testing, heel-to-shin testing and heel and toe-walking. Examination of manual strength is particularly useful for PNS/muscular disease, but less so for CNS disease when compared to functional tests.

> A major purpose of the reflex examination is to distinguish between central nervous system (CNS) and peripheral nervous system (PNS) disease.

> The reflex examination is susceptible to both misinterpretation and faulty technique making reflex findings often less valuable than functional testing.

Method of Examination

Reflexes are obtained by tapping near the tendon insertions and should avoid hitting the muscle itself which can always generate a reflex.

Patients are best examined sitting in relaxed fashion with the arms flexed at the elbows and hands in the lap. The angle between the forearm and upper arm should approach 90°. Reflexes are obtained by tapping at the tendon insertions and should avoid hitting the muscle itself which can always generate a reflex. Reflexes routinely evaluated are the biceps, triceps, brachioradialis, Hoffmann's, patellar (knee), Achilles (ankle) and plantar to detect a Babinski sign. Biceps and brachioradialis are innervated by C5–6 roots, triceps by C6–7, Hoffmann's C8, patellar L3–4 and ankle S1.

Hoffmann's sign is elicited by hyperextending the third finger and flicking the nail downward; a positive sign is quick flexion of the distal phalanx of the thumb. Only an asymmetry is abnormal.

The biceps reflex (see Fig. 4.16) is elicited by the examiner placing her thumb on the biceps tendon and tapping it. Triceps and brachioradialis reflexes are usually more easily elicited (see Fig. 4.17 and 4.18). A different position can be used for the triceps reflex; the arm can be held up in the abducted position at the shoulder without the patient's assistance before tapping the tendon. Hoffmann's sign is elicited by hyperextending the third finger and flicking its nail downward. A positive Hoffmann's is a quick flexion of the distal phalanx of the thumb (see Fig. 4.19). Only an asymmetry is definitely abnormal. Bilaterally positive Hoffmann's signs are commonly found in normal individuals. When examining knee and ankle reflexes (see Figs. 4.20, 4.21, 4.22, 4.23 and 4.24) it is often best for the patient to be sitting with good body support, the popliteal fossa just at the edge of the examining table. When sitting far forward many patients have a tendency to flex the knees and thus inhibit free extensor movement. The suprapatellar reflex is occasionally useful to replace the standard knee reflex when patients object to the latter for various reasons such as previous knee surgery or painful arthritis (see Fig. 4.22). The ankle reflex requires both hands of the examiner, one for the reflex hammer and the other to put slight upward pressure on the ball of the foot (see Fig. 4.23). When patients are confined to bed different techniques are required (see Fig. 4.21 and 4.24).

Reflexes are judged by velocity of movement, amplitude and relaxing phase in descending order of importance.

Reflexes are judged by velocity of movement, amplitude and relaxing phase in descending order of importance. Velocity of movement is most sensitive. Reflexes can be graded by using a system of trace, 1+, 2+, 3+, or 4+ with 4+ indicating clonus.

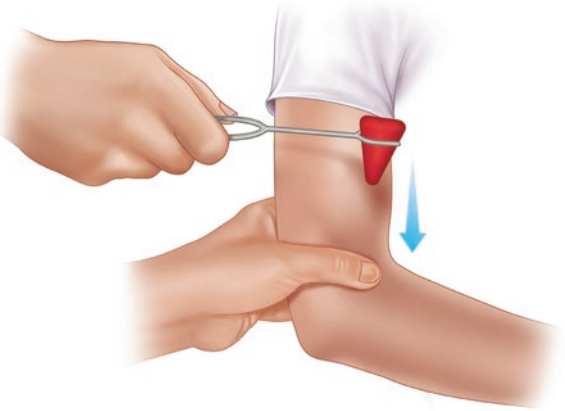

Fig. 4.16 Biceps reflex. Method of obtaining biceps reflex

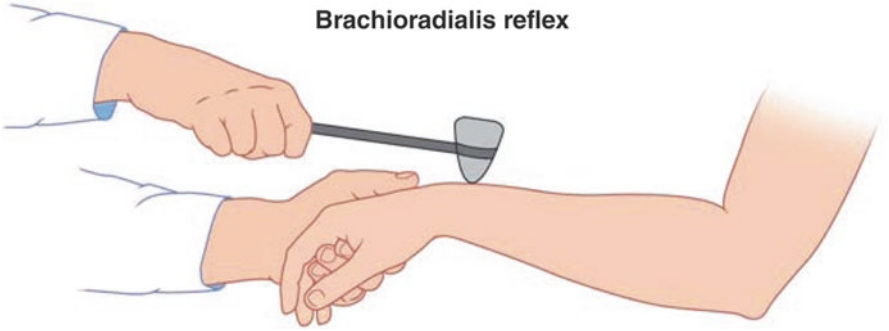

Fig. 4.17 Brachioradialis reflex. The arm is held in flexion at the elbow a little less than 90° and pronated halfway. The tendon is struck just above the styloid process

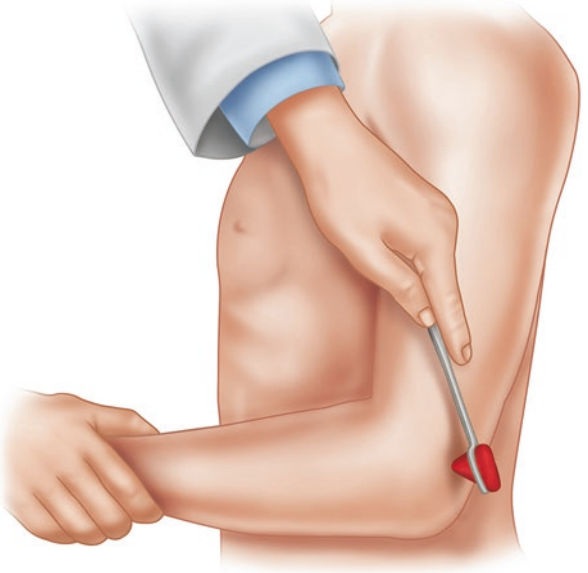

Fig. 4.18 Triceps reflex. Method of obtaining triceps reflex

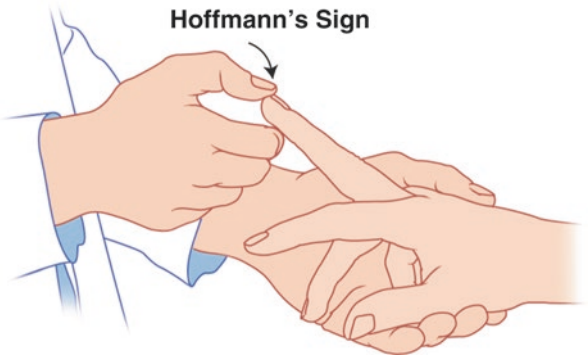

Fig. 4.19 Hoffmann's sign. The patient's hand is fixed in the pronated position and the middle finger is hyperextended. The patient's nail is then strongly and firmly flicked downward by the examiner's thumb. A positive response is flexion of the terminal phalanx of the patient's thumb

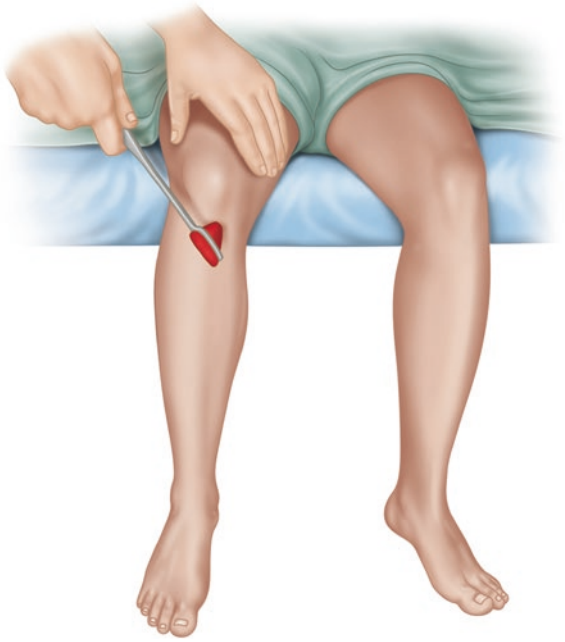

Fig. 4.20 Knee reflex sitting. Method of obtaining knee reflex

Some neurologists use only 1+ to 4+ thus eliminating the option of trace. Clonus is a series of repetitive jerks, usually three or more, elicited by a single tap. Clonus is considered sustained if it does not stop at a maintained position held by the examiner. Sustained clonus is usually elicited at the ankles and ordinarily requires persistent mild upward pressure on the ball of the foot. Sustained clonus is always abnormal. Unsustained clonus is abnormal only if asymmetric.

The jaw jerk is seldom useful to test since most people have minimal or no reflex. Prompt closure of the jaw is the abnormal response and supports the presence of pathology affecting corticobulbar fibers above the trigeminal motor nucleus (see Fig. 4.12). An exaggerated jaw reflex suggests bilateral pathology involving corticobulbar fibers which may support a diagnosis of generalized hyperreflexia as seen in amyotrophic lateral sclerosis.

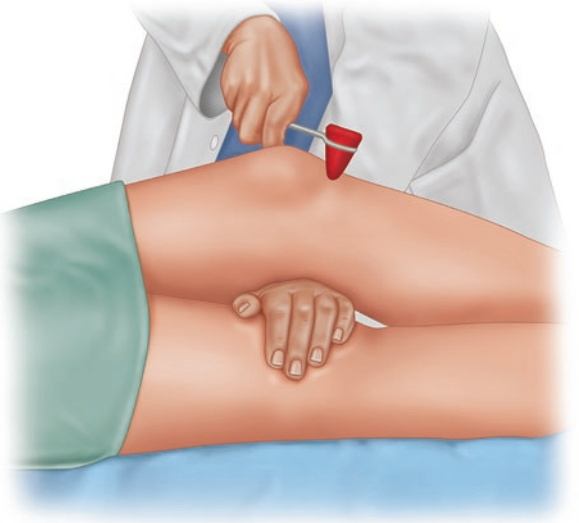

Fig. 4.21 Knee reflex supine. Method of obtaining knee reflex when patient is unable to sit

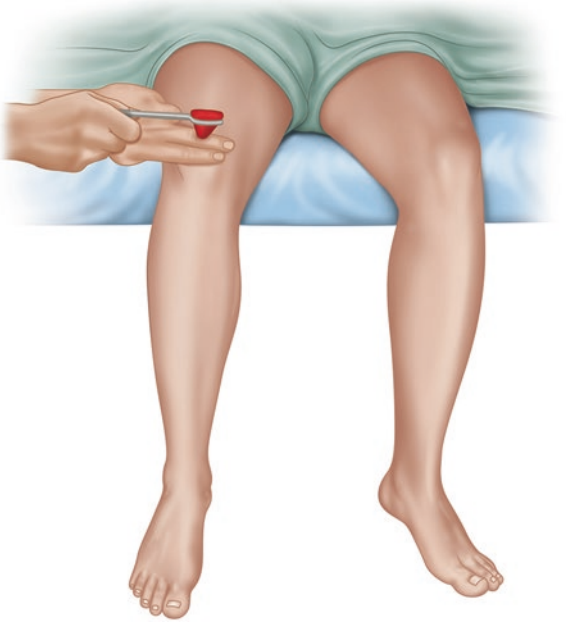

Fig. 4.22 Suprapatellar reflex. Method of obtaining the suprapatellar reflex

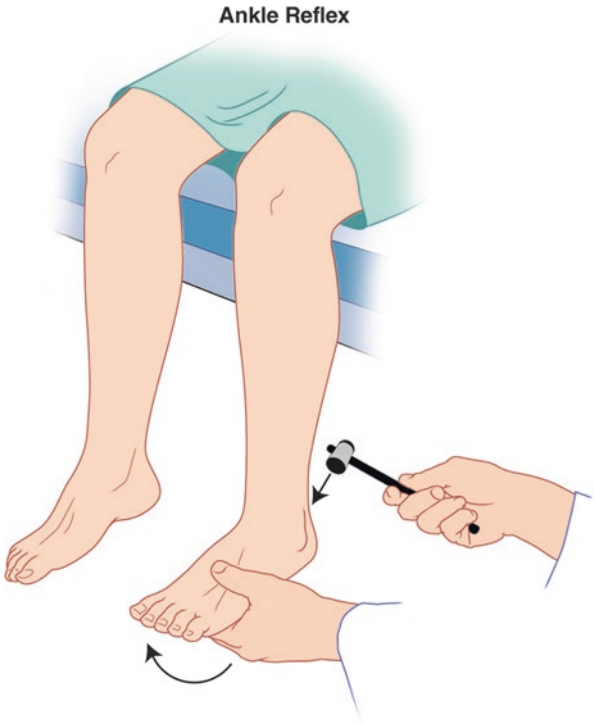

Fig. 4.23 Ankle reflex sitting. This is best obtained with the patient seated at the table edge with his legs dangling. The foot is partially dorsiflexed by placing upward pressure on the ball of the foot. The Achilles tendon is then firmly-to-strongly tapped

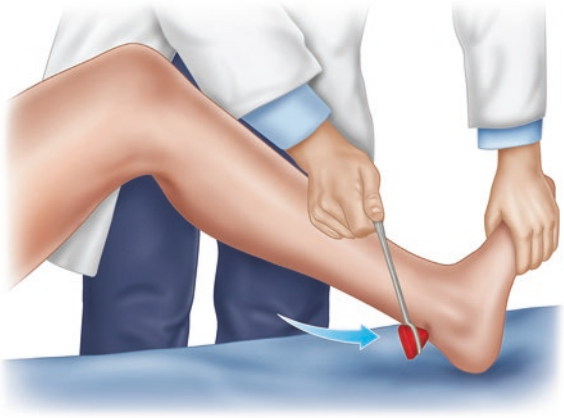

Fig. 4.24 Ankle reflex supine. Method of obtaining ankle reflex when patient is unable to sit

Enhancement Technique

When a reflex cannot be obtained enhancement techniques can be useful.

When a reflex cannot be obtained enhancement techniques can be useful. If unobtainable in the arms, the patient can be requested to grit his teeth. If knee or ankle reflexes cannot be elicited, gritting the teeth, making a fist or the Jendrassik maneuver can be utilized. The Jendrassik maneuver is to have the patient interlock the fingers of both hands and then pull on them. One or two seconds after the maneuver is made the reflex should be assessed. (See Fig. 4.25) Occasionally, the originally absent reflex on both sides becomes asymmetric such as present on one side, absent on the other, or 2+ on one side and 1+ on the other, thus indicating localizable pathology. (Fig. 4.26)

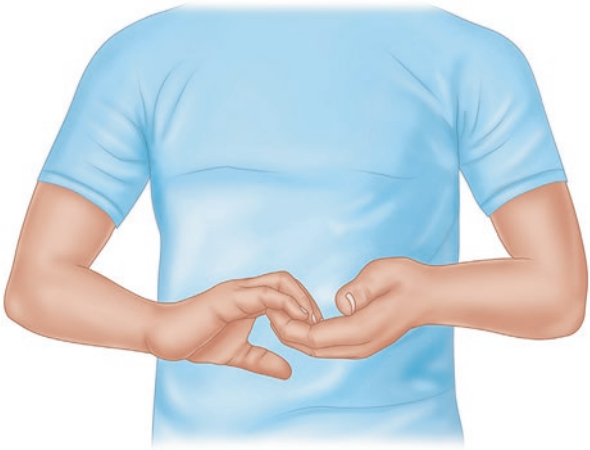

Fig. 4.25 Jendrassik maneuver. Method of reinforcing an ankle or knee reflex when either is not obtained by the usual method. The patient is instructed to pull on his interlocked fingers and the reflex is checked 1 or 2 s later

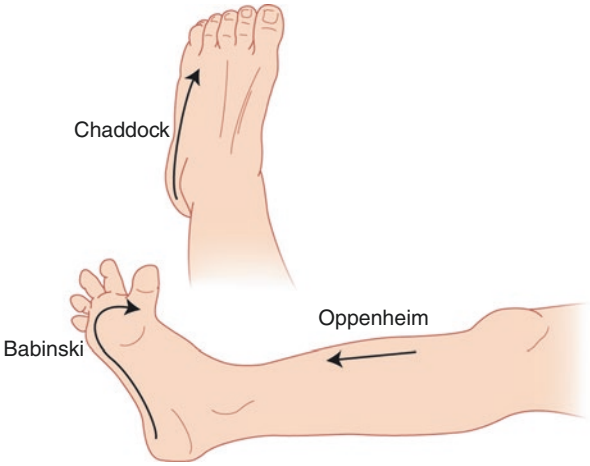

Fig. 4.26 Extensor plantar responses. The Babinski, Oppenheim and Chaddock signs are most useful. The Babinski sign is elicited with slow firm pressure beginning at the lateral part of the heel and moving upward as shown above. The first definitive movement of the big toe should end the test. This is often obtained within 2 in. of beginning the stimulus. The same movement may be obtained with Chaddock and Oppenheim tests, as demonstrated

Reflex Aberrations

Reflex spread should be noted. For example, a tap on the brachioradialis tendon may generate both the intended reflex and finger flexion. The knee reflex may induce adduction at the hip. These responses are common with corticospinal tract lesions but they are definitely significant only if asymmetric since some normal individuals exhibit reflex spread. An inverted reflex is an absent reflex associated with reflex spread. For instance, tapping the triceps tendon produces flexion rather than extension at the elbow. One possible explanation could be a C7 root lesion associated with a myelopathy. This does not always indicate obvious pathology. Slow relaxing phases of reflexes, especially the ankle jerk, have been found to be a good predictor of hypothyroidism.

Superficial Reflexes

> The superficial abdominal reflex is abnormal on the absent side. Bilateral absence is not an abnormal sign.

The abdominal and cremasteric reflexes are the two most commonly used. The former is elicited by scratching the abdomen, in an oblique fashion, in each of the four quadrants (see Fig. 4.27). This reflex, which is multisynaptic, pulls the umbilicus towards the stimulus. The side of the absent reflex is abnormal and indicates

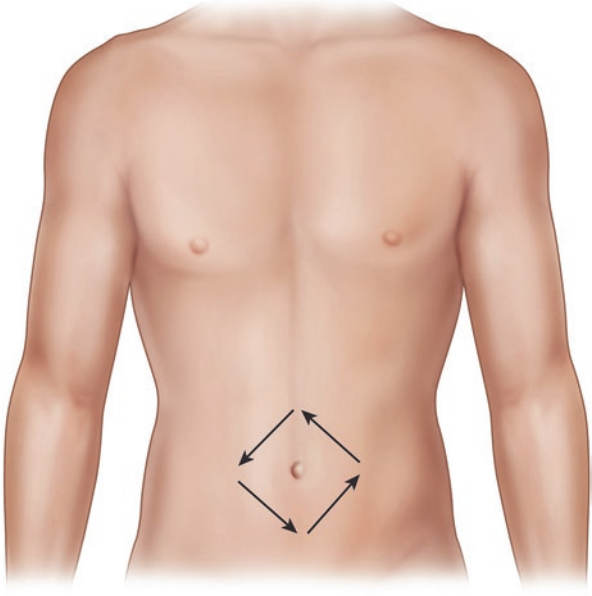

Fig. 4.27 Abdominal reflex. The abdomen is scratched once in each of the 4 quadrants as shown. The umbilicus may be pulled toward the stimulus

ipsilateral pathology affecting the corticospinal tract usually in the spinal cord. If only the upper abdominal reflexes are present, there may be a lesion at T10 or T11 suppressing the lower abdominal reflexes. Beevor's sign may then be present; head flexion causes the umbilicus to move upward. It is important to realize that normal individuals often have absent abdominal reflexes. The cremasteric reflex is elicited by scratching the inner thigh which causes the cremasteric muscle to contract, thereby elevating the testicle on that side. Unilateral absence may indicate ipsilateral pathology in the corticospinal tract.

Two other reflexes are infrequently useful. The superficial anal reflex (S2 through S5) is manifested by contraction of the anal sphincter when pricking the mucus membrane in the perianal area. The bulbocavernosus reflex (S3–S4) is a contraction of the anal sphincter detected by a gloved finger in the rectum when the glans penis is pinched.

Abnormal Reflexes

The Babinski sign indicates corticospinal tract disease, located in cerebrum, brainstem and spinal cord.

Testing the plantar response may elicit the Babinski sign, the prototypical finding of corticospinal tract disease (see Fig. 4.26). Therefore, it is present only with lesions affecting the motor portions of the cerebral hemispheres, brainstem and spinal cord. Strictly localized lesions of other parts of the CNS such as cerebellum, hypothalamus, occipital lobes, etc., will not produce a Babinski sign.

The elicitation of this sign should begin with a brief explanation to the patient as to what the stimulus will feel like. Demonstrating it first on the patient's hand can put the patient at ease. A simple statement might be, "This is a reflex test to check the spinal cord and brain." Otherwise, many patients believe it is a test to determine whether they feel the stimulus and often evokes immediate distrust and dislike of the examiner.

The patient's leg should be extended at the knee. A firm pressure with a key, broken tongue blade, or other similar object is applied to the lateral portion of the sole of the foot near the heel and slowly moved up to the base of the fifth toe. It is an uncomfortable stimulus, but does not have to be painful and certainly should not break the skin. Infrequently, when there is no response, the stimulus can be turned and continued along the base of the other toes. The first movement of the big toe determines the reflex. Once this movement is clearly visible continuing this stimulus is of no value. Upward movement is abnormal and is usually obtained within 2–3 in. of beginning the stimulus. Occasionally, it may be difficult to distinguish between a withdrawal response and a Babinski sign. Fanning or abduction of the toes is not required and its presence without big toe extension has no diagnostic

significance. Asymmetry of the plantar response, strong flexion on one side, and no response (mute) on the other may have diagnostic import.

The Babinski sign is determined by the first movement of the big toe; when this movement is definite continuing the stimulus is unnecessary.

There are other methods of obtaining an abnormal plantar response, extensor movement of the big toe. The two most commonly used when there is an equivocal Babinski sign are the Chaddock and Oppenheim methods (see Fig. 4.26). The Chaddock is probably the most reliable second choice. It is performed by using the same stimulus as that used for the Babinski sign applied along the lateral surface of the foot beginning near the heel and extending up to the fifth toe. The stimulus is a slow deep pressure. The examiner may evoke Oppenheim's sign by dragging his knuckles slowly and firmly down the tibia from knee to ankle and this can be combined with the plantar or Chaddock methods. An advantage of Chaddock method is a reduced chance of eliciting a withdrawal response. Oppenheim's sign is the least sensitive but the most specific, since withdrawal responses are not elicited. Other seldom used methods are Gordon and Bing signs. The former is squeezing the calf muscles and the latter by tapping the dorsum of the big toe repeatedly with a pin.

Terminology will be briefly mentioned at this time. A Babinski sign is present or absent. There is no such thing as a negative Babinski (−/+) or a positive Babinski (+/+).

The grasp reflex is elicited by placing two fingers in the palm of the patient's hand and drawing the fingers out between the thumb and the index finger.

The grasp reflex is elicited by placing two fingers in the palm of the patient's hand and drawing the fingers out between the thumb and the index finger. When the patient involuntarily grasps the examiner's fingers the reflex is present. This is a normal reflex in the first few months of life, but reappears most commonly with cerebral degenerative diseases. A unilateral grasp reflex usually indicates contralateral frontal lobe pathology.

The glabellar reflex is obtained by repeatedly tapping just above the bridge of a patient's nose. A positive response, also known as Myerson's sign in Parkinson's disease, is manifested by repeated eye blinks, whereas a normal response is usually no more than two or three blinks. This is also commonly present in cerebral degenerative diseases.

The glabellar reflex is obtained by repeatedly tapping just above the bridge of a patient's nose and a positive sign (Myerson's sign) is manifested by several or continuous repeated eye blinks.

The sucking reflex is elicited by asking the patient to open his mouth about 2 cm, then moving a wet Q-tip from the lateral lips to the midline. The lips curve around it. A rooting reflex may be obtained by tactile stimulation just lateral to the mouth. The response is a turn of the lips, mouth and sometimes the head toward the stimulus. These reflexes are observed primarily as a late development in cerebral degenerative diseases with diffuse involvement of the frontal lobe or bilateral corticobulbar tract.

Reflexes of Questionable Significance

The snout reflex is elicited by tapping the upper lip of the patient. The response is a prompt pouting and protrusion of the lips. In essence, it is hyperreflexia of the orbicularis oris and mentalis muscles and thus commonly present with lesions affecting frontal lobes and corticobulbar pathways in subcortical and midbrain regions. However, it has been occasionally well documented in healthy individuals and thus of no definite pathologic significance. It is common, however, in patients with degenerative cerebral disease.

The palmomental reflex is obtained by scratching the palm of a patient's hand. This may cause ipsilateral contraction of the mentalis and, less often, the orbicularis oris muscles. As it is often present in normal individuals it has no clear diagnostic significance. This reflex is, however, more common in patients who have cerebral degenerative diseases.

Synopsis

See Table 4.9.

Table 4.9 Anatomic site of lesion/reflex change

Site of lesion	Reflexes
Cerebral (cortical and subcortical)	Increased
Extrapyramidal	Unchanged
Brainstem	Increased
Cerebellum	Unchanged or pendular
Spinal cord	*Increased[a]
Root	Decreased
Plexus	Decreased
Nerve	Decreased
Neuromuscular junction	Unchanged
Muscle	Unchanged

[a]Exceptions: Anterior horn cell involvement such as occurs with amyotrophic lateral sclerosis will decrease reflexes

Major Principles

Reflexes are commonly normal with diseases involving the central nervous system or the peripheral nervous system.

1. Reflexes are commonly normal with diseases involving the CNS or PNS.
2. Generalized symmetrical hyperreflexia is not, as an only sign, pathologic.
3. Generalized symmetrical hyporeflexia or even areflexia is not, as an only sign, pathologic.
4. Unilateral hyperactive reflexes are usually abnormal on the side that is hyperactive and indicates pathology involving the corticospinal tract in cerebrum, brainstem or spinal cord.
5. Asymmetric reflexes affecting only one limb may indicate a CNS lesion involving the corticospinal tract affecting the hyperactive side or a plexus/root/nerve lesion on the hypoactive side. The decision will hinge on a good history and other abnormal neurologic findings.

Babinski signs, unilateral or bilateral, and sustained clonus are always abnormal.

6. Babinski signs, unilateral or bilateral, are always abnormal indicating pathology affecting the corticospinal tract in cerebrum, brainstem or spinal cord. When unilateral, the lesion is in the ipsilateral spinal cord, the contralateral cerebral hemisphere or the contralateral brainstem.
7. Hoffmann's sign, when unilateral, usually indicates pathology affecting the corticospinal tract in the ipsilateral spinal cord or contralateral cerebral hemisphere and brainstem.
8. Marked asymmetry of reflexes in arms vs. legs, particularly hyperactive only in the legs, is suggestive of thoracic myelopathy.
9. Sustained clonus is always abnormal. Unsustained clonus is only abnormal if asymmetric.
10. Absence of a single reflex is most common with a root or focal nerve lesion.

Sensory Examination [15]

The sensory examination of one patient by two physicians performed hours apart is seldom identical unless the lesion is acute and severe. A pin or vibration stimulus is not likely to be given with the same force. Testing position sense can be done with different degrees of movement and at different speeds.

The sensory exam may be affected by fatigue, somnolence, fear and drug effect.

There are confounding factors which may alter the patient's responses such as fatigue, somnolence, fear and drug effect. Oppositional and pessimistic attitudes must be detected and taken into account. The patient's demeanor and verbal responses should be a tip off.

Delayed responses may be due to bradyphrenia (slow thinking) associated with dementia, mental retardation, depression or malingering. An obsessive, indecisive individual or one who is somatically preoccupied may cogitate over each answer and magnify minor sensory differences. One method which may compensate for these responses is to ask the patient; "If the good side is worth $1.00, what is the bad side worth?" Many answers are in the range of 70–95 cents and can be construed as unimportant. Clinical judgment is required in equivocal instances. There are patients who wish to control the results of the examination and willfully or subconsciously deny perception of a stimulus. Willful denial occurs with patients who are malingering. Subconscious denial is characteristic of a conversion reaction. Distinguishing between these two diagnoses can be quite vexing. There are a few patients who erroneously report perception of a stimulus perhaps to reduce the chances of discovering and facing a serious illness.

The examiner must take all of the above-noted influences into consideration before reaching a final conclusion about the sensory examination. An additional cautionary note is to avoid premature dismissal of the results of the exam as indicative of psychogenic causes or malingering. Numerous embarrassing and dangerous errors have been made with such impetuous diagnoses. It is safer to err on the side of organicity.

The purpose of the sensory examination is to uncover unilateral deficits, distal sensory loss, and to search for specific patterns of sensory loss depending on the history. Checking for sensory levels when spinal cord disease is suspected is critical. Sacral sensation, perianal especially, may be particularly involved with conus medullaris and cauda equina lesions. A neurogenic bladder mandates this assessment. Root, plexus or focal nerve pathology require a specific outline of the distribution of sensory loss.

There are four primary sensory modalities, pain/temperature, vibration, position sense and touch. Large myelinated fibers, fast conducting, carry sensations of vibration, position sense and touch. Small unmyelinated, slower conducting fibers mediate pain and temperature.

Small unmyelinated, slower conducting fibers mediate pain and temperature. Large myelinated, fast conducting fibers mediate vibration, position and touch sensitivity.

Nerve fibers conducting pain and temperature enter the spinal cord via the dorsal horn, usually descend one or two segments and synapse there. Then the fibers cross immediately via the anterior commissure, ascend in the lateral spinothalamic tract, synapse in the ventral posterior lateral (VPL) nucleus of the thalamus and subsequent axons terminate in the parietal lobe. Sensory testing is done with pin and/or cold stimulus. The latter is most simply done with the tines of the tuning fork although they may become warm quickly with prolonged or repeated use. Patients are occasionally frightened of pins and thus temperature testing is an excellent substitute. Either stimulus is applied at the toes first and slowly moved upward to find a sensory level. When the patient's responses to pin are inconsistent, observing the patient's expression or wince is more reliable. Distal sensory loss, sensory levels, dermatomal and nerve distribution patterns are sought.

When the patient's responses to pin are inconsistent, observing the patient's expression or wince is more reliable.

Vibration, proprioception and most touch fibers are mediated by large myelinated, rapid conducting axons. They enter the dorsal horn, ascend in the posterior (dorsal) columns, decussate in the medial lemniscus (medulla), ascend to the VPL nucleus of the thalamus where they synapse and subsequent axons terminate in the parietal cortex. Perception of vibration depends at least partially on the intensity of the stimulus which is best kept approximately uniform with each test. Loss of vibration sense at the toe joints mandates a search for a vibration sensory level at ankle, knee, hip and spine in that order. In addition to immediate perception of vibration, the stimulus should be kept in place for several seconds. There are patients who perceive the stimulus for only 1 or 2 s, known as rapid adaptation. This is probably an abnormal finding in patients under age 70, although there are no established criteria. Vibration sense is nearly always lost before position sense for lesions involving thalamus and below. Hence a sensory examination is never complete without examination of vibration sense with a 128 Hz tuning fork.

Loss of vibration sense at the toe joints mandates a search for a vibration sensory level at ankle, knee, hip and spine in that order.

Proprioception loss (position sense) is examined with either of two methods. These are the direction of movement or whether the resultant position is above or below the resting position. Clearly, the patient must be given the appropriate instructions. Slow movements are harder to detect, so the examiner needs to have a uniform approach. The exam begins with the metatarsal-phalangeal joint of the big toe and a distal interphalangeal joint of a finger. If either is abnormal, a sensory level is

sought for at wrist, elbow and shoulder and/or ankle, knee and hip. Severe proprioception impairment may result in an ataxic gait, positive Romberg, finger-to-nose and heel-to-shin ataxia. Pseudoathetosis, wandering movements of the limb, usually an arm, may occur. Cerebral lesions cause position sense loss far more frequently than loss of vibration sense.

Severe proprioception impairment may result in an ataxic gait, positive Romberg, finger-to-nose and heel-to-shin ataxia.

Loss of light touch perception on the toes is a strong confirmatory finding of a significant neuropathy.

The sensation of light touch is mediated mainly by large myelinated fast-conducting fibers which ascend in the posterior columns and, to a limited extent, small unmyelinated fibers which ascend in the ventromedial part of the spinothalamic tract. Since touch fibers are widely distributed the assessment of light touch seldom yields diagnostic information. One exception is the occasional loss of light touch on the toes which is a strong confirmatory finding of a significant neuropathy.

Sensory Abnormalities According to Lesion Site

1. Neuropathy.

Large fiber neuropathies are first detected by testing of vibration sense. Initially, there is usually rapid adaptation to the stimulus which may be perceived for only a few seconds. Position sense loss is a much later development. Small fiber neuropathies are manifested by distal loss of pain and temperature perception, the latter usually being more sensitive. The legs are invariably involved first. Loss of light touch usually occurs after pain and temperature sensitivity is impaired. However, when impaired, the diagnosis of neuropathy is definite.

2. Plexopathy.

There is a predilection for motor dysfunction in plexopathies even though sensory symptoms, especially pain, are prominent.

There is a predilection for motor dysfunction in plexopathies even though sensory symptoms, especially pain, are prominent. There may be patchy loss to pin. An

example is the lumbosacral plexopathy which typically occurs with diabetes (diabetic amyotrophy). This causes excruciating pain, disabling weakness of quadriceps and iliopsoas musculature, yet just minimal sensory loss along the medial calf (saphenous nerve). The saphenous nerve is a branch of the femoral nerve.

3. Radiculopathy.

> Most patients with radiculopathy have little or no sensory impairment even if sensory symptoms such as pain and paresthesias are prominent.

Most patients with radiculopathy have little or no sensory impairment even if sensory symptoms such as pain and paresthesias are prominent. A dermatomal pattern of sensory loss to pinprick and, infrequently, light touch may be present. However, a meticulous search for touch and pinprick impairment is seldom worth the time investment. Vibration and position sense are nearly always intact, presumably because multiple roots mediate these sensory functions. Multiple extensive radiculopathies and dorsal root ganglionopathies will impair all sensory modalities.

4. Myelopathy.

> Myelopathies may cause sensory loss to pin and temperature contralateral to the lesion, typically a sensory level one or two segments below the level of the lesion.

Myelopathies may cause sensory loss to pin and temperature contralateral to the lesion, typically a sensory level one or two segments below the level of the lesion. The sensory level, however, is often considerably below the lesion level which thus mandates neuroimaging of the entire spinal cord. The rough anatomic landmark levels are L1 at the groin, T10 at the umbilicus, T6–T7 at the edge of the ribcage, and T4 at the nipple. A higher level on the chest requires a search for a sensory level on the hand and arm from T1 through C5. C4 and higher will be evident on the shoulder, neck, and occipital region.

Vibration and position sense loss is ipsilateral with vibration loss occurring first. Sensory dissociation is a term which refers to preservation of vibration and position sense and impairment of perception of pin and temperature. This is a common phenomenon in patients with intramedullary (within cord) lesions such as syringomyelia or astrocytoma, and spinal cord compression from anterior-placed lesions.

> Sensory dissociation is a term which refers to preservation of vibration and position sense and impairment of perception of pin and temperature.

Light touch is usually preserved because it is mediated by both ipsilateral (dorsal column) and contralateral (spinothalamic) pathways. It should be noted that rapid adaptation to a stimulus, either pin or vibration, may occur prior to total loss of perception.

Sacral sensation should be evaluated since intramedullary lesions (inside spinal cord) may spare sacral fibers ("sacral sparing") which are situated in the lateral portion of the spinothalamic tract. Conversely, cauda equina and conus medullaris lesions typically cause asymmetric sacral sensory loss along with the expected bowel, bladder and sexual dysfunction and motor involvement of sacral innervated musculature.

Sacral sensation should be evaluated since intramedullary lesions (inside spinal cord) may spare sacral fibers ("sacral sparing").

5. Brainstem.

Brainstem lesions cause contralateral hemihypesthesia to pain/temperature, vibration and position sense, the latter two provided the lesion is above the decussation of the medial lemniscus in the medulla. After partial recovery from a brainstem lesion, typically an infarction, sensory levels may be present sometimes sparing one leg or only exhibiting segmental sensory loss. The recognition of this residual deficit is important as it may obviate the need for additional neuroimaging. Painful paresthesias and burning sensations may be residual symptoms which require treatment.

6. Thalamus.

Thalamic pain syndromes may produce excruciatingly painful paresthesias, burning sensations, hyperesthesia and hyperpathia.

Thalamic lesions involving the VPL nucleus may cause dense sensory loss involving all primary sensory modalities. Concomitant or subsequent thalamic pain syndromes manifested by excruciatingly painful paresthesias, burning sensations, hyperesthesia and hyperpathia are not uncommon residua. Thalamic stroke, infarction or hemorrhage, is the usual etiology. Posterior cerebral artery branches irrigate this region.

7. Cerebral.

Sensory cortex lesions have a predilection for involvement of the hand and position sense loss is preferentially involved.

Sensory cortex lesions, mainly parietal but also posterior frontal, are less likely to cause complete hemihypesthesia. There is a predilection for involvement of the hand and position sense is preferentially involved. There is seldom loss of vibratory sense.

Double simultaneous stimulation, stereognosis, graphesthesia and two-point discrimination are useful tests for cerebral lesions.

More complex sensory abnormalities are often present. The proviso for making that judgment is intact primary sensory modalities, pin, touch and vibration. Such sensory findings as described below may also be discovered in high cervical cord lesions and thus the term cortical sensory loss is not entirely appropriate.

A common abnormality is astereognosis, the inability to detect form, shape, size and texture. This is easy to demonstrate by simply using, for example, a key, rubber band and cotton. Differentiating hard from soft may be possible but identification of substance or object may be missed. Two-point discrimination is usually assessed at the fingertips where asymmetries are most easily demonstrated. A normal detectable separation is 2–4 mm. Agraphesthesia is the inability to accurately detect numbers written on the palmar surface of the hand. The test is done quickly using the blunt end of a safety pin or a Q-tip.

Double simultaneous stimulation with touch may result in perception of the stimulus on only one side with extinction (loss of perception) on the abnormal side. This finding is most common with cerebral pathology, usually parietal lobe and the lesion is contralateral to the extinguished extremity. Sensory hierarchy can be employed to elicit the abnormality. This refers to the dominance of sensory perception in descending order, face-chest-leg-hand. Thus, right face, right chest, or right leg touch simultaneous with a left hand touch may result in the absence of perception of the touch on the left hand. Yet bilateral hand touches may be easily perceived and is thus a less sensitive method of examination.

Nonorganic Sensory Loss

Nonorganic sensory loss should be suspected when the findings do not follow an anatomic pattern. For example, sensory loss should not stop precisely at the midline since sensory fibers for pain overlap the midline.

The sensory findings do not follow an anatomic pattern. There may be loss of all sensory modalities – vision, hearing, vibration, position, pin, touch, even smell – on one side. Sensory loss typically stops precisely at the midline even

though sensory fibers for pain and temperature overlap and thus the stimulus should be perceived prior to reaching the midline. On the face the overlap is minimal. Responses are commonly inconsistent if the examination is repeated the following day or even a few hours later. Sensory responses may occasionally be obtained in patients who complain of complete unilateral anesthesia. A wince or withdrawal with pinprick stimulation of the palm of the hand or the sole of the foot can often be elicited.

Sensory Terminology

1. Allesthesia – Stimulation on the side contralateral to a hemisphere (especially parietal) lesion is perceived on the normal side.
2. Allodynia – Pain evoked by a nonpainful stimulus.
3. Anesthesia – Absence of any sensation.
4. Anesthesia dolorosa – Spontaneous pain located in an area of anesthesia. This is characteristic of herpes zoster.
5. Dysesthesia – Unpleasant sensations provoked by an ordinary stimulus.
6. Hyperesthesia – Acute sensitivity to a sensory stimulus.
7. Hypesthesia – Decreased perception of a stimulus.
8. Hyperpathia – Exaggerated response to a painful stimulus.
9. Paresthesias – Spontaneous sensations occurring without stimulation often described as prickling, burning, crawling and itching.

Dermatome Patterns (Fig. 4.28)

A familiarity with dermatome patterns is useful for the everyday examination of patients. The commonly used landmarks with frequent variations include:

C6, C7 and C8 are on the hand. The thumb is largely C6; the index, third and part of the fourth fingers are C7; and part of the fourth plus fifth finger is C8.

C4 is at the clavicle and just beneath it is T2.

T4 is at the nipple.

T6-T7 is at the edge of the ribcage.

T10 is at the umbilicus.

L1 is at the groin.

L4, L5 and S1 are on the foot. L4 is the medial part of the big toe, L5 is the medial portion of the dorsum and sole of the foot from the big toe to the fourth toe.

S1 is the lateral part of the foot, dorsum and sole including the fifth toe.

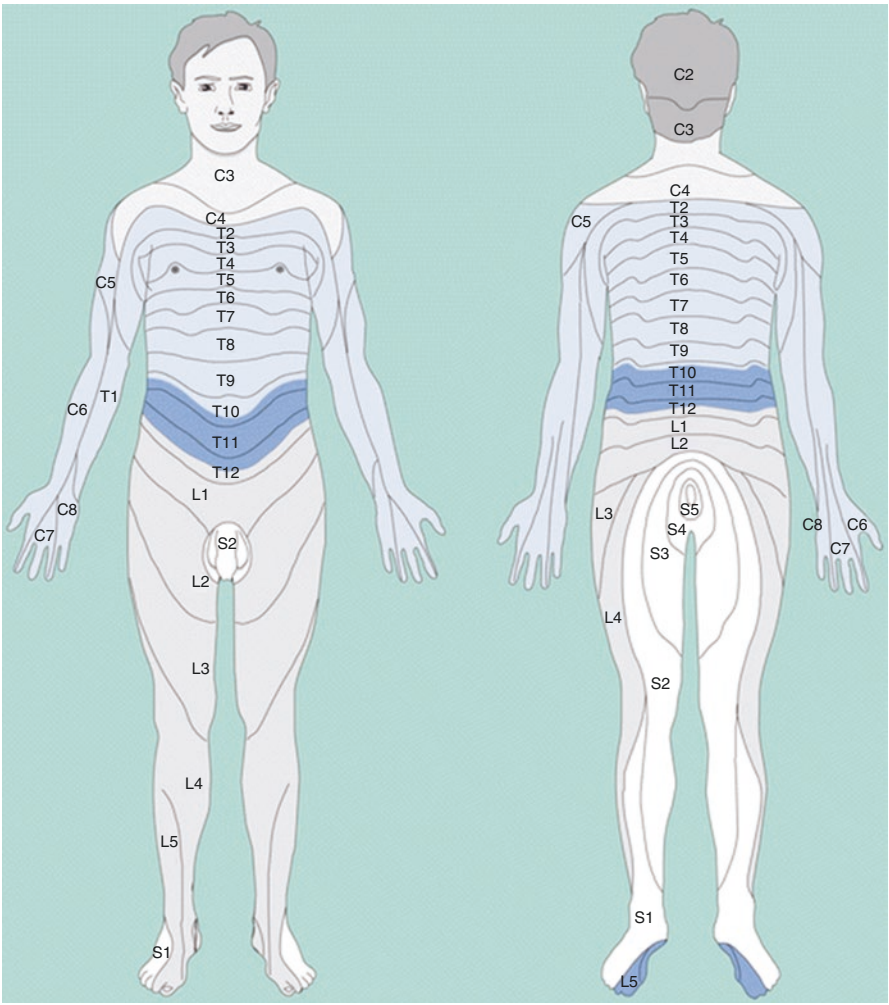

Fig. 4.28 Dermatomes

Mechanical Signs

Meningeal Disease

Nuchal rigidity is the cardinal manifestation of meningeal irritability. The patient is unable to voluntarily put his chin on his chest. When supine and at rest, the patient's neck cannot be fully flexed by the examiner. There are variable degrees of resistance ranging from immediate, severe and rock hard to minimal, detectable only at the final few centimeters, called "end nuchal rigidity."

Brudzinski's sign is obtained by placing one hand firmly on the patient's chest, then lifting the back of the head. When positive, the patient will flex the hips and knees.

Kernig's sign is described in a few ways, both in sitting and supine positions. In the supine position, the hip and knee are both flexed to 90°. Then the leg is extended at the knee another 45° which results in resistance and pain. Straight leg raising produces similar results. This sign is rarely of clinical utility for meningeal disease.

The interpretation of nuchal rigidity is affected by limitations of head movement in other directions and the presence or absence of fever.

The significance of nuchal rigidity is determined by the absence of other signs. These are limitations of head tilt, head turn and head extension. These findings, when unaccompanied by fever or systemic illness, imply other etiologies. They include cervical muscle strain, anterior interlocking osteophytosis, neck trauma and the severe rigidity of extrapyramidal disorders. Parkinson-plus syndromes such as progressive supranuclear palsy commonly produce nuchal rigidity.

Rare etiologies to be cognizant of in puzzling clinical situations include incipient cerebellar tonsillar herniation and retropharyngeal abscess.

Ultimately, clinical judgment based on personal experience will be required to make the decision about performing a lumbar puncture. In critically ill patients a normal CT (head) associated with or without papilledema should ease the fears of provoking a herniation syndrome. For patients who have questionable signs of nuchal rigidity and a nondiagnostic CT scan it is best to opt for performance of a lumbar puncture since possible etiologies are meningitis, subarachnoid hemorrhage and, least likely, leptomeningeal carcinomatosis. Needless to say, nuchal rigidity associated with fever, even without a CT scan, mandates a lumbar puncture.

Cervical and Lumbar Radiculopathy

Head extension is the most useful mechanical test for the diagnosis of cervical radiculopathy.

Head extension is the most useful mechanical test for the diagnosis of cervical radiculopathy since it narrows the intervertebral foramina and is likely to augment compression of a nerve root. Brief extension for a few seconds is commonly not diagnostic. Prolonged extension for 1 min is a very sensitive and specific sign which frequently reproduces the patient's symptoms of pain and/or paresthesias. Head tilts, turns, and axial compression are much less sensitive.

Head flexion which causes neck pain supports the presence of muscular etiology.

Head flexion which causes neck pain supports the presence of muscular etiology.

It may also elicit Lhermitte's sign, electricity-like sensations which radiate down the spine and sometimes the legs. This may be due to increased sensitivity to mechanical stimulation of damaged or demyelinated nerve fibers in the posterior columns. Although classically associated with multiple sclerosis it may occur with any pathology affecting the spinal cord, especially degenerative diseases such as a herniated cervical disk or spinal stenosis.

When arm movements at one joint alone provoke radiating pain, even neck pain, the source is generally in the involved painful joint, most commonly the shoulder. Etiologies include tendonitis, rotator cuff injuries, capsulitis and impingement syndrome.

Straight leg raising is positive if pain is provoked between the elevations of 30° and 70°.

Straight leg raising is positive if pain is provoked between the elevations of 30° and 70°.

The straight leg raising test (Lasègue) is the primary test for lumbar root irritation. When the patient is supine the extended leg is slowly elevated. If pain is elicited between 30° and 70°, lumbar root irritation is suspected. However, a tight sensation in hamstring muscles is relatively common and not pathologic. If back pain or radicular pain below the popliteal fossa is elicited, then the test is positive. The addition of ankle dorsiflexion is a valuable provoking maneuver.

Crossed positive straight leg raising is a particularly useful sign. When the patient is supine, elevation of the asymptomatic leg elicits radicular pain in the symptomatic leg. This virtually secures a diagnosis of lumbar radiculopathy.

Pain produced with elevation of the leg over 70° is of questionable significance, quite doubtful if only in the posterior thigh. Pain provoked by less than 30° elevation suggests psychological factors or malingering. Pain which is worse with knee flexion or hip rotation points to a source in the hip, muscle or is nonorganic.

Straight leg raising in the sitting position is a valuable additional test to assess for the presence of lumbar radiculopathy. When the supine straight leg raising test is questionable, this test, especially with the addition of ankle dorsiflexion and head flexion, may evoke lumbar root pain and clinch the diagnosis. If the test is negative the presence of lumbar root pathology is much less likely.

Tinel's sign is produced by tapping over any peripheral nerve. Paresthesias are elicited in the distribution of that nerve when the test is positive. Phalen's sign is produced by forced flexion at the wrist. This may evoke paresthesias in the distribution of the median nerve, especially when the position is maintained for 30–60 s. Both tests are commonly used to support a diagnosis of a carpal tunnel syndrome.

The thoracic outlet syndrome is rare and false positive tests are common.

Thoracic outlet syndrome maneuvers are the sternoclavicular, Adson's and hyperabduction. Unfortunately, false positive tests are common and the syndrome itself is rare. The sternoclavicular test is performed by a retraction and downward movement of both shoulders. Adson's adds turning of the patient's head to one side and taking a deep breath. The hyperabduction maneuver adds to the Adson's maneuver by abduction of the shoulder with flexion at the elbow of the arm opposite the direction of head turn. A positive test is reproduction of symptoms sometimes accompanied by obliteration of the pulse and production of a supraclavicular bruit on the side opposite the head turn.

Questions (True or False)

1. Orthostatic hypotension may be a cause of loss of balance.
2. Dysarthria is a good localizing sign.
3. Complete destruction of the superior temporal gyrus causes contralateral hearing loss.
4. Involuntary tongue movements may be due to tardive dyskinesia.
5. Asymmetric palpebral fissures may occur with cerebral lesions.
6. Light-near dissociation of pupillary reactions does not occur with optic nerve disease.
7. The pupil with Horner's syndrome reacts briskly to light.
8. Seizures may cause multidirectional nystagmus.
9. Peripheral vestibular disease causes horizontal gaze-evoked nystagmus.
10. The hallmark of an internuclear ophthalmoplegia is ipsilateral medial rectus weakness.
11. Impaired rapid alternating movements are pathognomonic of cerebellar system disease.
12. Paratonic rigidity is a common sign in patients with dementia.
13. Prolonged head extension is a useful diagnostic test for cervical radiculopathy as it can provoke radicular pain.
14. When swallowing provokes ear pain glossopharyngeal neuralgia must be suspected.
15. Loss of position sense in an arm may cause an upward arm drift.
16. A positive Romberg occurs only with proprioception loss.
17. Reflexes are increased with a cerebellar hemisphere lesion.
18. Tonic downward eye deviation may occur with metabolic encephalopathies.
19. Naming is impaired in most aphasias.
20. Good repetition occurs with lesions outside the perisylvian region.
21. In a conduction aphasia repetition is normal.
22. Relative afferent pupillary defects occur with both retinal and optic nerve disease.

23. When disk margins are blurred, no hemorrhages are present and venous pulsations are seen the patient does not have papilledema.
24. Gerstmann's syndrome is manifested by finger agnosia, acalculia, agraphia, and right–left confusion.
25. Periodic alternating nystagmus occurs with lesions at the foramen magnum.
26. Inability to imitate a gesture is a sign of an ideomotor apraxia.
27. Adie's syndrome occurs with lesions of the optic nerve.
28. The Dix-Hallpike test is useful to diagnose any peripheral vestibular disorder.
29. Corticolingual fibers supply both sides of the tongue.
30. Severe motor restlessness of the legs is called akathisia.

Answers

1. T
2. F
3. F
4. T
5. T
6. F
7. T
8. F
9. F
10. T
11. F
12. T
13. T
14. T
15. T
16. F
17. F
18. T
19. T
20. T
21. F
22. F
23. T
24. T
25. T
26. T
27. F
28. F
29. T
30. T

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Chapter 5
Evaluation of the Poorly Responsive Patient

Evaluation of the poorly responsive patient requires an organized approach. One aim of this chapter is to meticulously outline an examination technique, delineate the anatomic basis for the observed abnormal neurologic signs, review pertinent neurophysiology, and lastly, discuss the differential diagnosis. The differential diagnosis is formulated after answering a primary question. Does this patient have a focal lesion, multifocal lesions, or global cerebral dysfunction? This seemingly simple problem is often a formidable one.

> The primary question when evaluating a poorly responsive patient is distinguishing between a focal lesion, multifocal lesions, or global cerebral dysfunction.

Common specific diagnostic problems of critically ill patients will be reviewed afterwards. These include the encephalopathies of metabolic and hypoxic-ischemic origin. Herniation syndromes due to focal lesions with mass effect are next. Lastly, the chronic disorders of consciousness and brain death will be discussed.

The definition of the levels of impaired consciousness has been a source of debate for many years. Employing specific terms is fraught with hazard since there are often differing views as to what term is most appropriate. The best approach is to simply outline what the patient is able to do spontaneously and to verbal, visual, and other sensory stimuli. Nevertheless, it is worthwhile to review the most succinct descriptions as outlined in "Diagnosis of Stupor and Coma" [1].

J. N. Alpert, *The Neurologic Diagnosis*,
https://doi.org/10.1007/978-3-319-95951-1_5

Clouding of Consciousness (Lethargy)

This state is manifested by reduced wakefulness and awareness. The patient is inattentive, distractible, and incompletely oriented. Nocturnal agitation is common.

Delirium

The typical patient is disoriented, frightened, irritable, and often delusional. Hallucinations are common and typically visual. The anatomic basis is bilateral cerebral dysfunction but, on rare occasions, there is right posterior cerebral hemisphere pathology. Sepsis, especially urosepsis, metabolic and toxic encephalopathies are the most common etiologies of delirium.

Defined alterations of consciousness include lethargy, delirium, obtundation, stupor and coma.

Obtundation

The obtunded patient is somnolent, shows little to no interest in the environment and displays bradyphrenia (slowed thinking) when roused.

Stupor

Only vigorous stimuli can arouse a stuporous patient. The stimulus must be maintained as a brief interruption results in a prompt return to an unresponsive state.

Coma

The comatose patient is unarousable with eyes closed. In light coma pain may produce facial grimacing, posturing or withdrawal responses. There is no localization of pain as demonstrated by the absence of defensive movements. In deep coma there is no response to pain.

Neurologic Examination

Inspection

The examination begins with a brief inspection of the patient lying in bed. What are the positions of the limbs, head and eyes? For example, eye deviation to the right may indicate a right cerebral, right subcortical, right midbrain or a left pontine lesion. Are there abnormal involuntary movements or postures? For example, nystagmus or nystagmoid jerks only to the right may indicate focal seizures emanating from the left cerebral cortex, especially the frontoparietal eye fields. A leg externally rotated may be a sign of a hemiparesis or a hip fracture. Other abnormal movements or postures to search for include myoclonus, seizures, tremor, dystonia, and dyskinesias.

Respiration (See Fig. 5.1)

What Is the Respiratory Pattern?

Inspection of the patient must include observation of the respiratory pattern.

Post hyperventilation apnea is induced by asking the patient to take five deep breaths. Patients with bilateral frontal lobe pathology may have a period of apnea that lasts more than 10 s. Apnea less than 10 s may be seen in normal individuals.

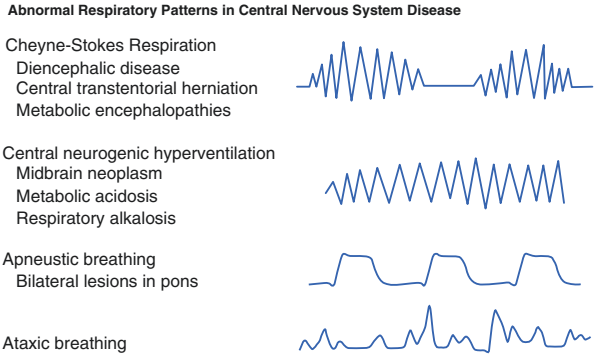

Fig. 5.1 Abnormal respiratory patterns in central nervous system disease or metabolic encephalopathies

Cheyne-Stokes respiration is hyperpnea followed by apnea in a crescendo-decrescendo fashion with apnea ranging from 10 to 20 s. It may occur with bilateral subcortical and diencephalic lesions and indicates preserved brainstem function. It is most common in the absence of neurologic disease in patients with severe congestive heart failure because of slowed velocity of aerated blood from the weak left ventricle to chemoreceptors in the carotid body.

Central neurogenic hyperventilation is a rare phenomenon that may occur with upper brainstem lesions, especially neoplasms. The neoplasm is believed to cause localized lactic acidosis which provokes a compensatory respiratory drive. Additionally, the diagnosis of pure central neurogenic hyperventilation requires an increased pO_2, decreased pCO_2 and an increased pH. This diagnosis implies the absence of more common causes of hyperventilation such as respiratory compensation for metabolic acidosis, neurogenic pulmonary edema, sepsis, hypoxia, hepatic failure, psychogenic hyperventilation, and toxic factors such as salicylate poisoning. Psychogenic hyperventilation disappears in sleep.

Apneustic breathing is apnea for 2–3 s at full inspiration. There may also be a similar, brief apneic event after full expiration. Apneustic breathing is rare and may occur with pontine lesions or very severe metabolic encephalopathies.

Ataxic breathing could be called agonal respirations because of the irregular pattern and gasping quality. It is ordinarily a preterminal event due to medullary damage and typically occurs with herniation of the cerebellar tonsils through the foramen magnum. Ondine's curse may result from bilateral lesions of the medulla involving chemosensory structures. The loss of automatic respiratory drive, yawning, hiccupping, and vomiting are associated features with lesions of the medulla.

Mental Status Examination

This examination can be performed whether or not the patient is intubated.

> Intubated patients must be evaluated for orientation.

1. Greet the patient. If the patient can be roused to speak, immediately check orientation to person, place, and date. Continue with the mental status examination to the patient's limit. An intubated patient should be requested to nod yes or no to these simple commands. To determine if the responses are accurate, he is given a few questions in succession such as, "Are you at home? Are you in the hospital? Are you in a drug store?" The patient is requested to nod yes or no to each option. The response to a question such as, "Do you know where you are?" has no reliable meaning, especially if the response is a nod yes.
2. If the patient does not speak, check for the ability to follow commands, one through four steps. A one-step or simple command is "close your eyes." A four-step

command would be, for example, "with your *right hand* touch your *left ear*." Each underlined word is a single step of identification. If right–left confusion is suspected, nonlateralizing commands should be employed such as, "Open your mouth, touch your ear, cross your legs and close your eyes." If the patient is deaf, large written commands on a blank sheet of paper may be required. If the patient cannot follow any commands, can he imitate gestures? This disparity may be present in patients with aphasia.

3. If the patient does not respond to verbal or visual stimuli, a painful stimulus should be given. There are four common types of pain stimuli, supraorbital pressure, nail-bed pressure, bilateral temporomandibular joint pressure, and sternal rub. Supraorbital pressure is efficacious, the least aggressive or violent and is therefore preferable. The sternal rub produced by grinding one's knuckles on the pectoralis major can be the most potent stimulus but it may be disturbing to onlookers and should be a last resort.

Supraorbital pressure is a preferred method of assessing the response to pain.

4. Reactions to pain in an otherwise unresponsive patient are often the most revealing elements of the examination. The aim is to elicit the presence of a focal lesion which obviously has a differential diagnosis that is distinct from nonfocal dysfunction, an encephalopathy.

The reaction to pain often elicits focal signs.

Some responses indicating a focal lesion include:

(a) Production of an asymmetric facial grimace.
(b) Production of asymmetric movements of extremities thus uncovering the presence of one or more paretic limbs.
(c) Attempting to remove a stimulus may unmask a paresis and/or demonstrate some awareness of self not previously appreciated.
(d) Decorticate posturing (see Fig. 5.2) is manifested by slow flexion of the arms and extension of the legs. The arms are adducted at the shoulders, flexed at the elbows, wrists, and fingers; the legs are extended, internally rotated, and plantar flexed. The lesions which produce decorticate posturing are subcortical, involve the diencephalon and may extend to the midbrain. Fragments of this response have the same diagnostic significance.

Decorticate posturing is flexion of the arms at the elbows and leg extension while decerebrate posturing is extension of all limbs.

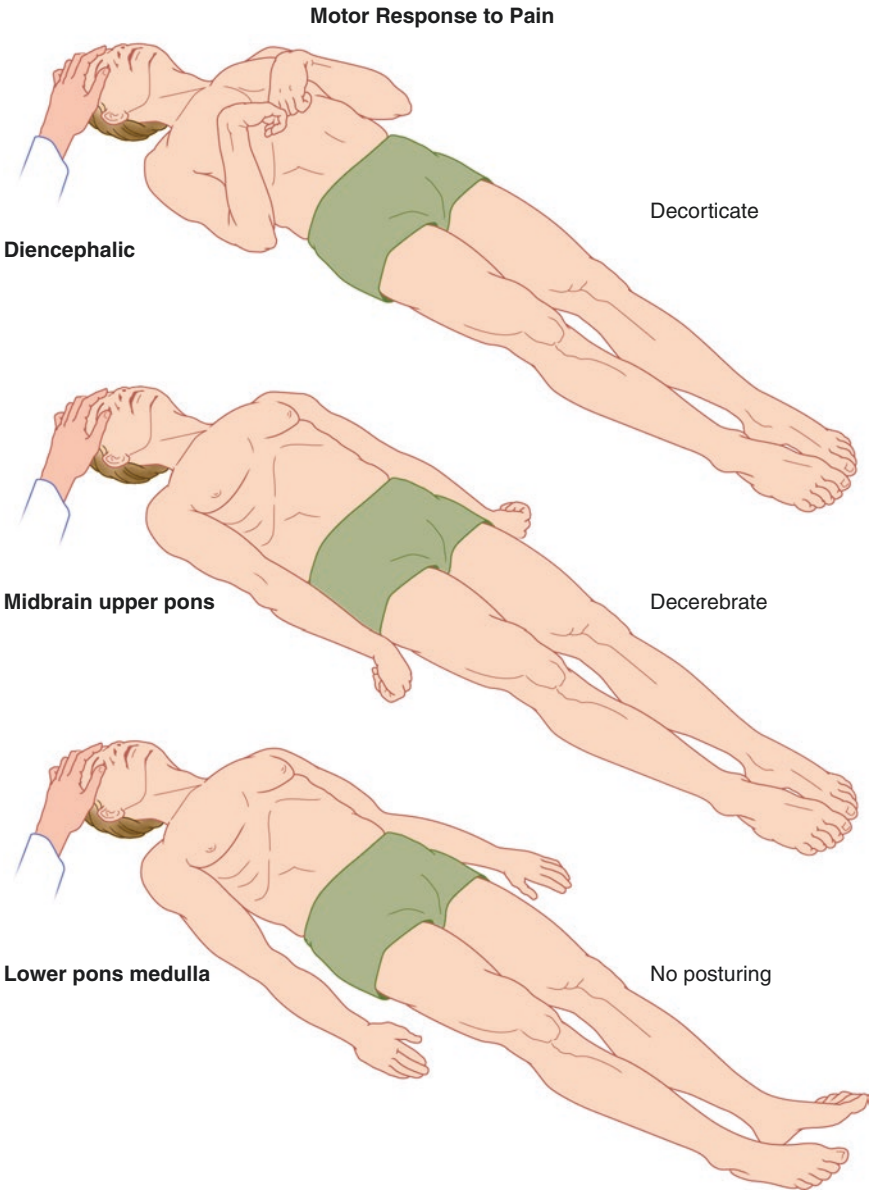

Fig. 5.2 Movement responses to painful stimuli (supraorbital pressure) at diencephalic, midbrain-upper pons and lower pons-medullary levels

(e) Decerebrate posturing (see Fig. 5.2) is characterized by extensor posturing of all extremities. Additionally, the arms are adducted and pronated. Although this posture is usually provoked by a stimulus, especially a painful one, it may occur spontaneously. Lesions which produce decerebrate posturing typically involve midbrain and upper pons, thus sparing the vestibulospinal tracts. The release of these vestibulospinal postural reflexes from forebrain control is the presumed mechanism of decerebrate posturing. Severe metabolic encephalopathy, especially hepatic, may also cause decerebrate posturing, an important point to remember.

Cranial Nerves

Funduscopic examination is mandatory even though the diagnostic yield is relatively small. Subhyaloid hemorrhages occur with subarachnoid hemorrhage (see Fig. 4.8). Bilateral blurred disk margins with adjacent flame and/or splinter hemorrhages indicate papilledema (see Fig. 4.4). Venous stasis retinopathy, dot and blot hemorrhages in the mid portion of the retina, occurs with common or internal carotid artery high grade stenoses or occlusions. The retinal stigmata of longstanding hypertension and diabetes may aid in making the diagnosis.

The visual field examination can be tried using double simultaneous stimulation of finger motion if the patient is arousable and can respond verbally or by pointing to the fingers that move. It must be remembered that vigorous motion may be perceived in a hemianopic field (Riddoch's phenomenon). Finger counting is often more reliable as patients whose speech is impaired can mimic the number of fingers flashed in the intact field. Quick exposure of different numbers of fingers in each field is the most sensitive approach. The use of visual threat by *slowly* bringing the finger into the patient's visual field from the periphery may elicit an attempted ipsilateral and/or contralateral eye blink. The eyelid on the side being examined may have to be held open gently. The presence of a blink only on one side indicates weakness of the orbicularis oculi on the side of the absent blink.

Visual fields can be assessed by using visual threat, double simultaneous stimulation of finger motion and rapid finger counting in some patients who are lethargic or obtunded.

Vestibuloocular reflexes are composed of the oculocephalic maneuver and caloric testing.

Vestibuloocular reflexes are composed of the oculocephalic maneuver and caloric testing. The oculocephalic maneuver involves moving the head quickly in one direction to determine whether the eyes move completely to the limbus in the contralateral direction. The normal alert patient does not display this reflex since normal random saccades will be interposed. A poorly responsive patient with an intact oculomotor system will move his eyes to the left when his head is quickly moved to the right and vice versa. This can also be assessed in the vertical plane as quickly moving the head upwards elicits down eye movements and vice versa. Thus, one purpose of the oculocephalic maneuver is to expose paretic eye movements due to pontine lesions involving the 6th nerve, medial longitudinal fasciculus (MLF), 3rd nerve or paramedian pontine reticular formation (PPRF) lesion in the horizontal plane and midbrain lesions involving the 3rd nerve, interstitial nucleus of Cajal, posterior commissure, and the rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF) lesion in the vertical plane. Bilateral lesions of the riMLF will eliminate both upward and downward saccades but only a lesion of the interstitial nucleus of Cajal is likely to eliminate the vertical oculocephalic response as it is a relay station for vestibular projections. Unmasking a 4th nerve lesion is difficult as it requires a vertical oculocephalic maneuver with the head turned sufficiently in one direction to maintain complete adduction whence down eye movements are strictly mediated by the superior oblique muscle. In deep coma no eye movements can be induced.

An important purpose of oculocephalic and caloric testing is the exposure of an eye movement paresis.

Caloric testing with 20–30 cc of ice water can be done at the bedside. Hot water irrigation requires careful temperature control and is therefore not practical. The head of the bed is elevated 30° to bring the horizontal canal into a vertical position for a maximum response. Secondly, the ears are checked for cerumen which should be removed if completely blocking the canal. The irrigation is done slowly and steadily, usually over 2–3 min, and can be halted when an obvious response is elicited. An emesis basin placed under the ear will catch the water draining out. The opposite ear should be examined after a 5-min delay to eliminate a residual response from the first irrigation. Both ears must be examined since, otherwise, a focal lesion affecting the lateral rectus and medial rectus muscles or a gaze paresis can otherwise be missed.

Utility of Caloric Testing

Caloric testing may be utilized to assess level of consciousness.

1. Assessing depth of unresponsiveness.

For the patient with an altered level of consciousness and without extraocular muscle paresis, there are four caloric responses to cold water irrigation that assess the degree of unresponsiveness. This can be done in serial fashion to measure either a decline or improvement in the neurologic status.

The first response is contralateral nystagmus which occurs in a normal alert person.

The second response is ipsilateral deviation with contralateral nystagmus. This response is common when the patient is lethargic or obtunded.

The third response is ipsilateral deviation only. This response occurs in a patient who is obtunded, stuporous, or in light coma.

The fourth response is no eye movement in a patient who is in deep coma.

2. Psychogenic unresponsiveness.

Caloric testing is an infallible method of checking for the depth of unresponsiveness, provided the patient has an intact peripheral vestibular apparatus. Thus it is used to diagnose malingering or a conversion reaction.

> Caloric testing is an infallible method of diagnosing psychogenic unresponsiveness assuming an intact peripheral vestibular apparatus.

3. Caloric testing can uncover a medial rectus paresis (3rd nerve or MLF lesion), gaze paresis (lesion of the oculomotor pathway, especially the PPRF), and lateral rectus paresis (6th nerve lesion).
4. Bilateral, simultaneous cold water irrigation produces downward eye deviation with upbeat nystagmus. The absence of upbeat nystagmus indicates a posterior commissure or bilateral pretectal lesion. The absence of down deviation supports the presence of pathology affecting the riMLF.

Spontaneous Eye Movements in a Poorly Responsive Patient

1. Aside from drug toxicity all forms of nystagmus suggest brainstem pathology, less often purely cerebellar lesions.

> In the unresponsive patient suspect seizure when horizontal, unidirectional jerk nystagmus is seen.

2. Horizontal, unidirectional jerk nystagmus is always a suspected manifestation of seizure. For example, a seizure focus in the left cerebral hemisphere may cause unidirectional right-beating nystagmus.

3. Specific types of abnormal eye movements.
   (a) Ocular bobbing. Rapid, conjugate, downward eye movement with a slow return to primary position at a rate of 3–6 per minute.
   (b) Reverse ocular bobbing. Rapid, conjugate upward eye movement with a slow return to primary position.
   (c) Ocular dipping. Slow downward and rapid up movement to primary position.
   (d) Reverse ocular dipping. Slow up and a rapid down movement to primary position.
   (e) Ping-pong gaze. Rapid alternating gaze deviation every few seconds.
   (f) Periodic alternating gaze deviation. Each deviation lasts approximately 2 min.
4. All of the above specific eye movement abnormalities may be due to metabolic, toxic, hypoxic, or ischemic encephalopathies. Ocular bobbing, however, is a characteristic finding after pontine strokes. Periodic alternating gaze deviation is relatively common in the vegetative state (to be discussed).

Eye Deviations [2]

Conjugate eye deviations have both anatomic and etiologic corollaries. For example, conjugate eye deviation to the left indicates a lesion above the oculomotor decussation (pontomesencephalic junction) on the left or below it on the right (PPRF). Conjugate downward eye deviation has been reported with thalamic hemorrhage, thus implicating compression of the posterior commissure; but most often it is secondary to metabolic or hypoxic-ischemic encephalopathy. Conjugate upward deviation is almost invariably due to hypoxic-ischemic encephalopathy.

Skew deviation is a vertical misalignment of the eyes due to a supranuclear lesion disrupting otolith (utricle, saccule) to oculomotor nuclei pathways (see Fig. 4.11). These pathways include the 8th nerve, vestibular nuclei, medial longitudinal fasciculus (MLF) and the fibers decussating in the pons. They ascend to the contralateral interstitial nucleus of Cajal (INC) and oculomotor neurons mediating vertical gaze. Eighth nerve lesions causing skew deviation are extremely rare. Hence, skew deviation is for practical purposes diagnostic of brainstem/cerebellar system pathology. The hypotropic (lower) eye is usually ipsilateral to a pontomedullary lesion which may include the MLF. Since the fibers decussate, midbrain lesions may cause contralateral hypotropia. Diplopia often occurs which violates the rule that supranuclear lesions do not cause double vision.

The ocular tilt reaction includes skew deviation, head tilt and ocular cyclotorsion. When the head is tilted left the right eye is hypertropic (higher) and both eyes rotate to the lower ear. The opposite occurs with head tilt right. This is usually a tonic reaction but can be paroxysmal thus causing a torsional nystagmus.

There are forms of simulated skew deviations which include the “double elevator palsy” and 4th nerve lesions. The former occurs with supranuclear pretectal lesions which interrupt efferent pathways from the riMLF to superior rectus and inferior

oblique subnuclei. (Fig. 5.3) Fourth nerve lesions, however, follow a three-step pattern of ipsilateral hypertropia, increased displacement on contralateral gaze and a positive Bielschowsky test. (Fig. 4.10)

Skew deviation, a vertical misalignment of the eyes, is caused by supranuclear lesions disrupting otolith-ocular pathways.

Pupils

Pupils are discussed in detail in the chapter on the autonomic nervous system. Pupillary size, shape, and reactivity are assessed. Significant asymmetry in light is greater than 0.5 mm. Parasympathetic or sympathetic nervous system pathology should explain the asymmetry in the absence of confounding ocular pathology such as prior surgery, ocular trauma, or diseases of the iris. It should be remembered that unilateral, optic nerve lesions are associated with equal pupils of normal size but asymmetric reactivity.

In the absence of local eye pathology pupillary asymmetry greater than 0.5 mm indicates impaired sympathetic or parasympathetic function. Exceptions are infrequent.

In the unresponsive patient, the following findings have anatomic and/or etiologic significance.
Diencephalic lesions and metabolic encephalopathy: 2–3 mm reactive pupils.
Midbrain lesions: 4–5 mm irregular nonreactive pupils.
Pretectal lesions: 5–6 mm round nonreactive pupils.
Pontine lesions – pinpoint, reactive pupils.
Medullary lesions – Horner's syndrome.

Corneal Reflexes

The corneal reflex tests the trigeminal-facial-oculomotor reflex connections. A unilateral corneal stimulus using a wisp of cotton to touch the cornea (over the iris) causes a bilateral blink response and elevation of the eyes (Bell's phenomenon). Thus, when the left cornea is touched, an absent or slow blink on the right with intact left blink indicates right orbicularis oculi weakness or a right seventh nerve, right seventh nucleus, or left supranuclear pathway lesion. An absent or slow ipsilateral response has the same meaning with opposite lateralization. Unilateral absence of Bell's phenomenon, upward deviation of the eye when it closes, usually

indicates a superior rectus paresis and possible third nerve lesion. Bilateral absence of Bell's phenomenon is not necessarily pathologic since it occurs in some normal individuals.

The corneal reflex requires touching the cornea, which is located over the iris, with a wisp of cotton.

The corneomandibular reflex is manifested by contralateral jaw deviation and bilateral eye blink. It usually indicates a structural lesion rather than metabolic dysfunction. It may occur with upper brainstem lesions. Conversely, the corneomental reflex, an ipsilateral twitch of the mentalis muscle when the cornea is touched, is a common finding both in degenerative diseases of the nervous system and, less often, in the normal elderly population.

Eyelids

The eyes are closed in a comatose patient. Incomplete closure of one eye indicates orbicularis oculi weakness and possibly a facial paresis. Unilateral orbicularis oculi weakness can be demonstrated via the corneal reflex and sometimes a weak or slow response (asymmetric) to visual threat. The examiner has to gently open both eyes to check for that response. The blink response to a sound stimulus may be asymmetric thus unmasking a weak orbicularis oculi on one side.

The eyes are closed in coma and open in a vegetative state.

Patients in a vegetative state, which develops after at least 2 weeks in coma, have normal sleep–wake cycles which result in an eyes open unresponsive state during the awake period. Ptosis may be observed in which case there may be levator palpebrae superioris (third nerve lesion) or Müller's muscle weakness (Horner's syndrome).

Palate

An absent gag response is a necessary finding in suspected brain death assuming the patient is not intubated. Unilateral loss indicates a focal lesion of the ipsilateral 9th and/or 10th cranial nerves or ipsilateral nucleus ambiguus in the medulla.

Motor Function

Are there asymmetric spontaneous movements which indicate focal disease? Is there decorticate or decerebrate posturing which is spontaneous or provoked by a painful stimulus? Multifocal myoclonus is common in metabolic, toxic, septic, or hypoxic-ischemic encephalopathies. Jerking of one limb or both arm and leg on one side should be presumed to be seizure activity.

> The patient must be constantly observed for asymmetric movements and abnormal posturing.

Paratonic rigidity (Gegenhalten) is a nonspecific, frequent abnormality of muscular tone found in patients with metabolic encephalopathy. It is manifested by an active resistance to passive movements and often misinterpreted as oppositional or noncooperative behavior. Spasticity is best elicited in the arms by quick pronation and supination movements of the forearms. With one or both hands under the popliteal fossa and with the patient supine, a sudden high amplitude jerk upward may elicit a "hang up," a slow fall of the leg indicating a spastic catch. Spasticity indicates pathology affecting the corticospinal tract. If both legs are held up under the popliteal fossa and suddenly released, a more rapid unilateral fall can signify focal weakness of that leg and thus, in the absence of peripheral pathology, structural disease probably involving the corticospinal tract. Consequently, metabolic encephalopathy cannot be the sole cause of the altered mental status. Similarly, holding both arms up at the same level and suddenly removing support may disclose focal weakness on the side which falls more quickly.

> Paratonic rigidity (Gegenhalten) is especially common in patients with metabolic encephalopathies.

Reflexes

Detecting reflex asymmetry between the left and right side is essential. In the patient with cerebral or brainstem disease the hyperactive reflexes are abnormal and contralateral to the lesion. Symmetrical brisk or absent reflexes are seldom significant in unresponsive patients. Sustained clonus, unilateral Hoffmann's sign and unilateral or bilateral Babinski signs are always abnormal and indicate a lesion involving the corticospinal tract. The presence of these abnormalities is not compatible with a purely metabolic encephalopathy.

> The reflex exam focuses on discovering asymmetric and abnormal reflexes, useful in distinguishing metabolic-toxic disorders from structural disease.

Sensory

A patient, whether or not intubated and who can be roused, may cooperate with vibration, position, and pinprick testing. In an intubated patient these modalities can be examined provided the patient is sufficiently alert. The patient may gesture yes or no by head shake as well as raising or lowering his finger in response to movement of his digits by the examiner. The obtunded or stuporous patient is tested by noting the facial grimace or limb withdrawal after pinprick stimulation of each limb. If unilateral hypesthesia is suspected, repeated checking with pinpricks on the trunk beginning on the presumed abnormal side and moving horizontally across the abdomen or chest may elicit a response such as a facial grimace or an attempt to remove the stimulus as it approaches but not yet reached the midline. This is due to nerve fibers which overlap the midline.

If the patient is arousable a complete sensory examination can be performed.

Meningeal Signs

Is the patient's neck sufficiently supple to bring the chin to rest on the chest? Nuchal rigidity may be obvious or detectable only at the termination of head flexion, so-called end nuchal rigidity. Testing for Brudzinski and Kernig signs may be necessary. If the patient's head cannot be moved in any direction, one must consider local pathology affecting bone, tendon, or muscle.

Metabolic and Hypoxic-Ischemic Encephalopathies

Metabolic Encephalopathy

Metabolic encephalopathy is the most common cause of altered mental status among hospitalized patients. It is relatively simple to discover the etiology in most instances. Occasionally, abnormal neurologic signs are misinterpreted as indicating a primary neurologic process and, conversely, a neurologic disease may be dismissed as an expected metabolic alteration. Therefore, an analysis of the signs and symptoms of these disorders is worth reviewing.

The cardinal manifestations of central nervous system complications of metabolic derangements can be separated into four categories. These are alterations of the mental status, abnormal respiratory patterns, characteristic oculomotor and pupillary findings, and typical motor phenomena.

Delirium is usually the first manifestation of an overt metabolic encephalopathy. The one exception is the rare occurrence of delirium associated with acute non-

dominant hemisphere lesions. The recognition that delirium has occurred is thus very useful when questions arise about the differential diagnosis, particularly if a primary neurologic etiology is suspected.

Delirium is usually the first manifestation of an overt metabolic encephalopathy.

Delirium is characterized by an altered level of consciousness, acute onset with fluctuating course, impaired attention, and disorganized thinking. There are delusions and primarily visual, not auditory hallucinations. Abnormalities of the sleep–wake cycle are almost invariably present. Confusion and hyperactivity ("sundowning") often occur at night.

The major alterations of the mental status are disorders of arousal. These can be divided into a hypervigilant and hypovigilant state. The hypervigilant state is distinguished by distractibility and accompanied by purposeless motor activity known as punding. An example would be fiddling with or manipulating the bedcovers. With requests to name the months of the year the patient may begin accurately, then stop suddenly to discuss another topic. Perseveration of responses is common.

The hypovigilant patient requires constant sensory stimulation to obtain responses. Otherwise, the patient is immobile, apathetic, and withdrawn. Thus there are features which may even suggest akinetic mutism, a condition of an alert-appearing (awake but unaware) motionless patient who can visually track a moving target. Patients who have metabolic encephalopathy often fluctuate between hypovigilant and hypervigilant states.

It is important to differentiate dementia from a metabolic encephalopathy. The former is marked by impaired cognition first; much later there is a change in alertness. The conspicuous elements of a metabolic encephalopathy are early changes in alertness and impaired attention. Disorientation and loss of short-term recall occur in both states.

Dementia begins with impaired cognition. The early signs of metabolic encephalopathy are impaired alertness and attention.

Another important clinical problem is the differentiation of encephalopathies from psychogenic disorders. Disorientation to self is nearly always psychogenic in origin and quite often there is no simultaneous disorder of alertness and no prior sign of abnormal cognition. If the patient is not fully responsive but when aroused is disoriented to self, caloric testing can be utilized to accurately ascertain the level of consciousness. An electroencephalogram (EEG) is less reliable since normal appearing records may occur in patients who are in coma.

Disorientation to self is nearly always psychogenic in origin.

Other features of encephalopathy include inappropriate behavior, paranoid ideation, and perceptual disorders. The latter are manifested by both illusions (distortion of a sensory perception) and visual hallucinations. Visual hallucinations can be combined with auditory hallucinations but auditory hallucinations alone do not occur with encephalopathies. Errors when spelling words backwards and doing serial subtractions are common but may be due to a primary problem of attention rather than a true cognitive disorder.

Visual but not auditory hallucinations are common in patients with metabolic encephalopathy.

Respiratory Disorders

Abnormalities of respiratory rates are a nearly invariable development in metabolic encephalopathies. Cheyne-Stokes respirations are characteristic and presumably due to impairment of frontal lobe function on respiratory drive assuming that congestive heart failure is not present.

Cheyne-Stokes respirations are common in patients with metabolic encephalopathies.

A determination of respiratory function at the bedside usually focuses on the respiratory rate. Consequently, a review of disorders of respiration will focus on the respiratory rate and the etiology of both hyperventilation and hypoventilation. This will be a brief summary which emphasizes the most common and important etiologies.

Hyperventilation may be due to neurologic disease or a respiratory attempt to compensate for metabolic acidosis. Structural pathology must be excluded. Some examples follow.

1. Hyperventilation causing respiratory alkalosis due to primary increased drive includes: psychogenic hyperventilation, hepatic encephalopathy, sepsis, hypoxia, pulmonary disease, neurogenic pulmonary edema, central neurogenic hyperventilation, and drug toxicities – especially salicylates. Psychogenic hyperventilation is easily diagnosed as it disappears in sleep.
2. Hyperventilation as a respiratory compensation for metabolic acidosis includes: uremia, diabetic ketoacidosis (Kussmaul breathing), treatment with metformin, lactic acidosis (especially due to hypoxia), diarrhea, and drug toxicity (especially salicylates).

Hypoventilation may be due to neurologic disease or a respiratory attempt to compensate for metabolic alkalosis. Structural pathology must be excluded. Some examples follow.

1. Hypoventilation causing respiratory acidosis due to a decreased respiratory drive includes: central nervous system disease due to head trauma, sedatives, stroke, and infection.

Restriction of chest expansion by structural abnormalities or weak muscles may cause respiratory acidosis. Some examples are severe kyphoscoliosis, chest injury, myasthenia gravis, and Guillain–Barré syndrome. Intrinsic lung disease such as chronic obstructive pulmonary disease should be considered.

2. Hypoventilation as a respiratory compensation for metabolic alkalosis includes: vomiting, gastric drainage, acute and chronic pulmonary disease, volume contraction, diuretic therapy, potassium deficiency associated with acid shift into the cell, Cushing's syndrome, and primary aldosteronism.

Eye Signs

Pupils

Patients with metabolic encephalopathy have pupils which are usually 2–3 mm, equal and normally reactive to light. A significant size asymmetry (>0.5 mm) or abnormal reactivity indicates the presence of focal disease and thus metabolic factors may not be the sole or primary etiology. Nonreactive pupils are due to neurologic diseases or caused by anticholinergic drugs, prior eye surgery, ocular trauma or eye diseases that affect the pupil. These latter conditions should be excluded after review of the history.

Patients with metabolic encephalopathy have pupils which are usually 2–3 mm, equal and normally reactive to light.

Eye movements [2]

Downward and rarely upward eye deviation may occur with metabolic, ischemic, and hypoxic encephalopathies. Lateral eye deviation does not; it nearly always indicates a structural focal central nervous system disease process. If the eyes are deviated to the right there is a lesion in the oculomotor pathway on the right side above the oculomotor decussation which is at the pontomesencephalic junction or below it, near or in the left PPRF. Skew deviation, which is a vertical separation of the globes due to a supranuclear lesion disrupting pathways between the otolith organs and ocular motor nuclei, and dysconjugate eye movements also establish the presence of structural pathology. Nystagmus, vertical or horizontal, indicates drug toxicity or structural disease most often affecting the brainstem and less likely the cerebellum. Rotatory nystagmus (torsional) indicates a brainstem lesion probably affecting vestibular nuclei.

Vestibuloocular examinations in the poorly responsive patient are composed of the oculocephalic maneuver and caloric testing. The oculocephalic reflex generates conjugate horizontal or vertical eye movements with brisk horizontal or vertical movements of the head, respectively. Failure of either oculocephalic or caloric testing to elicit eye movements in one direction is an indication of a focal lesion which is either superimposed on a metabolic encephalopathy or alone explains the patient's altered mental status. In the latter case there is likely to be brainstem pathology that elucidates the patient's clinical picture. Midbrain pathology affecting the mesencephalic reticular formation is likely. Caloric testing is a stronger stimulus which produces a more varied and reliable response. The details have been previously discussed in the section "Utility of Caloric Testing."

Vertical eye deviations may occur with metabolic/hypoxic-ischemic disease or focal brainstem-thalamic lesions.

Horizontal gaze deviation always indicates a focal lesion.

Abnormalities of Motor Function

Multifocal myoclonus, generalized and focal motor seizures may occur with metabolic encephalopathies. The focal seizures usually shift locations and may shift sides. Multifocal myoclonus is common and manifested by migrating twitching of muscle groups in random fashion. It is particularly prominent in facial musculature. This occurs in severe encephalopathy and typically is not recorded on electroencephalographic tracings.

Multifocal myoclonus, generalized and focal motor seizures may occur with metabolic encephalopathies.

Tremor of the hands is a frequent accompaniment. It is of moderate to high amplitude, asynchronous, postural, and action in type. The rate is about 8–10 Hz. It may also involve the tongue, face, and legs. It is distressing to the patient as it usually interferes with purposeful activity.

Asterixis is elicited in an awake or lethargic patient by extending the arms with the palms face down and hands and fingers dorsiflexed by the patient. This is a position as if one is pushing against a wall. A quick bilateral flapping, asynchronous downward movement occurs, usually fingers first and commonly with a latency of a few to several seconds. It will be repeated continuously as long as the position is maintained. The flap frequency is variable. Dorsiflexing the feet with the legs extended may elicit the same response. The etiology was once thought to be specific

for hepatic encephalopathy but is now known to occur in practically all metabolic derangements and is perhaps most common with hypercapnia.

Asterixis may occur with any metabolic encephalopathy.

Paratonic rigidity is a hallmark finding. Its features are active resistance by the patient in response to the examiner's attempt to move his arm usually at the elbow. This occurs despite the examiner's admonition to "relax" or "don't resist." A quick movement of the patient's arm is most likely to elicit this resistance.

Decerebrate rigidity and rarely decorticate rigidity may occur with severe metabolic encephalopathies. There may be severe sudden extensor spasms, especially of the legs. These postures quite naturally raise fears of an unexpected mass lesion causing central herniation. The presence of normally reactive, symmetrical pupils should ameliorate these fears. Any severe metabolic disorder may cause spontaneous decerebrate posturing.

Decerebrate rigidity may occur with severe metabolic encephalopathies.

The emergency workup for an unresponsive patient with a suspected metabolic encephalopathy includes: complete blood count, electrolytes, glucose, BUN, creatinine, PT/INR, PTT, liver functions, calcium, phosphorus, arterial blood gases, TSH, blood cultures, drug screen, urinalysis and urine culture. A stat noncontrast CT scan follows. In the absence of a diagnostic finding, a lumbar puncture is done with fluid sent for cell count, protein, glucose, Gram stain, fungal smear, India ink prep, cryptococcal antigen, VDRL, routine and fungal cultures. Polymerase chain reaction studies may be considered. An extra sample should be obtained and saved for possible additional testing. Finally, an electroencephalogram (EEG) may be necessary to exclude nonconvulsive status epilepticus and to grade the severity of the encephalopathy.

Differential Diagnosis of Metabolic Disorders

In order to avoid overlooking an important immediate etiology, it may be useful to think anatomically. Once a metabolic encephalopathy is diagnosed, the disease process causing the metabolic abnormality must be identified and treated.

1. Neck
   (a) Hypothyroidism or hyperthyroidism.
   (b) Parathyroid disease. Hypercalcemia and hypocalcemia.

2. Chest
   (a) Pulmonary disease. Hypoxia and hypercapnia.
   (b) Cardiac disease. Severe congestive heart failure with low cardiac output.
3. Abdomen
   (a) Liver – hepatic encephalopathy.
   (b) Pancreas – hyperglycemia, hypoglycemia, pancreatic failure.
   (c) Adrenal – Addison's disease, Cushing's disease.
   (d) Kidney – renal failure.
4. Electrolyte and pH disorders
   (a) Hyponatremia, hypernatremia.
   (b) Metabolic acidosis, metabolic alkalosis, respiratory acidosis, respiratory alkalosis.

Specific Diseases Which Mimic the Confusion of Metabolic Encephalopathy

Most of these disorders are uncommon, with the exception of pure fluent aphasias, as the only manifestation of an acute illness. All require prompt diagnosis and therapy but several (1–5) demand immediate diagnosis and urgent treatment.

These include:

1. Fluent aphasias, especially Wernicke's and transcortical sensory, due to acute middle cerebral artery (MCA) distribution stroke.
2. Complex partial status epilepticus (nonconvulsive status epilepticus).
3. Wernicke's encephalopathy.
4. Herpes simplex encephalitis.
5. Bacterial and fungal meningitis.
6. Other infectious diseases.
   (a) Viral meningitis and encephalitis.
   (b) Other opportunistic infections.
   (c) Human immunodeficiency virus (HIV) encephalopathy.
   (d) Malaria. Plasmodium falciparum may present as cerebral malaria.
7. Vascular diseases
   (a) Multiple cerebral infarctions of any etiology. For example, multiple cerebral embolism, large and small vessel disease, systemic vasculitis, isolated granulomatous angiitis of the central nervous system, infectious vasculitis and Behcet's disease.
   (b) Antiphospholipid antibody syndrome.
   (c) Disseminated intravascular coagulation (DIC).
   (d) Thrombotic thrombocytopenic purpura (TTP).

(e) Nonbacterial thrombotic endocarditis (marantic endocarditis).
(f) Cerebral autosomal dominant arteriopathy with subcortical infarctions and leukoencephalopathy (CADASIL).
(g) Posterior reversible encephalopathy syndrome (PRES).
(h) Reversible cerebral vasoconstriction syndrome (Call-Fleming syndrome).

8. Drug intoxication.
9. Acute encephalopathy of systemic lupus erythematosus (SLE).
10. Hashimoto's encephalitis.
11. Progressive multifocal leukoencephalopathy.
12. Prolonged postictal state following an unwitnessed generalized seizure.
13. Migraine with brainstem aura.
14. Acute demyelinating encephalomyelitis (ADEM).
15. MELAS (mitochondrial encephalopathy with lactic acidosis and stroke-like episodes).
16. Prion diseases (rare) are unlikely to present for the first time with an encephalopathy. These include Creutzfeldt-Jakob disease (CJD), both variant CJD (vCJD) and sporadic CJD (sCJD). Gerstmann-Straüssler-Scheinker syndrome nearly always begins with dementia.

Fluent aphasias, complex partial status epilepticus and Wernicke's encephalopathy require an immediate diagnosis. Acute fluent aphasias customarily occur with an MCA distribution stroke, ischemic or hemorrhagic. An acute ischemic origin may not be readily diagnosed by CT imaging; thus, it mandates careful attention to language function, especially the presence of paraphasias. Herpes simplex encephalitis may also present in this fashion since unilateral temporal lobe involvement is characteristic. Complex partial status epilepticus (nonconvulsive status epilepticus) requires an urgent EEG often forgotten in this era of sophisticated neuroimaging. Furthermore, an EEG may reveal features diagnostic of herpes simplex encephalitis. Wernicke's encephalopathy is manifested by the triad of an altered sensorium, eye signs such as ocular pareses and nystagmus, and limb or gait ataxia. Cerebrospinal fluid evaluation is essential to exclude bacterial or fungal meningitis. All of these diagnoses necessitate immediate recognition and treatment.

Hashimoto's encephalitis is rare but is usually preceded by thyroid dysfunction, especially hypothyroidism. There are elevated antithyroglobulin and antithyroperoxidase antibodies. Encephalitis must always be considered when an overt metabolic etiology is not apparent. Fever and signs of meningeal disease are often absent. Therefore, as noted above, a lumbar puncture is mandatory.

Creutzfeldt–Jakob disease (CJD) usually manifests other signs such as seizures, myoclonus, extrapyramidal findings and prior dementia. Cerebrospinal fluid may be sent for 14-3-3 protein which is frequently present but not pathognomonic for this disease. Urine studies have detected prion protein in both variant CJD, such as mad cow disease, and sporadic CJD. These urine studies are not yet available for general use. [4]. Most recently nasal brushings have detected misfolded prion proteins with nearly 100% specificity and 97% sensitivity for sporadic CJD [5]. An EEG commonly exhibits diagnostic features. Progressive multifocal leukoencephalopathy

caused by the JC virus occurs in the immunosuppressed patient and ordinarily presents with multifocal signs; but initially the diagnosis is often obscure. Opportunistic infections, primarily fungal disease, must always be suspected in patients on long-term steroid treatment or those who are immunosuppressed for various reasons. HIV encephalopathy is well-described but a rare initial neurologic presentation.

The vascular diseases listed above are essential to recognize. Multiple small infarctions of any etiology can cause an encephalopathy. A few specific ones include the antiphospholipid antibody syndrome which may lead to arterial thromboses and less often venous sinus thromboses. TTP, which may be a complication of clopidogrel treatment, causes microvascular thrombi. Associated features include hemolytic anemia and renal failure. DIC should be suspected in patients with sepsis and malignancies. Nonbacterial thrombotic endocarditis is associated with platelet fibrin vegetations in patients with underlying adenocarcinomas and hematologic malignancies. Multiple systemic emboli are common but neurologic manifestations predominate. CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarctions and leukoencephalopathy) is usually associated with a longstanding history of stroke but in rare instances can present as an acute encephalopathy usually preceded by a severe headache, migraine with aura. A positive family history is usually available. Reversible cerebral vasoconstriction syndrome (Call-Fleming syndrome) typically presents with thunderclap headache usually reaching a peak intensity at 1 min and ordinarily lasting less than 3 min. Nausea, vomiting, photophobia and phonophobia are frequent and triggering factors include physical exertion, sexual activity, stress, coughing and other similar provocations. Agitation, confusion, hypertension, carotid dissections and diffuse segmental narrowing and beading on angiography will confirm the diagnosis. There is complete reversibility of the vasoconstriction [6].

Other unusual considerations include migraine with brainstem aura manifested by a transient confusional state, stupor and even coma but with complete rapid (less than 1 h) remission. Only a careful, meticulous history will uncover this diagnosis. A postictal state following an unwitnessed generalized seizure must always be considered. ADEM nearly always presents with additional focal abnormalities. MELAS begins in childhood with encephalopathy and myopathy, headache, seizures and stroke-like episodes. This is due to a mutation in genes of mitochondrial DNA; thus there is maternal inheritance.

Case Reports

Case 1 A 46-year-old man is admitted to the hospital because of rapid development of dementia progressing over 2 weeks. On the night of admission he has a tonic-clonic seizure and 1 h later went into generalized status epilepticus. Treatment with lorazepam is followed by a loading dose of fosphenytoin with achievement of a therapeutic level at 1 h. The seizures cease and then recur 5 h later. Subsequently, over the ensuing 2 days he averages one generalized tonic-clonic seizure every 1–3 h. Levetiracetam is added without benefit.

Past medical history is remarkable only for hypercholesterolemia. His only medicine is atorvastatin.

Medical examination on admission reveals a blood pressure of 120/70 and pulse 58, regular. He is pale and has mild peripheral edema. The interictal examination reveals a patient who can be roused by painful stimuli only for several seconds. He neither answers questions nor follows simple commands. Pain stimulus using supraorbital pressure elicits symmetrical facial movements. The pupils are 3 mm equal and have a 3+/4 reaction to light. Caloric testing elicits ipsilateral eye deviation without nystagmus or an element of eye movement paresis. The oculocephalic maneuver yields full horizontal and vertical eye movements. He withdraws all extremities to pain. Reflexes are 1+ and symmetrical except for absent ankle jerks. Plantars are flexor.

A CT scan of the brain is normal and cerebrospinal fluid studies disclose 23 white blood cells of which 60% are neutrophils. A CBC shows a hemoglobin of 9 gm. with an MCV of 101 fL, white blood cell count of 13,200 with 81% neutrophils. Oxygen saturation is 96% on room air. Liver functions, BUN, creatinine, electrolytes, calcium and phosphorus are normal.

Questions:

1. How can the mental status exam be classified?
2. How can the increased white blood cell count with left shift plus the CSF pleocytosis be explained?
3. What test not ordered is diagnostic and based on the refractory seizures?
4. What medical finding is common?
5. What part of the history supports the diagnosis?
6. What neurologic abnormality is discovered on the basis of the diagnosis?

Case 1 Analysis:

1. Stupor.
2. Both are common with a recent seizure, especially status epilepticus.
3. The TSH is 80. Macrocytic or microcytic anemia and seizures refractory to treatment may occur in myxedema.
4. Peripheral edema.
5. Hypercholesterolemia.
6. Reflexes show a slow relaxing phase most noticeable at brachioradialis. Ordinarily this abnormality is discovered at the ankles.

Diagnosis: Myxedema with encephalopathy, tonic-clonic seizures, macrocytic anemia and hypercholesterolemia.

Case 2 A 55-year-old man becomes lethargic the morning following an anterior cervical fusion performed for a herniated disk at C6-C7. An urgent neurologic consultation is requested. The patient cannot give a lucid history when roused.

His past medical history is remarkable for hypertension and Type II diabetes. Medications are atenolol and metformin. The patient's wife reports that he is a nonsmoker and has two gin and tonics with dinner every night.

Neurologic examination reveals a blood pressure of 140/100 and a regular pulse of 64. Oxygen saturation is 92% and respiratory rate is 30/min. Temperature is 98.6F. The patient can be roused with supraorbital pressure which elicits a symmetrical facial grimace. Then he is oriented to person, city and state but not month or year. He follows only one- or two-step commands. He responds to visual threat in both fields, has 2 mm pupils with 3+/4 reaction to light. The oculocephalic maneuver produces eye movements in all planes. Caloric testing elicits ipsilateral deviation with minimal contralateral nystagmus and no ocular paresis. Corneal reflexes are intact. He moves all extremities spontaneously, has a rapid postural and action tremor which also involves the tongue. He has frequent myoclonic jerks and paratonic rigidity. Asterixis is prominent. Reflexes are 3+, symmetrical and plantar responses are flexor. He responds to pinprick in all extremities by withdrawal.

Laboratory data CBC, liver functions, electrolytes, BUN, creatinine, calcium, TSH and glucose are normal. O_2 saturation is 92% on room air.

Questions:

1. What is the primary diagnosis? What are the main neurologic signs that support the diagnosis?
2. What additional lab work is required?
3. What is the most likely diagnosis?
4. What is the mechanism?

Case 2 Analysis:

1. Metabolic encephalopathy. Altered mental status, myoclonus, asterixis, paratonic rigidity, and changes in respiratory pattern.
2. Laboratory studies show a normal arterial ammonia of 40 μgN/dL and an elevated PCO_2 of 60 mmHg.
3. Hypercapnic encephalopathy.
4. CT (neck) reveals a hematoma compressing the trachea causing CO_2 retention. Remember that asterixis is a nondiagnostic sign.

Diagnosis: Hypercapnic encephalopathy due to tracheal compression by a hematoma.

Case 3 A 25-year-old woman is brought into the Emergency Room because of a sudden fall followed by unresponsiveness. She has no illnesses and her only medication is a birth control pill.

Neurologic examination: Blood pressure 140/106, pulse 64 and regular, respiratory rate 20. Temperature is 99.2F. She responds to pain only (nailbed pressure) with a symmetrical facial grimace. There is no response to visual threat. Oculocephalic responses are absent. Pupils are 2 mm, equal and with a 3+/4 reaction to light. Corneal reflexes are absent. She has no spontaneous movement and exhibits slight withdrawal of all extremities to pain. Reflexes are 3+, symmetrical and plantars are flexor on the right and neutral on the left (no movement).

Laboratory Data: CBC, liver functions, electrolytes, BUN, creatinine, glucose, calcium, arterial blood gases and TSH are normal. CT scan (brain) is normal.

Questions:

1. What critical bedside test has been omitted?
2. What could it show?
3. Where is the lesion?
4. What is the suspected etiology? Are there any predisposing factors?

Case 3 Analysis:

1. Caloric examination. This is a stronger stimulus than oculocephalics.
2. Ice water A.D. with head elevated 30° elicits no movement.

   Ice water A.S. with head elevated 30° elicits O.S. to left and no movement O.D.

   This is the 1–1/2 syndrome due to ischemia affecting right PPRF and right MLF. Other findings which could be uncovered by caloric testing include skew deviation, gaze palsy, and perverted nystagmus (vertical rather than horizontal).

3. Right paramedian pons.
4. Basilar artery thrombosis documented by urgent angiography. Treatment is given with tissue plasminogen activator (TPA). Birth control pills containing estrogen may be a risk factor.

Diagnosis: Pontine ischemia due to basilar artery thrombosis.

Hypoxic-Ischemic Encephalopathy

Although the most common cause of hypoxic-ischemic encephalopathy is cardiac arrest, there are numerous instances when oxygenation is maintained but hypotension produces severe cerebral ischemia. Conversely, cardiac function and blood pressure may remain normal, yet hypoxia is severe. It is important, therefore, to be precise in these definitions. Ischemic encephalopathy is often more devastating than hypoxic encephalopathy. One need only look at intrepid mountain climbers who summit Himalayan peaks and function well despite pO_2's in the 30 mmHg range.

> Ischemic encephalopathy is often more devastating than hypoxic encephalopathy.

The sequelae of ischemic and hypoxic-ischemic encephalopathy are watershed infarctions. These are located in the border zones between the middle cerebral artery (MCA) and anterior cerebral artery (ACA), MCA and posterior cerebral artery (PCA), and the border zone between the deep and superficial branches of the MCA.

> The sequelae of ischemic and hypoxic-ischemic encephalopathy are watershed infarctions.

Clinical correlates of anterior infarctions (ACA-MCA) include crural paresis (leg greater than arm) and myoclonic jerks of leg or arm. Dominant hemisphere lesions result in transient mutism, dysnomia, and especially, transcortical motor aphasia (decreased output, good comprehension and good repetition). Nondominant hemisphere lesions can be manifested by apathy and abulia.

Clinical correlates of posterior infarctions (MCA-PCA) are homonymous hemianopsia or homonymous inferior quadrantanopsia and hemisensory deficits which may include sensory extinction with double simultaneous stimulation, astereognosis, poor 2 point discrimination and agraphesthesia. Dominant hemisphere lesions are associated with transcortical sensory aphasia manifested by paraphasias, fluent speech, good repetition, and poor comprehension. Nondominant infarctions often cause anosognosia and hemispatial neglect.

Clinical correlates of subcortical infarctions, involving the superficial and deep branches of the MCA, invariably include hemiparesis and commonly aphasias of various types in dominant hemisphere lesions.

Pure hypoxic encephalopathies do not cause watershed infarctions, but rather neuronal damage in specific populations of neurons which are particularly sensitive to hypoxia. These are located in the striatum (caudate and putamen nuclei), cerebral cortex, CA1 region of the hippocampus and the cerebellum, especially Purkinje cells. Loss of Purkinje cells may be responsible for action myoclonus, a debilitating, often prolonged disorder known as the Lance-Adams syndrome.

Pure hypoxic encephalopathies do not cause watershed infarctions.

Prognostic Factors in Comatose Survivors After CPR

Circumstances surrounding a cardiac arrest, including the etiology, cannot be relied upon for prognosis.

1. Circumstances surrounding CPR such as time of anoxia, duration of CPR, etiology of cardiac arrest cannot be relied upon for prognosis [7].
2. Hyperthermia is associated with a poor outcome but is also not a sufficiently reliable prognostic factor.
3. Features of the neurologic examination which indicate poor prognosis are:
   (a) Absent pupillary reactions 3 days after cardiac arrest.
   (b) Absent corneal reflexes 3 days after cardiac arrest.
   (c) Absent or extensor motor responses 3 days after cardiac arrest.
   (d) Myoclonic status epilepticus within 24 h of cardiorespiratory arrest.
4. Electrophysiologic studies.
   (a) Somatosensory evoked potentials. Bilateral absence of cortical SSEPs (N20 response) 1–3 days post arrest is a strong indicator of a poor prognosis.

(b) Electroencephalography patterns. Burst suppression or generalized epileptiform discharges are associated with poor outcomes but not with good prognostic accuracy.
(c) Neuroimaging [8]. Ideal timing of MRI after cardiac arrest is 2–5 days. It is useful to prognosticate a poor outcome and is then 38% sensitive but with 100% specificity. Diffusion-weighted imaging is the preferred sequence. Bilateral hippocampal hyperintense signals are a poor prognostic sign.
(d) Biochemical markers. Serum neuron-specific enolase levels of greater than 33 μg/L show good predictive value for poor prognosis.

5. Figure 5.3 is an excellent summary even though published in 1981.

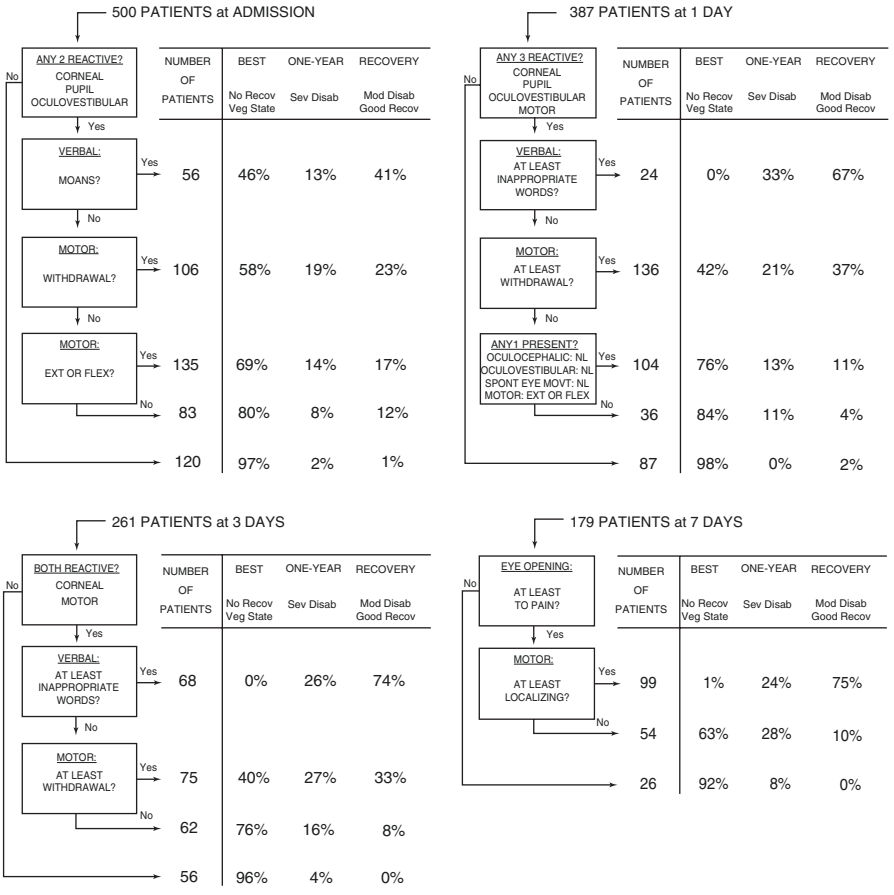

Fig. 5.3 Estimating prognosis in nontraumatic coma. All patients surviving various early intervals after onset of coma are categorized on the basis of sequential criteria relating to their clinical examinations. Best levels of recovery within 1 year are given for each of the prognostic groups. *No Recov* no recovery, *Veg State* vegetative state, *Sev Disab* severe disability, *Mod Disab* moderate disability, *Good Recov* good recovery, *Mot* motor responses, *Ext* extensor, *Flex* flexor, *Spont Eye Movt* spontaneous eye movements, *Nl* normal. Nonreactive motor responses means the absence of any motor response to pain. (Levy et al. [3], with permission)

Traumatic Brain Injuries (TBI)

TBI requires a different assessment. For the immediate evaluation in the Emergency Room a standard approach is the use of the Glascow Coma Scale. The prognosis is distinct from non-traumatic coma and recovery after prolonged unresponsiveness is not uncommon.

A few broad principles can be stated regarding prognosis for a possible good recovery.

1. Coma lasting minutes results in post-traumatic amnesia (PTA) lasting hours to days with recovery over days to weeks.
2. Coma lasting hours to days results in PTA lasting days to weeks and recovery over months.
3. Coma lasting weeks leads to PTA for months and recovery over months to 2 years.

Major determining factors.

1. There is a poor prognosis for patients over age 60 or less than age 2.
2. The location of contusions and hemorrhages.
3. Recovery from diffuse axonal injury takes longer than from focal contusions. The former is not usually well-defined by neuroimaging.

Major adverse factors.

1. Poor pupillary responses.
2. Hyperthermia.
3. Increased intracranial pressure.
4. Hypoxia.

Rule of thumb.
After 2 years post-head trauma the chance of significant recovery is negligible.

Glascow Coma Scale

Eye Response

4 = eyes open spontaneously
3 = eye opening to verbal command
2 = eye opening to pain
1 = no eye opening

Motor Response

6 = obeys commands
5 = localizing pain
4 = withdrawal from pain
3 = flexion response to pain
2 = extension response to pain
1 = no motor response

Verbal Response

5 = oriented
4 = confused
3 = inappropriate words
2 = incomprehensible sounds
1 = no verbal response

A GCS score of 13 or higher indicates mild brain injury, 9–12 indicates modest brain injury, and 8 or less indicates severe brain injury.

The Glascow Coma Scale is primarily applicable to the assessment of patients with head trauma. Because of its ubiquitous use familiarity with its standards is useful.

Herniation Syndromes

Mass lesions of any etiology which affect only one cerebral hemisphere will not ordinarily alter the level of consciousness. If the mass effect from the lesion alone or secondary edema causes a shift of midline structures to affect the contralateral hemisphere, diencephalon (hypothalamus, thalamus, and subthalamus), or midbrain, the patient becomes poorly responsive.

Mass lesions of any etiology which affect only one cerebral hemisphere will not alter the level of consciousness.

If there is a mass lesion in the posterior fossa such as a tumor or hemorrhage within the cerebellum, the patient will remain alert unless there is compression and secondary dysfunction of the brainstem, especially the midbrain reticular formation.

Because of the different mechanisms which are involved, herniations can be divided into supratentorial and infratentorial. It is essential to recognize their clinical signs at the bedside since they convey the ominous signals of impending demise.

There are three supratentorial herniations, falcine (cingulate gyrus), central transtentorial, and uncal (see Fig. 5.4). The clinical signs of all of them can be divided into the effects on level of consciousness, respiration, pupils, eye movements, and motor function. All descriptions will focus on these five elements. An emphasis will be placed on eye signs which are often the most reliable diagnostic features (see Table 5.1).

There are three supratentorial herniations: falcine, central transtentorial, and uncal.

Falcine Herniations

Falcine herniations are associated with herniation of the cingulate gyrus under the falx cerebri. This results in compression of branches of the ACA (pericallosal and callosomarginal) which supply the medial portion of the cerebral hemisphere; this causes edema and thus increases the shift if no treatment is given. Progression into central transtentorial herniation usually ensues. The clinical signs of falcine herniation are those which accompany the mass lesion itself.

Falcine herniation may be followed by central transtentorial herniation.

Central Transtentorial Herniation

Central transtentorial herniation can be divided into diencephalic, midbrain-upper pons and lower pons-upper medulla stages.

Central transtentorial herniation can be divided into diencephalic, midbrain-upper pons, and lower pons-upper medulla stages.

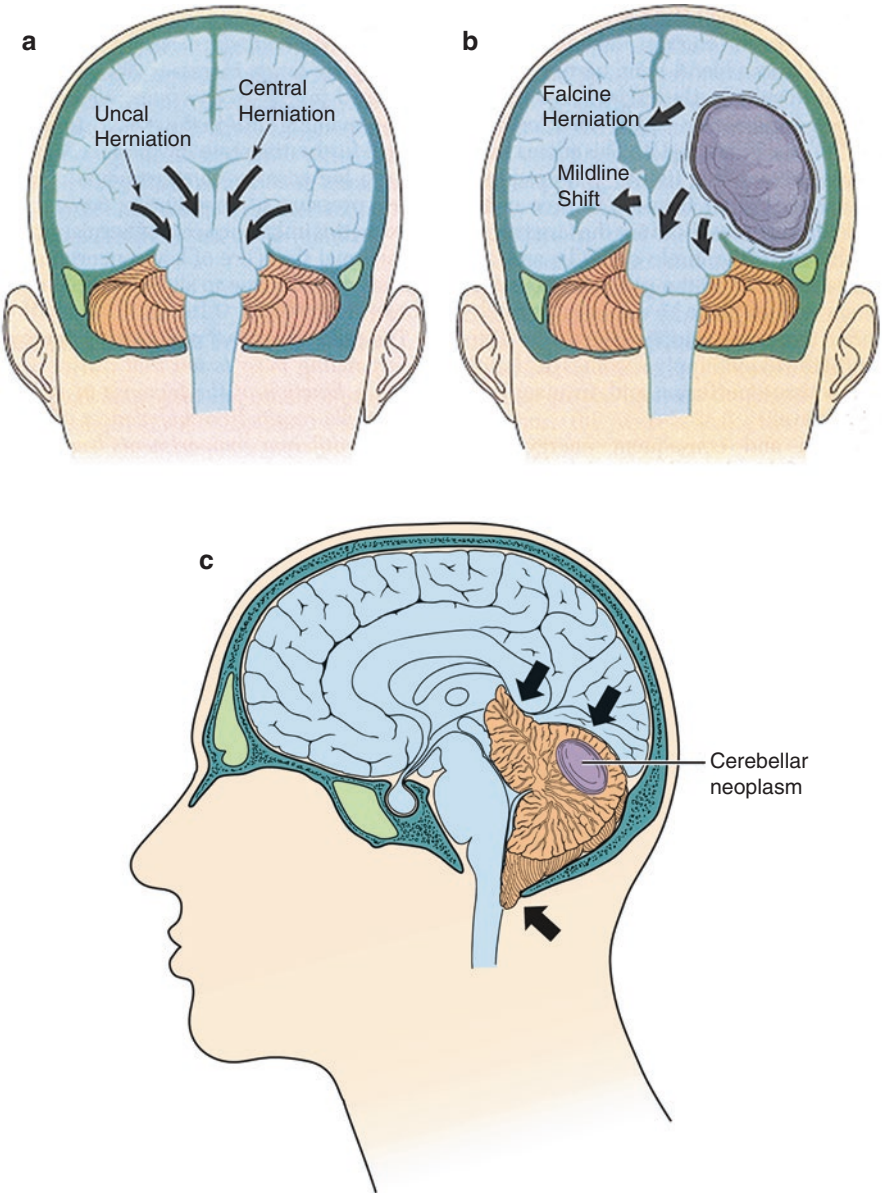

Fig. 5.4 Obtained with permission from Plum and Posner (2007). Supratentorial herniation. (**a**) When mass effect is symmetrical both central and uncal herniation are likely to occur. (**b**) Mass lesion causing falcine herniation, midline shift, central and uncal herniation. Infratentorial herniation. (**c**) The *uppermost arrow* shows ascending transtentorial herniation of the superior vermis of the cerebellum. The *lower adjacent arrow* discloses mass effect of a cerebellar neoplasm causing upward bulging of the tentorium cerebelli. The *lowest arrow* indicates herniation of the cerebellar tonsils

Table 5.1 Eye signs in herniation syndromes

	Pupil (size and light reaction)	Oculocephalic reflex	Oculovestibular response (cold calorics)
Central transtentorial herniation			
Diencephalic	1–3 mm, reactive	Full horizontal and vertical eye movements elicited	Ipsilateral deviation with or without contralateral nystagmus
Midbrain/upper pons	Midposition, 4–5 mm, irregular, fixed	Sluggish, may be dysconjugate	Sluggish, ipsilateral deviation, may be dysconjugate, no nystagmus
Lower pons/ upper medulla	Midposition, 4–5 mm, fixed	Absent	Absent
Uncal herniation			
Early 3rd nerve	5–7 mm, sluggish reaction, ipsilateral	Full horizontal and vertical eye movements except occasional ipsilateral medial rectus paresis	Ipsilateral deviation with or without contralateral nystagmus and occasional ipsilateral medial rectus paresis
Late 3rd nerve	5–7 mm, no reaction, ipsilateral	Full horizontal and vertical eye movements except ipsilateral medial rectus paresis	Ipsilateral deviation, no nystagmus and ipsilateral medial rectus paresis
Transtentorial upward herniation	4–6 mm, nonreactive	Vertical oculocephalics, no upgaze	With bilateral cold caloric stimulation, no upbeat nystagmus

The diencephalic stage occurs when downward displacement of the cerebral hemispheres forces the diencephalon through the tentorial notch. The etiologies are mass lesions affecting or within the frontal, parietal, and occipital lobes. There is traction on the pituitary stalk and buckling of the diencephalon against the midbrain. Subsequently, there is further downward movement associated with clinical signs of pontine and medullary dysfunction.

Clinical signs of the diencephalic stage in its early development are drowsiness and rarely agitation. Respirations are normal or Cheyne-Stokes. The pupils are 1–3 mm, equal and show a normal reaction to light. Uncommonly, a brief Horner's syndrome may be seen due to unilateral hypothalamic injury. Vestibuloocular reflexes (oculocephalics and calorics) are intact, showing full horizontal eye movements. Ice water calorics induce ipsilateral eye deviation and occasionally horizontal contralateral nystagmus. Spontaneous eye movements may be roving. Patients exhibit paratonic rigidity and often attempt to remove a noxious stimulus.

In the later diencephalic stage Cheyne-Stokes respirations are present and caloric irrigation elicits ipsilateral eye deviation without contralateral nystagmus. A painful stimulus provokes decorticate posturing which may develop asymmetrically.

The midbrain-pons stage carries ominous sequelae as complete recovery from this stage is rare even if the offending lesion is completely removed. Diabetes insipidus and fever are common due to traction on the pituitary stalk and hypothalamus. Central neurogenic hyperventilation supervenes, the pupils become midposition

(4–5 mm), irregular, and fixed. Vestibuloocular reflexes elicit horizontal eye movements only with maximal stimulation. Decerebrate rigidity replaces decorticate posturing when painful stimuli are applied.

Low pontine-medullary stage clinical signs are deep coma and shallow respirations which eventually become ataxic. Apneustic breathing rarely occurs. Pupils are midposition, fixed to light and vestibuloocular reflexes are absent. There is no response to pain other than occasional flexor movements at the knees with plantar stimulation.

Uncal Herniation

Uncal herniation occurs with temporal lobe lesions or any laterally placed lesion. The hippocampus and uncus bulge over the edge of the tentorium trapping the 3rd nerve against it. The midbrain is flattened and the posterior cerebral artery (PCA) which surrounds it is compressed. This may cause an ipsilateral occipital lobe infarction with associated edema which aggravates the herniation process. The opposite cerebral peduncle can be compressed against the incisura of the tentorium cerebelli (Kernohan's notch) producing an ipsilateral hemiparesis. The Sylvian aqueduct is commonly compressed causing ventricular enlargement. The subsequent increase in supratentorial volume causes further downward displacement of the diencephalon. Herniation produces brainstem ischemia and stretching of the medial perforating branches of the basilar artery which is attached to the circle of Willis. The results are midline hemorrhages in the midbrain and pons (Duret's hemorrhages).

Uncal herniation occurs with temporal lobe lesions or any laterally placed lesion.

An ipsilateral hemiparesis, due to Kernohan's notch, is caused by compression of the opposite cerebral peduncle.

Uncal herniation can be divided into the early 3rd nerve, late 3rd nerve, and midbrain-upper pons stages.

The early 3rd nerve stage is an ipsilateral enlargement of the pupil with a sluggish light reaction. Breathing is normal. Oculocephalic testing elicits full horizontal and vertical eye movements with the occasional presence of ipsilateral medial rectus weakness due to 3rd nerve compression. Caloric testing produces ipsilateral eye deviation with or without contralateral nystagmus and the occasionally demonstrable ipsilateral medial rectus weakness also due to the 3rd nerve compression.

Painful stimuli provoke an attempt to remove the stimulus. Paratonic rigidity in the contralateral limb may be present. Contralateral hemiparesis, hyperreflexia, and Babinski signs are usual and, infrequently, there is an ipsilateral hemiparesis due to Kernohan's notch.

The late 3rd nerve stage is manifested by a rapid decline into coma. Respirations are hyperpneic (central neurogenic hyperventilation), less likely Cheyne-Stokes. There is an ipsilateral fixed large pupil (5–7 mm) and medial rectus paresis is evident with vestibuloocular reflex testing. Posturing occurs with painful stimuli, bilateral decerebrate or asymmetric, decorticate on one side and decerebrate on the other.

The midbrain-upper pontine stage which follows reveals a deeply comatose patient with fixed midposition (4–5 mm) pupils and absent vestibuloocular reflexes. Decerebrate posturing prevails. The subsequent decline follows the pattern of central herniation described in the foregoing section.

Infratentorial herniations are tonsillar and upward transtentorial.

Tonsillar herniation results in medullary infarctions and respiratory arrest.

Infratentorial Herniations

Infratentorial herniations are twofold, tonsillar and upward transtentorial.

1. Tonsillar herniation is caused by mass effect in the posterior fossa which shoves the cerebellar tonsils through the foramen magnum. Normally the tonsils can be as low as 5 mm below the foramen magnum. When they descend below this critical level, they may be compressed against the edge of the foramen magnum along with the medulla and high cervical cord. These structures become infarcted and the medullary centers for respiratory and circulatory control are destroyed. An early clinical sign of tonsillar herniation may be a slightly stiff neck. This augurs an impending rapid respiratory and circulatory collapse.
2. Transtentorial upward herniation occurs with posterior fossa mass lesions which push the cerebellum and midbrain upward through the tentorial notch. Aqueductal compression usually occurs with secondary ventricular enlargement. The superior cerebellar artery is compressed causing cerebellar infarctions, secondary edema and augmented pressure aggravating the upward herniation. The veins of Rosenthal and Galen are compressed causing venous congestion and further increase in intracranial pressure.

Transtentorial upward herniation causes pretectal and posterior commissure compression with bilateral large, fixed pupils and upgaze paresis, respectively.

Clinical signs are impairment of upward gaze and enlarged round fixed pupils (5–6 mm) due to pressure on the posterior commissure and adjacent pretectum, respectively. There may be central neurogenic hyperventilation and occasionally downward eye deviation. Retractory nystagmus may occur due to simultaneous contraction of all eye muscles which pulls the eyes back into the orbit. With sufficient pressure on the midbrain, impaired function of the mesencephalic reticular formation will result in coma.

Chronic Disorders of Consciousness

The conscious state depends on two characteristics, wakefulness and awareness [9]. The reticular formation, primarily in the thalamus, is the substrate required for wakefulness. Awareness depends on additional structures, the cerebral cortex, and subcortical white matter connections with the thalamus.

> The conscious state depends on two characteristics, wakefulness and awareness.

Coma

Coma is a state of unresponsiveness and unarousability with closed eyes. Thus, the reticular formation is not functioning. In deep coma there is no withdrawal or posturing to painful stimuli. In light coma painful stimuli will produce posturing and withdrawal responses. After a few weeks the comatose patient transitions into a vegetative state if treatment efforts have failed. Any etiology can lead to a vegetative state, be it hypoxic-ischemic, infectious, metabolic, toxic, or structural pathology.

> In coma, the reticular formation is not functioning, the patient is unarousable, and the eyes are closed.

Vegetative State

The vegetative state, awake but unaware, indicates preservation of the reticular formation alone. Usually it begins to emerge after 10–14 days of coma. It can be associated with a flat EEG (electrocerebral silence) or a severely abnormal EEG. The vegetative state is characterized by the absence of meaningful interaction with people or environmental stimuli. The patient has normal sleep–wake cycles and therefore the eyes are open for long periods. There is spontaneous breathing, eye blinks, and roving eye

movements. Pain may provoke facial grimacing, decorticate posturing and limb withdrawal. The patient may utter sounds but never words; he may yawn, chew, and swallow saliva. Cranial nerve reflexes are intact. There is fecal and urinary incontinence. Because the patient is awake and may have roving eye movements, both medical personnel and nonmedical individuals are often seduced into a belief that the patient is aware. The vegetative state becomes clearly evident at 1 month. It becomes permanent at 3 months if the etiology is nontraumatic, 12 months if traumatic. Although absolute certainty is not attainable, the veracity of the diagnosis is supported by numerous neuroimaging, neurophysiologic, and neuropathologic correlations.

In the vegetative state the reticular formation is functioning and the eyes are open. There are normal sleep–wake cycles.

Additional seldom used terminology applied to these patients includes the persistent vegetative state, permanent vegetative state, coma vigil, apallic state and akinetic mutism. Akinetic mutism is a term which cannot be used for the vegetative state and requires a separate discussion.

Akinetic Mutism

This is a self-defining term. The patient does not speak, is immobile or nearly so, but appears hypervigilant. The semblance of attentiveness derives from the presence of visual tracking with conjugate eye movements. Additional features of this state which differentiate it from the vegetative state is the possibility of an acute or subacute origin as well as prompt recovery if due to a mass lesion which can be surgically treated. Rupture of an anterior communicating artery aneurysm may cause this condition and it may become permanent. It is a result of bilateral lesions of the anterior cingulate cortex and medial prefrontal cortex as well as structural lesions involving the dorsomedial nucleus of the thalamus, midbrain tegmentum and occasionally bilateral injuries to the nigrostriatal bundle in the lateral hypothalamus. The latter may be reversible through treatment with dopaminergic agonists.

Akinetic mutism differs from the vegetative state since it may be of acute origin and resolve quickly if the lesion is treatable.

Minimally Conscious State

The minimally conscious state can be defined as a near vegetative state [10, 11]. The presence of fragments of awareness of self and environment are infrequently or

rarely witnessed. This is determined by an appropriate but often inconsistent verbal or gestural response to yes–no questions, ability to follow simple commands and purposeful behavior. Rarely there is intelligible verbalization. The patient may reach for objects and demonstrate pursuit eye movements to moving stimuli. The diagnosis depends on accurate observations by caregivers who will likely need coaching on reliable methods of communication.

The minimally conscious state is a near vegetative state as there are rare meaningful responses to verbal commands and/or purposeful behavior.

The patient's physician will usually not be present when behavior indicating awareness is exhibited. Neurologic examinations are notorious for variability which may be related to time of day, fatigue, fever, or other physiologic and environmental changes. Consequently, repeated careful examinations are essential to provide an accurate diagnosis.

Attention must be paid to the patient's family and their observations. Even though unrealistic assumptions and conclusions are made, a grain of an accurate observation may emerge which changes the diagnosis from vegetative state to minimally conscious state, a critical distinction. An inaccurate diagnosis of a vegetative state instead of minimally conscious state has been estimated to range up to 40%.

Attention must be paid to the patient's family and their observations since physicians are unlikely to be present when responses are witnessed.

The etiology of a vegetative state or minimally conscious state is most often hypoxic and/or ischemic encephalopathy due to cardiac arrest, respiratory failure, prolonged hypotension, or head trauma. The pathology of nontraumatic cases especially involves cortical and thalamic neurons but less so of subcortical white matter tracts, hypothalamus, and brainstem. The pathology of head injury is typically manifested by diffuse axonal injury, white matter greater than gray matter.

In view of the pathology described above, the prognosis of the patient in a traumatic vegetative or minimally conscious state is far better than nontraumatic etiology. Observation for at least 1 year is required before a reasonably accurate prognostic statement can be made, especially for young patients. Approximately 50% of patients in a minimally conscious state due to trauma will be able to function independently at 1 year.

The prognosis of the patient in a traumatic vegetative or minimally conscious state is far better than a nontraumatic etiology, usually hypoxic-ischemic encephalopathy.

Patients who are in a vegetative state for 3 months due to a nontraumatic etiology, ordinarily hypoxic-ischemic encephalopathy, have a near zero chance of a meaningful recovery. At 1 month the prognosis is extremely poor, probably less than 1%.

Neuroimaging studies, especially MRI, functional MRI, and PET scan have demonstrated abnormalities that may be useful for estimating prognosis. Details of these findings are beyond the scope of this text.

Locked-in State

Although this is not a disorder of consciousness it must be distinguished from the vegetative state and akinetic mutism. This state is usually due to a pontine lesion causing quadriplegia, paralysis of horizontal eye movements but preservation of downward eye movements. Upward eye movements above the horizontal plane are usually not retained. The etiology is ordinarily a stroke, ischemic, or hemorrhagic, with destruction of the basis pontis and PPRF. A rare etiology is central pontine myelinolysis, which is demyelination of the basis pontis commonly due to an excessively rapid correction of hyponatremia. Communication with patients who have locked-in syndrome is technically possible through downward eye movements or eye blinks; however, the prognosis for significant recovery is poor.

Brain Death

There are four clinical settings in which the determination of death is made. First is the total collapse of cardiac and pulmonary function in the patient without mechanical support. Second is the collapse of cardiac function in the intubated ventilated patient. Third is pulmonary failure despite maximum oxygenation and ventilator support. The fourth is absence of brain function in the intubated patient despite adequate artificial ventilation and sustained cardiac function. There is general acceptance of the principle that absence of brain function is absence of life.

There is general acceptance of the principle that absence of brain function is absence of life.

The most common situation is the total collapse of cardiac and pulmonary function which nowadays occurs primarily out of the hospital. Emergency code blue teams in the hospital have been extraordinarily successful in resuscitating patients after cardiac and/or respiratory arrest. But the majority of recipients have serious hypoxic-ischemic sequelae. This clinical scenario requires careful and accurate definitions of brain dysfunction. Furthermore, organ transplantation mandates precision.

Every hospital has its own protocol for brain death, although the differences between them are now negligible. A typical brain death protocol is described below:

1. Diagnostic criteria for clinical diagnosis of brain death (for patients older than 18 years) [12].

   (a) Prerequisites. Brain death is the absence of clinical brain function when the proximate cause is known and demonstrably irreversible.

      (i) Clinical findings with or without neuroimaging evidence of an acute CNS catastrophe that are compatible with the clinical diagnosis of brain death.
      (ii) Exclusion of complicating medical conditions that may confound clinical assessment (no severe electrolyte, acid–base, or endocrine disturbance).
      (iii) No drug intoxication or poisoning.
      (iv) Core temperature ≥ 32 °C (90 °F).

   (b) The three cardinal findings of brain death are coma or unresponsiveness, absence of brainstem reflexes, and apnea.

      (i) Coma or unresponsiveness – no motor response of any extremity to deep painful stimuli.
      (ii) Absence of brainstem reflexes.

   Pupils.

   No response to bright light.
   Size: midposition (4 mm) to dilated (9 mm).

   Ocular movement.

   No oculocephalic reflex (testing only when no fracture or instability of the cervical spine is apparent).
   No deviation of the eyes to irrigation in each ear with 50 mL of cold water (allow 1 min for observation after irrigation and at least 5 min between testing on each side).

   Facial sensation and facial motor response.

   No corneal reflex to touch with a cotton swab.
   No jaw reflex.
   No grimacing to deep painful stimuli.

   Pharyngeal and tracheal reflexes.

   No response after stimulation of the posterior pharynx with tongue blade.
   No cough response to bronchial suctioning.

   (iii) Apnea – testing performed as follows:

   Prerequisites.

   Core temperature ≥ 36.5 °C or 97 °F.

Systolic blood pressure ≥ 90 mmHg.
Euvolemia. *Option*: positive fluid balance in the previous 6 h.
Normal pCO_2. *Option*: arterial $pCO_2 \geq 40$ mmHg.
Normal pO_2. *Option*: preoxygenation to obtain arterial $pO_2 \geq 200$ mmHg.

Connect a pulse oximeter and disconnect the ventilator.
Deliver 100% O_2, 6 L/min into the trachea. *Option*: place a cannula at the level of the carina.
Look closely for respiratory movements (abdominal or chest excursions that produce adequate tidal volumes).
Measure pO_2, pCO_2, and pH after approximately 8 min and reconnect the ventilator.
If respiratory movements are absent and arterial pCO_2 is ≥60 mmHg (*option*: 20 mmHg increase in pCO_2 over a baseline normal pCO_2), the apnea test result is positive (i.e., it supports the diagnosis of brain death).
If respiratory movements are observed, the apnea test result is negative (i.e., it does not support the clinical diagnosis of brain death) and the test should be repeated after a suitable interval.
Connect the ventilator if, during testing, the systolic blood pressure becomes ≤90 mmHg or the pulse oximeter indicates significant oxygen desaturation and cardiac arrhythmias are present; immediately draw an arterial blood sample. If pCO_2 is ≥60 mmHg or $pCO_2 \geq 20$ mmHg over baseline normal pCO_2, the apnea test result is positive (it supports the clinical diagnosis of brain death); if pCO_2 is <60 mmHg or pCO_2 increase is <20 mmHg over baseline normal pCO_2, the result is indeterminate, and an additional confirmatory test can be considered.

2. Pitfalls in the diagnosis of brain death
   The following conditions may interfere with the clinical diagnosis of brain death, so that the diagnosis cannot be made with certainty on clinical grounds alone. Confirmatory tests are recommended.

   (a) Severe facial trauma.
   (b) Preexisting pupillary abnormalities.
   (c) Toxic levels of any sedative drugs, aminoglycosides, tricyclic antidepressants, anticholinergics, antiepileptic drugs, chemotherapeutic agents, or neuromuscular blocking agents.
   (d) Sleep apnea or severe pulmonary disease resulting in chronic retention of CO_2.

3. Clinical observations compatible with diagnosis of brain death [13]

   (a) Spontaneous movements of limbs other than pathologic flexion or extension response.
   (b) Lazarus sign: slow body movements producing flexion at the waist.

(c) Respiratory-like movements (shoulder elevation and adduction, back arching, intercostal expansion without significant tidal volumes).
(d) Sweating, blushing, tachycardia.
(e) Normal blood pressure without pharmacologic support or sudden increases in blood pressure.
(f) Absence of diabetes insipidus.
(g) Deep tendon reflexes; superficial abdominal reflexes; triple flexion response.
(h) All of these findings are due to preserved function of spinal cord pathways and neurons.

4. Confirmatory laboratory tests (*options*)
Brain death is a clinical diagnosis. A repeat clinical evaluation 6 h later is recommended, but this interval is arbitrary. A confirmatory test is not mandatory but is desirable in patients in whom specific components of clinical testing cannot be reliably performed or evaluated. It should be emphasized that any of the suggested confirmatory tests may produce similar results in patients with catastrophic brain damage, who do not (yet) fulfill the clinical criteria of brain death. The following confirmatory test findings are listed in the order of the most sensitive test first. Consensus criteria are identified by individual tests.

(a) Technetium-99 m hexamethylpropyleneamineoxime brain scan. No uptake of isotope in brain parenchyma ("hollow skull phenomenon").
(b) Electroencephalography. No electrical activity during at least 30 min of recording that adheres to the minimal technical criteria for EEG recording in suspected brain death as adopted by the American Electroencephalographic Society, including 16-channel EEG instruments.
(c) Transcranial Doppler ultrasonography.
    (i) 10% of patients may not have temporal insonation windows. Therefore, the initial absence of Doppler signals cannot be interpreted as consistent with brain death.
    (ii) Small systolic peaks in early systole without diastolic flow or reverberating flow indicate very high vascular resistance associated with greatly increased intracranial pressure and support the diagnosis of brain death.

5. Medical record documentation (*standard*)

(a) Etiology and irreversibility of condition.
(b) Absence of brainstem reflexes.
(c) Absence of motor response to pain.
(d) Absence of respiration with $pCO_2 \geq 60$ mmHg.
(e) Justification for confirmatory test and result of confirmatory test.
(f) Repeat neurologic examination. *Option*: the interval is arbitrary, but a 6-h period is reasonable.

Questions (True or False)

1. The most important question to solve in an unresponsive patient is whether a focal lesion, multifocal lesions, or diffuse dysfunction are present.
2. Cheyne-Stokes respiration is sustained hyperventilation.
3. Apneustic breathing is due to a pontine lesion.
4. An intubated patient cannot have a satisfactory assessment of his mental status for diagnostic purposes.
5. Decorticate posturing includes flexion of the legs.
6. Patients with papilledema may have hemorrhages which are located at the disk margins.
7. Caloric testing is a more powerful stimulus than the oculocephalic maneuver.
8. Caloric testing is the best method to detect psychogenic unresponsiveness.
9. Horizontal eye deviation generally indicates a focal lesion. Eye deviation in the vertical plane is common with metabolic or hypoxic ischemic encephalopathy.
10. Midbrain lesions produce larger pupils than pretectal lesions.
11. Paratonic rigidity is a common abnormality in patients with metabolic encephalopathy.
12. The sensory examination of an obtunded patient may yield focal signs.
13. Acute delirium usually indicates a metabolic or toxic encephalopathy.
14. Disorientation to self is frequently observed at the onset of a toxic encephalopathy.
15. Hyperventilation causes a respiratory acidosis.
16. Skew deviation is a horizontal divergence of the globes.
17. Multifocal myoclonus is a hallmark sign of a metabolic encephalopathy.
18. Asterixis is pathognomonic of hepatic encephalopathy.
19. Circumstances surrounding a cardiac arrest are a good prognostic indicator.
20. Falcine herniations may compress the anterior cerebral artery causing cerebral edema.
21. Cheyne-Stokes respirations may occur with both central transtentorial herniation and congestive heart failure.
22. Upward transtentorial herniation due to a cerebellar mass lesion is likely to compress the posterior commissure to produce paresis of upward gaze.
23. An intact thalamic reticular formation is required to preserve wakefulness.
24. In coma the eyes are closed; in a vegetative state they open periodically due to preserved wakefulness.
25. A vegetative state due to trauma is permanent at 3 months.
26. Akinetic mutism may not occur acutely.
27. The diagnosis of a minimally conscious state commonly depends on observations by nurses who may need instructions about recording their observations.
28. A patient with a locked-in state is unable to communicate.
29. Assessment for brain death does not include caloric testing.
30. The corneal reflex is part of the examination for brain death.
31. Deep tendon reflexes may be present in brain death.
32. Kernohan's notch is associated with an ipsilateral hemiparesis.

Answers

1. T
2. F
3. T
4. F
5. F
6. T
7. T
8. T
9. T
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32. T

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Chapter 6
The Six Major Anatomic Decussations with Clinical Correlation

Initially, the most confounding elements of neuroanatomy for many medical students are likely to be the decussations of the neural pathways. There are six major and partial decussations; most are simple, but they must be committed to memory as they are the kernel of neuroanatomic localization. These are the corticospinal tract, corticobulbar tract, oculomotor decussation with its associated pathways, visual pathway, lateral spinothalamic tract, and posterior column/medial lemniscus. This chapter will attempt to summarize these anatomic facts in a concise, proximate fashion to facilitate an easy review when required.

The Corticospinal Tract (Fig. 6.1)

There are three motor systems in the brain: corticospinal, extrapyramidal, and cerebellar. The corticospinal tract is the primary motor system pathway. It arises from both precentral (frontal) (60%) and postcentral (parietal) (40%) cortical areas. The fibers descend in the ipsilateral corona radiata, posterior limb of the internal capsule, central portion of the cerebral peduncle, basis pontis, medullary pyramids and 80–90% cross in the pyramidal decussation at the cervical-medullary junction. The fibers then descend in the contralateral corticospinal tract located in the lateral columns and terminate at lower motor neurons in the anterior horn of the spinal cord. Lamination of the fibers from medial to lateral are cervical, thoracic, lumbar, and sacral. The extrapyramidal and cerebellar systems have multiple pathways and thus are not amenable to precise anatomic and clinical correlations.

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The corticospinal tract arises from both precentral (frontal) and postcentral (parietal) cortical areas.

80–90% of corticospinal tract fibers cross in the decussation of the pyramids located at the cervical-medullary junction.

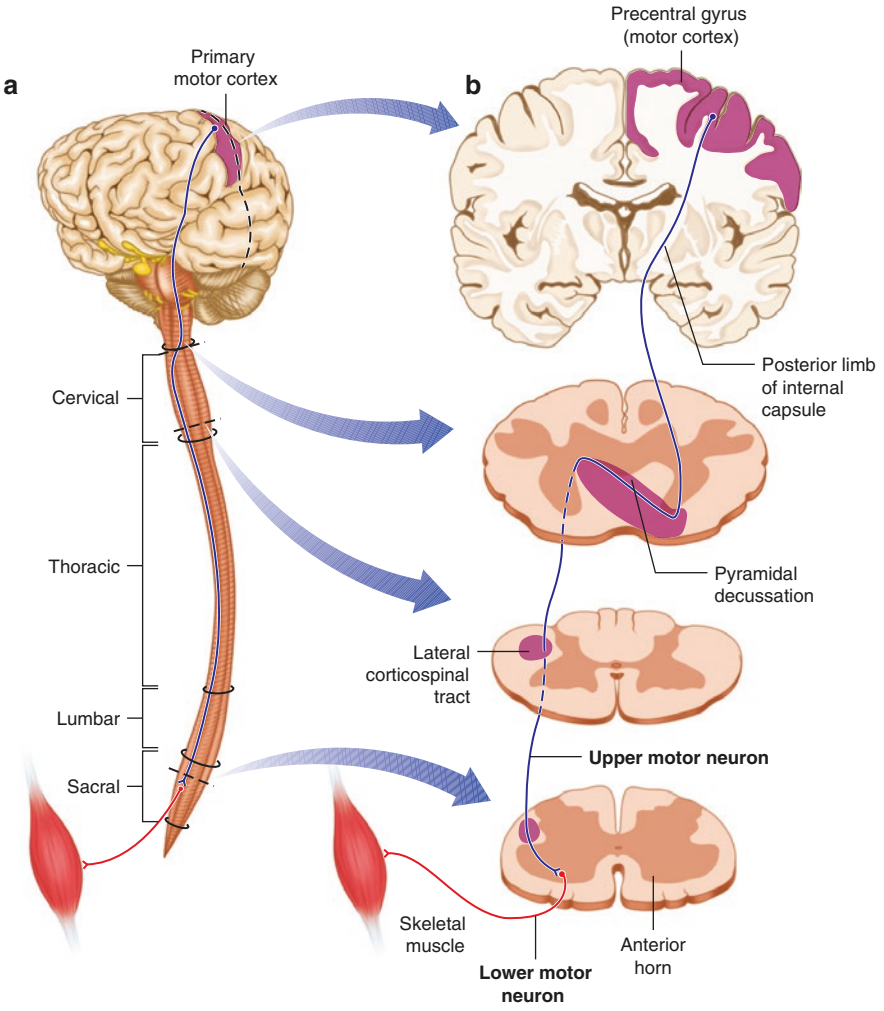

Fig. 6.1 Corticospinal tract pathways. (Adapted from Blumenfeld [1])

Neurologic abnormalities arising from lesions of the corticospinal tract may include physical weakness, poor dexterity, abnormal muscular tone, hyperreflexia and Babinski signs. The weakness has a predilection for distal musculature. Poor dexterity, which is tested by finger tap, foot tap, and rapid alternating movements, frequently occurs first. Muscular tone may be spastic and reflexes can be increased. The prototypical abnormal reflex is the Babinski sign. Any one of these findings can be noted in isolation or in different combinations.

1. Clinical summary:

   (a) Cerebral (cortical or subcortical) and brainstem lesions which affect the corticospinal tract may cause one or more of these findings: contralateral hemiparesis or monoparesis, spasticity, impaired dexterity, increased reflexes, and Babinski sign.
   (b) Unilateral cervical spinal cord lesions which affect the corticospinal tract in the lateral columns may cause one or more of these findings: ipsilateral hemiparesis or monoparesis, spasticity, impaired dexterity, increased reflexes, and Babinski sign.

> Cerebral and brainstem lesions cause contralateral hemiparesis or monoparesis and spinal cord lesions, ipsilateral hemiparesis or monoparesis.

   (c) Unilateral thoracic spinal cord lesions which involve the corticospinal tract may cause one or more of these findings: ipsilateral leg weakness, spasticity, impairment of rapid foot tapping, increased reflexes, and Babinski sign.
   (d) Lesions at the cervical-medullary junction may cause a triparesis, quadriparesis, cruciate paresis (such as involvement of left arm and right leg), and rarely bilateral arm paralyses (man-in-a-barrel syndrome).
   (e) Most spinal cord lesions produce bilateral abnormalities of the corticospinal tracts.

The Corticobulbar Pathways (Fig. 6.2)

1. Clinical correlation:

   (a) Contralateral facial weakness may occur with lesions affecting the corticobulbar pathways. Nerve fibers which control facial muscles originate from neurons in the lower 3rd of the cortical motor fields, descend in the corona radiata, genu of the internal capsule, medial portion of the cerebral peduncle, basis pontis, and decussate just above the 7th nerve nuclei. There is some bilateral innervation to the 7th nerve nuclei. The frontalis muscle has bilateral innervation and is usually, but not always, spared with contralateral

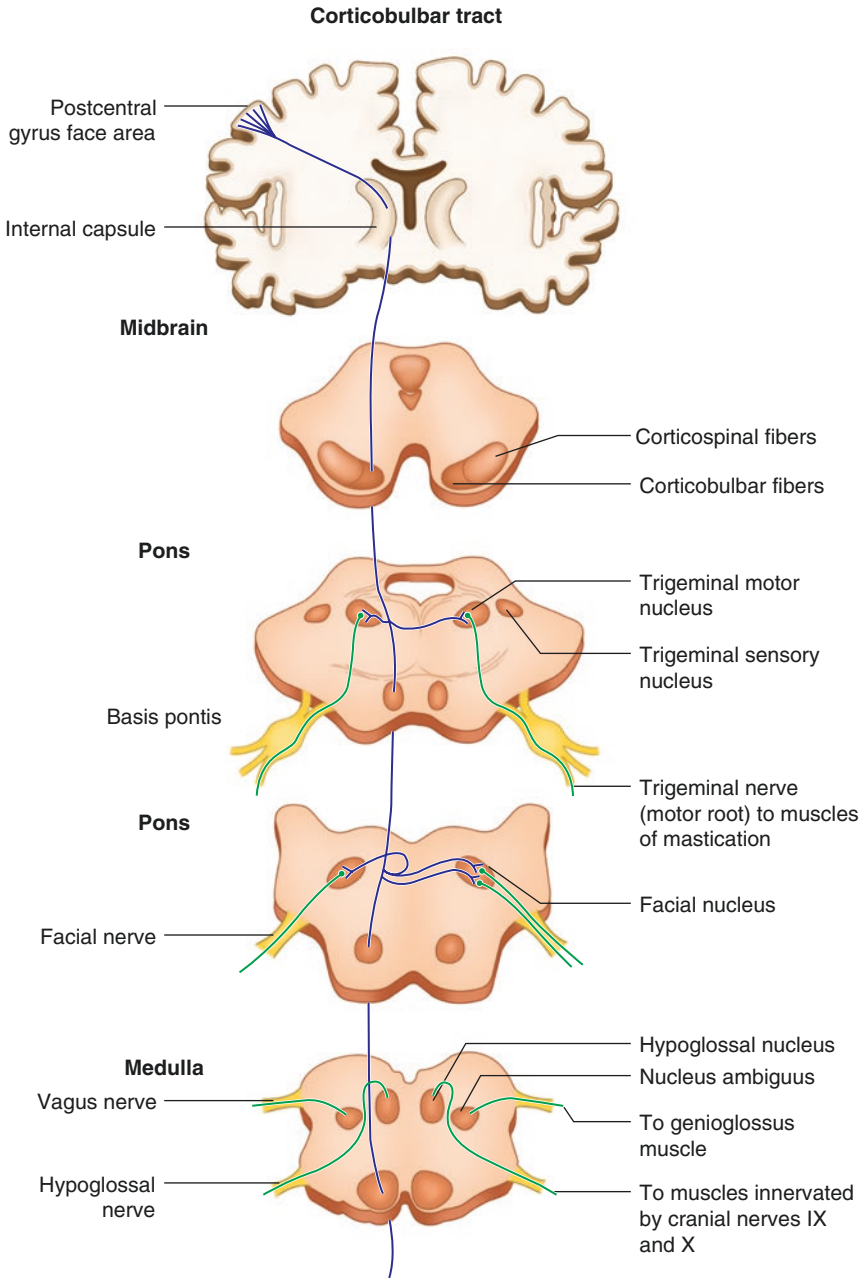

Fig. 6.2 Corticobulbar pathways. (Adapted from Brazis et al. [2])

lesions above the decussation. A wider palpebral fissure on the involved side is a common, subtle finding which may be the sole evidence for orbicularis oculi weakness. Emotional, involuntary facial movements are likely to be innervated by a separate pathway since voluntary movements and strength may be normal; but a brief laugh may expose an overt facial droop. A separate pathway to explain this disparity is likely as lesions of the frontal lobe, just anterior to the precentral gyrus, have been found to be associated with these clinical findings.

Corticobulbar pathway lesions often cause contralateral facial weakness which usually spares the frontalis and less often the orbicularis oculi muscles.

Emotional, involuntary facial movements are likely to be innervated by a separate pathway since voluntary movements and strength may be normal.

(b) Cerebral, thalamic, and midbrain lesions may cause contralateral facial numbness and, infrequently, a decreased corneal reflex. Sensory fibers from the main sensory nucleus of the trigeminal nerve cross the midline and ascend in the quintothalamic tract to terminate in the ventral posteromedial nucleus of the thalamus (VPM). Fibers from the VPM ascend to ipsilateral parietal lobe neurons.

Cerebral, thalamic and midbrain lesions may cause contralateral facial numbness.

(c) Nerve fibers which control jaw muscles via the motor root of the 5th nerve originate in the lower frontal motor cortex, descend through the corona radiata, internal capsule, medial portion of the cerebral peduncle, and decussate in the pons to synapse in the motor nucleus of V. Although there is bilateral control of motor function, there is primarily contralateral innervation of the masseter muscle. Thus jaw deviation to the contralateral side of the lesion may rarely occur.
(d) There is bilateral innervation of the nucleus ambiguus (9th through 11th cranial nerve nuclei). Consequently, dysphagia is generally not a symptom of an acute unilateral cerebral lesion unless it is extensive. An unusual exception is dysphagia associated with nonfluent aphasias due to an apraxia of tongue movements.

Because of bilateral innervation of the nucleus ambiguus, dysphagia is seldom caused by an acute unilateral cerebral lesion.

(e) Corticolingual fibers to the tongue arise from neurons in the lower portion of the precentral gyrus. These muscles are innervated bilaterally except for the genioglossus which is solely supplied by the contralateral cerebral hemisphere. Consequently, the tongue may deviate to the side of the hemiparesis. Dysarthria appears most often when corticolingual pathways are interrupted on either side. The lesions can be located in either cerebral hemisphere or in the brainstem.

Dysarthria appears most often when corticolingual pathways are interrupted.

(f) The corticobulbar pathway to the sternocleidomastoid muscles probably involves a double decussation. The trapezius muscle on the side of the hemiplegia is paretic. The sternocleidomastoid muscle, however, shows ipsilateral weakness. Consequently, the head is turned to the side of the lesion. Head turn without tilt is most common and can be explained as an isolated contraction of the sternomastoid portion of the muscle. This conception of the anatomic pathway is supported by the presence of focal seizures which cause contralateral jerking of the head (adversive seizure). It has been suggested that the pathway for sternomastoid control crosses the midline to the opposite side of the pons and then crosses back to the ipsilateral spinal cord via the pyramidal decussation (a second decussation). Thus, hemiplegia with contralateral head deviation implies a lesion between the first and the second decussations.

The head is turned to the side of a corticobulbar lesion because of ipsilateral sternocleidomastoid weakness.

2. Clinical summary:

(a) Unilateral cerebral lesions, right or left, may cause one or more of the following findings: contralateral facial numbness with or without a decreased corneal reflex, contralateral facial weakness, dysarthria due primarily to involvement of the corticolingual pathway, ipsilateral head deviation, and contralateral tongue deviation. Rarely, there is contralateral jaw deviation due to masseter weakness which is supplied mostly by the contralateral cerebral hemisphere, but still with significant bilateral innervation.
(b) Midbrain and rostral pontine lesions may cause the same clinical findings.

(c) Medullary lesions may result in contralateral head deviation and contralateral tongue deviation.
(d) Lesions immediately below the decussation of the pyramids may cause ipsilateral head deviation because it is below the second decussation of the pathway to the sternomastoid muscle.

3. Synopsis:

Unilateral lesions on either side of the corticobulbar pathway, cerebral or brainstem, commonly cause one or more of the following clinical symptoms or signs: (1) dysarthria, (2) contralateral facial numbness, (3) contralateral facial weakness, (4) contralateral tongue deviation, and (5) ipsilateral head deviation and rarely contralateral head deviation in some medullary lesions.

The Oculomotor Decussation and Associated Pathways (Fig. 6.3)

1. Saccadic system for horizontal eye movements.

Saccades are quick eye movements, both voluntary and reflexive. There are four major parts of the system that generate saccadic eye movements, frontal eye fields

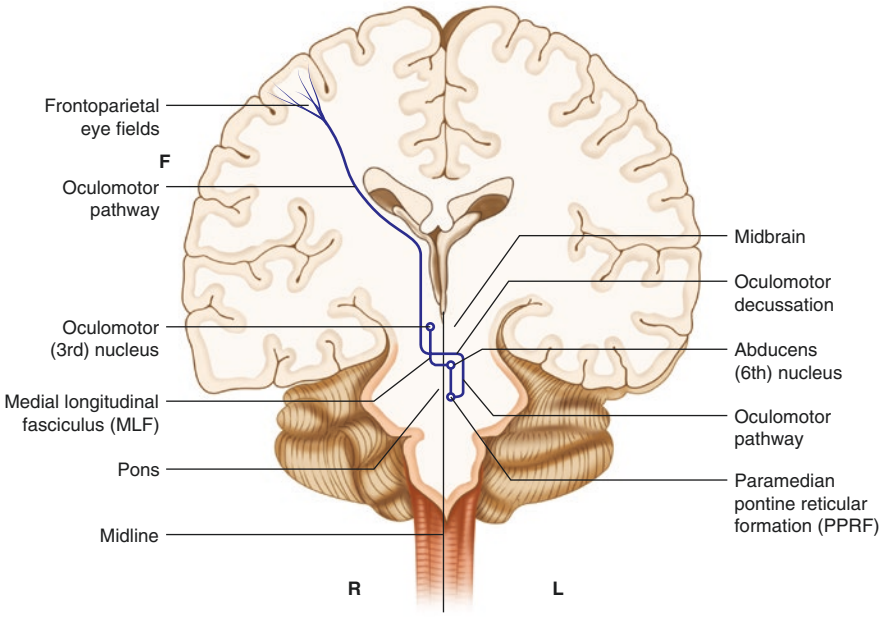

Fig. 6.3 Oculomotor pathway

(FEF), parietal eye fields (PEF), supplementary eye fields (SEF), and the superior colliculus. These are all interconnected in a complex array of pathways and therefore the following description is a substantial simplification.

The FEF is located in the rostral bank of the precentral gyrus at the caudal end of the middle frontal gyrus. It is concerned with triggering voluntary saccades [3]. There is a direct pathway from the FEF via the anterior limb of the internal capsule, medial portion of the cerebral peduncle to the ipsilateral mesencephalic reticular formation followed by a decussation at the pontomesencephalic junction and terminating at the contralateral paramedian pontine reticular formation (PPRF). This is the most clinically relevant pathway. There are additional pathways to the ipsilateral superior colliculus. There is a direct pathway concerned with voluntary saccades and an indirect pathway via the caudate nucleus and other basal ganglia structures which controls the maintenance and releasing of visual fixation [3].

The PEF is located in the intraparietal sulcus which is adjacent to the superior part of the angular gyrus and the supramarginal gyrus. It is concerned with reflexive saccades for exploration of the environment. It projects to the FEF and the superior colliculus.

The SEF is located in the rostral portion of the supplementary motor area which is on the midline surface of the hemisphere in front of the primary motor cortex leg representation. It is involved with gaze control and it plays an executive role in saccadic initiation.

The superior colliculus is essential for triggering saccades as it regulates accuracy, frequency, and velocities of saccadic eye movements. It receives its major input for this function from the FEF and PEF. Its neurons send projections across the midline of the midbrain joining other oculomotor pathways to terminate in the PPRF.

The most clinically relevant pathway is the projection from the FEF directly to the contralateral PPRF via the decussation of the fibers at the pontomesencephalic junction.

Voluntary and reflexive saccades are triggered from FEF and PEF, respectively.

The most clinically relevant pathway is the projection from the FEF directly to the contralateral PPRF via the decussation of the fibers at the pontomesencephalic junction.

The PPRF sends fibers to the ipsilateral 6th nerve nucleus to synapse with neurons whose axons form the 6th nerve and interneurons whose axons immediately cross the midline to constitute part of the medial longitudinal fasciculus (MLF). The

MLF ascends to the 3rd nerve nucleus where its axons synapse with neurons which are the source of nerve fibers to innervate the ipsilateral medial rectus muscle.

The 6th nucleus contains interneurons which send their axons to the contralateral MLF.

Thus, for example, the right cerebral eye fields (FEF and PEF) initiate gaze to the left. The pathway travels downward through the anterior limb of the internal capsule, right mesencephalic reticular formation, crosses the midline at the pontomesencephalic junction and synapses in the left PPRF. The left PPRF neurons send their axons to neurons and interneurons in the left 6th nerve nucleus. These neurons are the source of the left 6th nerve and, the interneurons, a source of fibers which cross the midline to form part of the right MLF which ascends to the right 3rd nerve nucleus. The right 3rd nerve which receives input from the MLF arises from the right 3rd nerve nucleus to innervate the right medial rectus.

2. Clinical correlation: Saccadic system pathways.

   (a) Lesions of frontoparietal eye fields cause ipsilateral eye deviation.
   (b) Lesions of the anterior limb of the internal capsule and adjacent structures may cause ipsilateral eye deviation. Thalamic lesions have rarely been associated with "wrong-way eye deviation," that is toward the hemiparetic side, an inexplicable observation. Irritation of adjacent oculomotor pathways may be an explanation.
   (c) Lesions of the midbrain cause ipsilateral eye deviation.
   (d) Lesions of the PPRF cause contralateral eye deviation.
   (e) Lesions of the MLF cause an internuclear ophthalmoplegia which is manifested by ipsilateral medial rectus weakness or an adductor lag with saccadic eye movements in the direction of ipsilateral medial rectus function. There is frequent nystagmus in the contralateral abducting eye. The etiology of this phenomenon remains speculative. Despite paresis of the medial rectus muscle on conjugate gaze, convergence is often preserved.
   (f) Lesions of the abducens nucleus cause ipsilateral lateral rectus weakness and, in rarely documented clinical cases, an ipsilateral gaze paresis.

The PPRF generates ipsilateral conjugate gaze; a lesion causes contralateral eye deviation.

The MLF generates ipsilateral adduction; a lesion produces ipsilateral adduction paresis.

3. Pursuit system for horizontal eye movements.

Pursuit (slow) eye movements are usually the only examined eye movement system at the bedside. This ignores the above-described saccadic system pathway, lesions of which generate important clinical data. Since the pursuit system is complex, its description will be condensed to the most important proposed elements.

Ipsilateral pursuit eye movements are generated from the ipsilateral occipitotemporal region. Fibers from this area project to the ipsilateral dorsomedial frontal cortex. Lesions involving these loci impair ipsilateral pursuit. The pathway probably descends through the thalamus and then crosses twice at the pontocerebellar level. Pontine nuclei project ipsilateral fibers via the middle cerebellar peduncle to the cerebellum where there are multiple synapses. Ultimately, Purkinje cells in the cerebellum send inhibitory projections to the ipsilateral medial vestibular nuclei (MVN). There are excitatory fibers from the MVN to the contralateral 6th nucleus. Smooth pursuit may not be initiated in the PPRF.

The cerebral hemisphere governs ipsilateral ocular pursuit.

4. Clinical correlation: Pursuit pathway.

(a) Bilateral occipital lobe lesions completely eliminate smooth pursuit.
(b) Brainstem lesions may cause ipsilateral or contralateral pursuit defects due to the double decussation.
(c) Cerebellar lesions, especially flocculus and vermis, interfere with pursuit eye movements in either direction, most often ipsilateral.
(d) Vestibulo-ocular reflexes are often enhanced in patients with impaired ocular pursuit.
(e) The substitution of saccades to catch up with a moving target is termed saccadic pursuit. This is the most commonly observed abnormality when lesions involve this pathway. The pursuit system cannot follow moving targets if they exceed a velocity of 30–40 degrees/seconds. Saccadic pursuit is not unusual in the elderly individual without an apparent neurologic illness.

Saccadic pursuit is the substitution of saccades to catch up with a moving target when pursuit eye movements are impaired.

5. Vertical eye movements.

(a) Saccadic system.

Vertical saccades are generated from neurons in the rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF) located in the midbrain. The neurons for

upward saccades are located in the lateral portion and downward saccades, medial. These neurons send fibers to the interstitial nucleus of Cajal (INC) which projects to the posterior commissure.

> The rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF) generates vertical saccades.

(b) Pursuit system.

The INC located in the midbrain mediates vertical smooth pursuit. It receives input from the cerebellum via the superior cerebellar peduncle, lower brainstem, and the medial longitudinal fasciculus. Projections to oculomotor nuclei from the riMLF and INC for up movements decussate in the posterior commissure.

6. Clinical correlation: Vertical eye movements.

(a) Vertical palsies first affect saccades, as pursuit eye movements and vestibulo-ocular reflexes are often initially spared.
(b) Upgaze paresis is more common than combined up and down palsies which are more common than isolated downgaze palsies.
(c) Paresis of upgaze is caused by lesions of the posterior commissure or nucleus of the posterior commissure. There are rare instances of upgaze paresis due to lesions of the median raphe in the pons. The basis for this finding has not been completely elucidated. Proposed pathways from pons to oculomotor complex include the MLF and the ventral tegmental tract.

> Paresis of upward gaze is most often due to lesions of the posterior commissure.

(d) Paresis of downgaze saccades occurs with bilateral dorsomedial lesions of the riMLF and, if the lesions extend laterally, upgaze saccades are also impaired.

> Combined paresis of downgaze and upgaze saccades result from bilateral riMLF lesions.

The Visual Pathways (Fig. 6.4)

The first neuronal elements are rods and cones which contain pigment that, when exposed to light, produce electrical activity. At the posterior pole is the macula and, nasal to it, the optic nerve. Cones, which perceive color, are in the macula and rods

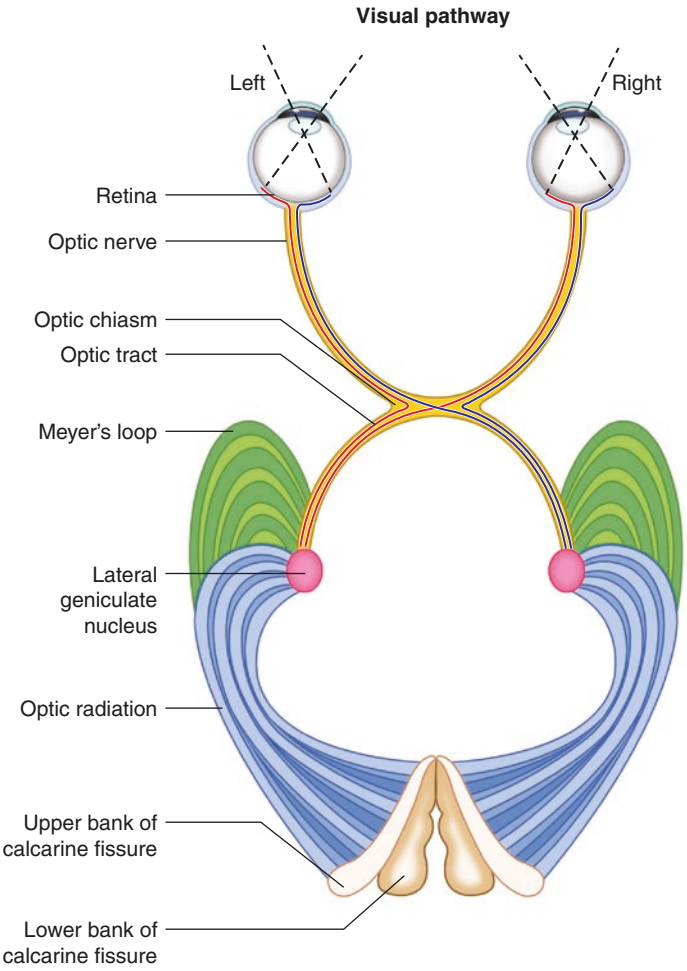

Fig. 6.4 Visual pathways

are located elsewhere. Both rods and cones convey activity to the ganglion cells, which provide the axons that comprise the optic nerve, optic chiasm, and optic tract. These synapse in the lateral geniculate nucleus.

Retinal ganglion cells provide the axons that comprise the optic nerve, optic chiasm, and optic tract.

The optic nerve has four sections. Average measurements include the optic nerve head (1 mm), intraorbital (25 mm), intracanalicular (9 mm), and the markedly variable intracranial segment (4–16 mm). The total length of the optic nerve averages about 45–50 mm.

The optic nerve fibers have a topical arrangement. Those which receive visual input from the temporal fields cross to the contralateral side of the chiasm. Optic nerve fibers receiving input from the nasal fields remain uncrossed. Macular fibers are both crossed and uncrossed, and believed to comprise approximately 90% of nerve fibers at the chiasm. The anterior–posterior diameter of the chiasm is approximately 1 cm and it varies from several millimeters to 1.5 cm above the diaphragma sellae.

Macular fibers are believed to comprise approximately 90% of the nerve fibers at the chiasm.

A prefixed chiasm (10%) is located over the anterior portion of the sella and postfixed (10%) behind the dorsum sella. About 80% of optic chiasms are just above the dorsum sella. Fibers from the inferior part of the nasal retina are in the ventral part of the chiasm. Fibers from the superior nasal retina remain dorsal in the chiasm. Consequently, pituitary neoplasms are more likely to affect superior temporal quadrants and lesions originating from above the chiasm, such as a craniopharyngioma, are more likely to cause inferior temporal quadrant defects.

The optic tract (2.5 cm) extends from the chiasm to the lateral geniculate nucleus of the thalamus. This nucleus receives the axons from the retinal ganglion cells. Neurons in the lateral geniculate nucleus provide axons which form the optic radiations. Meyer's loop is a portion of the radiations which run lateral to the temporal horn of the lateral ventricle about 5 cm behind the tip of the temporal lobe. The superior fibers correspond to the superior retina and, consequently, lesions in the parietal lobe may produce inferior homonymous (both eyes) quadrantanopsias. The inferior portion contains fibers from the inferior retina and, consequently, temporal lobe lesions may produce superior homonymous quadrantanopsias. The central portion of the optic radiations contains fibers from the macula which are both crossed and uncrossed. Thus, unilateral lesions of the optic radiations usually spare central vision.

Neurons in the lateral geniculate nucleus provide axons which form the optic radiations.

Parietal lobe lesions may cause inferior homonymous quadrantanopsias, and temporal lobe lesions may produce superior homonymous quadrantanopsias.

The visual cortex is located on the superior and inferior edges of the calcarine fissure in the occipital lobe. The right side, for example, contains fibers from the right temporal retina and left nasal retina. Thus, right occipital lobe lesions cause a contralateral homonymous hemianopsia. The occipital pole receives macular fibers

from both eyes such that central visual loss ordinarily occurs from bilateral involvement only. The term "striate cortex" is so named because the line of Gennari (a thick white band) is easily seen in the visual cortex without magnification. The striate cortex extends onto the convexity of the occipital lobe.

1. Clinical correlation: Visual impairments occurring with lesions of the visual pathways

Optic nerve lesions cause central scotomas first and decreased visual acuity second.

(a) Optic nerve lesions result in central scotomas (central, paracentral or cecocentral) first and decreased visual acuity second. Unilateral altitudinal or quadrantic visual field loss occurs most often with vascular pathology. Arcuate scotomas occur most often with glaucoma but can be secondary to virtually any other optic nerve pathology.
(b) Optic chiasm lesions usually produce central scotomas initially since approximately 90% of chiasm fibers represent macular vision. With progressive damage, bitemporal hemianopsias or unilateral temporal quadrantic field defects may occur. Lesions from below, such as pituitary neoplasms, typically produce superior visual field defects and lesions from above result in inferior visual field loss.
(c) Optic tract, lateral geniculate (rare), optic radiation, and occipital lobe lesions usually cause a contralateral homonymous hemianopsia.
(d) Incongruous (different amount of visual loss in each eye) homonymous hemianopsias or quadrantanopsias are most commonly noted with optic tract lesions, infrequently lateral geniculate lesions.
(e) Congruous (identical amount of visual loss in each eye) homonymous hemianopsias or quadrantanopsias may be observed with any lesion behind the chiasm.

Visual pathway lesions behind the optic chiasm cause contralateral homonymous hemianopsias.

(f) Parietal lobe lesions which involve the optic radiations are likely to produce inferior homonymous quadrantanopsias (pie-on-the-floor).
(g) Temporal lobe lesions are likely to cause superior homonymous quadrantanopsias (pie-in-the-sky).
(h) Occipital lobe lesions may produce homonymous hemianopsias, quadrantanopsias and, infrequently, homonymous scotomas which are easily overlooked on bedside examination. Commonly, homonymous scotomas are

seen in the process of recovering from a homonymous hemianopsia. Yet they frequently cause disabling symptoms.

(i) Medial occipital lobe lesions may cause a temporal crescent visual field loss affecting only one eye contralateral to the lesion as the temporal field is larger than the nasal field. Eight to ten percent of the anterior striate cortex has monocular innervation. This defect violates the general rule of homonymous visual field loss with involvement of visual pathways behind the chiasm.

Medial occipital lobe lesions may cause a temporal crescent visual field loss affecting only one eye contralateral to the lesion.

(j) The occipital tip represents foveal vision and receives macular fibers from both eyes. Consequently, with unilateral occipital lobe involvement there is usually macular sparing whereas bilateral lesions of the occipital tip can cause macular vision loss of the central 5 ° O.U. Stroke is a typical etiology of a macular sparing visual field defect and head injuries are the more common cause of macular involvement.

(k) Bilateral occipital lobe lesions are usually due to vascular disease involving the basilar artery system as both posterior cerebral arteries usually arise from the tip of the basilar artery. Visual field defects include superior or inferior altitudinal hemianopsias which have inverted representations. The upper banks receive innervation from the inferior visual fields and vice versa. Consequently, bilateral superior or inferior altitudinal field defects of abrupt onset are ordinarily due to basilar artery disease or cardioembolism to the basilar artery bifurcation where both posterior cerebral arteries usually originate.

Altitudinal homonymous hemianopsias are most often due to bilateral occipital lobe infarctions.

2. Synopsis: Visual impairments with visual pathway lesions.

(a) Optic nerve lesions: Central scotomas, unilateral altitudinal or quadrantic field defects, impaired visual acuity. (In order of clinical importance)

(b) Optic chiasm lesions: Central scotomas, bitemporal hemianopsia, unilateral temporal quadrant visual field loss, or combinations of central scotoma with temporal visual field loss. (In order of clinical importance)

(c) Optic tract lesions: Contralateral homonymous hemianopsia, often incongruous, rarely central scotomas, and homonymous scotomas. (In order of clinical importance)

(d) Lateral geniculate lesions (rare): Contralateral homonymous hemianopsia or quadrantanopsia, congruous or incongruous.

(e) Optic radiation lesions (temporal lobe): Congruous, contralateral homonymous hemianopsia or superior quadrantanopsia. Incongruity is uncommon.

(f) Optic radiation lesions (parietal lobe): Congruous, contralateral homonymous hemianopsia or inferior quadrantanopsia. Incongruity is uncommon.
(g) Occipital lobe lesions:

- Contralateral, congruous homonymous quadrantanopsias and hemianopsias, macular sparing, and with infrequent macular involvement.
- Homonymous scotomata, contralateral.
- Temporal crescent defect, contralateral.
- Altitudinal homonymous hemianopsias, inferior or superior.
- Bilateral incomplete homonymous hemianopsias or quadrantanopsias including checkerboard vision and cortical blindness. An example of checkerboard vision would be a right superior homonymous quadrantanopsia and a left inferior homonymous quadrantanopsia.
- Macular sparing (common) or, when there are bilateral lesions of the occipital tip, involvement of the central 5 ° O.U. (rare and typical of a traumatic etiology).

3. Extrastriate cortex and visual association areas.

(a) Extrastriate cortex encompasses all of the occipital lobe surrounding the primary visual cortex.
(b) Visual association areas extend from the extrastriate cortex to encompass adjacent posterior parietal lobe and much of the posterior temporal lobe.
(c) Lesions of visual association areas produce defects in higher order processing of visual information.
(d) Dorsal stream (occipitoparietal). Neurons are located in the parietal and superotemporal association areas. These areas are involved in spatial orientation, depth perception, location, movement in direction as well as velocity and visual guidance of movement.
(e) Lesions involving the dorsal stream may produce simultanagnosia, optic ataxia, oculomotor apraxia and hemispatial neglect.
(f) Ventral stream (occipitotemporal). Neurons are in the inferotemporal visual associated cortex. They are concerned with object recognition, color, shape and pattern.
(g) Lesions involving the ventral stream may produce alexia, anomia and agnosia.

The Sensory Systems

1. Decussation of the medial lemniscus (medulla) (Fig. 6.5).

The posterior (dorsal) columns mediate ipsilateral position and vibration sense. Lamination of its fibers from medial to lateral are sacral, lumbar, thoracic, and cervical.

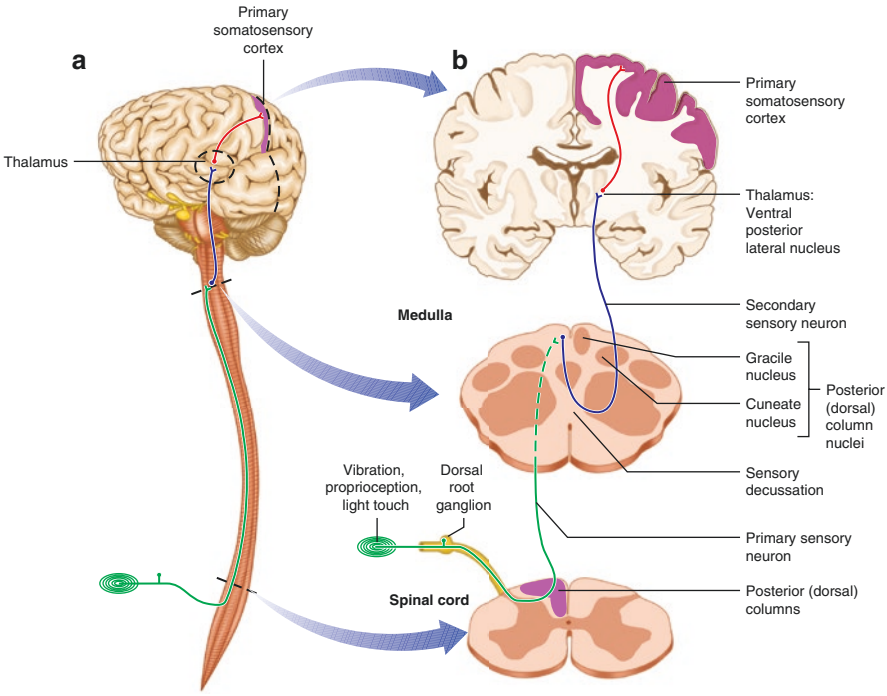

Fig. 6.5 Posterior column-medial lemniscus pathway. (Adapted from Blumenfeld [1])

This pathway primarily mediates position and vibration sense. Secondarily, with regard to clinical importance, are fibers for pressure and touch.

Large myelinated fibers exit from the dorsal horn to ascend in the ipsilateral posterior columns, the fasciculus gracilis (medial), and cuneatus (lateral). There is a somatotopic arrangement as sacral fibers are medially placed and subsequent fibers are gradually layered in adjacent fashion, leg next and arm lateral, as the tract moves rostrally to synapse in the nucleus gracilis and cuneatus in the medulla. Axons of cells in these nuclei decussate in the medial lemniscus which is midline in the medulla. They largely maintain the somatotopic arrangement as they ascend to the ventral posterolateral (VPL) nucleus of the thalamus. Axons from this thalamic nucleus project to the postcentral gyrus in the parietal lobe. The calf and foot are represented on the medial surface of the cerebral hemisphere followed by the thigh, abdomen, and chest. The shoulder neurons are on the tip of the convexity. The arm, hand, digits, and face are represented successively over the convexities. The three latter anatomic structures comprise the majority of the surface of the parietal lobe.

Lesions above the medial lemniscus decussation produce contralateral loss of position and vibration sense.

2. Clinical correlation:

   (a) Spinal cord lesions: Ipsilateral impairment of vibration and position sense. Vibration sense is lost first.
   (b) Brainstem lesions: Contralateral impairment of vibration and position sense. Vibration sense loss is more prominent.
   (c) Thalamic lesions (VPL nucleus): Contralateral impairment of vibration and position sense. Either sensory function can be affected first.
   (d) Parietal lesions: Contralateral loss of position sense much more prominent than vibration sense. Vibration perception is commonly preserved.

> Vibration sense is lost before position sense with any lesion of the central or peripheral nervous system except for those in the cerebral hemisphere. Thalamic lesions are variable.

3. Decussation of the anterior commissure of the spinal cord (Fig. 6.6)

Small, unmyelinated fibers mediating pain and temperature enter the spinal cord, descend one or two segments in the zone of Lissauer and synapse in the dorsal horn.

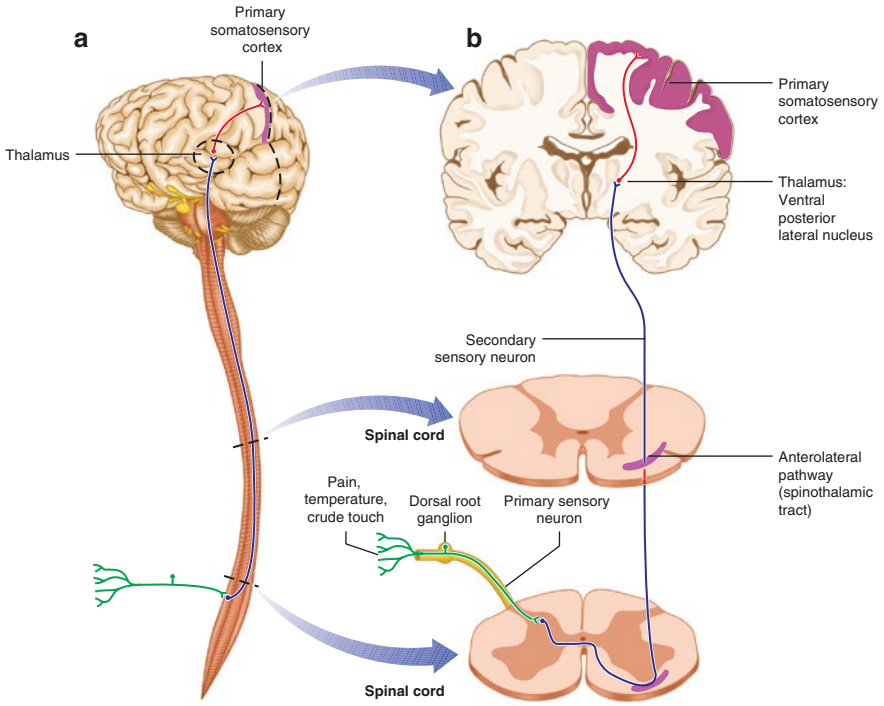

Fig. 6.6 Lateral spinothalamic pathway. (Adapted from Blumenfeld [1])

Axons from these neurons decussate in the anterior commissure and ascend in the ventrolateral portion of the spinal cord. There is a somatotopic arrangement with sacral fibers laterally placed followed by lumbar, thoracic, and cervical. The fibers are gradually layered, adjacent and medial, as the tract moves rostrally. This arrangement is unchanged as the tract ascends and synapses in the VPL nucleus of the thalamus. Axons from the VPL then ascend to the postcentral gyrus of the parietal lobe and are distributed in the same fashion as those mediating position and vibration sense.

The lateral spinothalamic tract which already contains crossed fibers mediating pain and temperature ascends and synapses with the ipsilateral VPL nucleus of the thalamus.

4. Clinical correlation:

   (a) Spinal cord lesions may cause contralateral loss of pain and temperature producing a sensory level, commonly one or two dermatomes below the level of the lesion. In clinical practice, it is not unusual to find sensory levels much below the location of the lesion.

   Spinal cord lesions may cause contralateral loss of pain and temperature producing a sensory level. Occasionally, the level may be far below the location of the lesion.

   (b) Cerebral, thalamic, and brainstem lesions may cause contralateral loss of pain and temperature sensation.

Questions (True or False)

1. The corticospinal tract arises solely from the frontal lobe.
2. Corticospinal tract lesions in the brainstem cause a contralateral hemiparesis.
3. Bilateral arm paralysis may be due to lesions of the high cervical cord.
4. Contralateral facial weakness can be caused by midbrain lesions.
5. Central facial weakness may be associated with weakness of orbicularis oculi.
6. The masseter muscle has equal bilateral innervation.
7. Dysphagia rarely occurs with an acute cerebral lesion.
8. Dysarthria has localizing significance.
9. The oculomotor pathway decussates between the midbrain and the pons.
10. The medial longitudinal fasciculus initiates conjugate gaze.
11. The right PPRF sends fibers to interneurons in the right 6th nucleus which provide axons forming part of the left MLF.

12. Lesions of the posterior commissure produce upgaze paralysis.
13. The majority of nerve fibers in the optic nerve come from the temporal fields.
14. The central scotoma is a hallmark finding with optic nerve disease.
15. The earliest sign of an optic chiasm lesion is a bitemporal hemianopsia.
16. Incongruous homonymous hemianopsias are often due to optic tract lesions.
17. Monocular visual field defects are always due to lesions anterior to the chiasm.
18. Neurons of the VPL nucleus of the thalamus receive input from the lateral spinothalamic tract and the medial lemniscus.
19. Heavily myelinated fibers mediating pain and temperature cross in the anterior commissure.
20. Bilateral occipital lobe lesions may cause altitudinal homonymous hemianopsias.

Answers

1. F
2. T
3. T
4. T
5. T
6. F
7. T
8. F
9. T
10. F
11. T
12. T
13. F
14. T
15. F
16. T
17. F
18. T
19. F
20. T

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Chapter 7
Cerebrovascular Anatomy with Clinical Correlation

Cerebrovascular disease ordinarily comprises about 5–10% of the outpatient practice of a general neurologist, but it is the predominant disorder in the hospital. Thus, the medical student experience is usually skewed toward evaluation and treatment of stroke, a critically important field. Adequate preparation to make the most of an inpatient experience requires a familiarity with vascular anatomy prior to beginning the mandatory rotation, presumably a minimum of 1 month. This will be summarized to emphasize salient features. Discussion of pathology is essential since ischemic strokes (85%) and hemorrhagic strokes (15%) have distinctive clinical and anatomic patterns. Treatment options will be only briefly mentioned since new therapies and management protocols will be constantly emerging. Case reports will be added to illustrate the importance of the history and neurologic examination to determine both the anatomic and pathologic diagnosis, the evaluation indicated, and some current treatment approaches.

Ischemic Stroke (Cerebral Infarction) and Transient Ischemic Attack (TIA)

> Cerebrovascular accident (CVA) is an unacceptable term since it does not distinguish between hemorrhage and infarction. Nor is this event an accident, an inappropriate designation.

Terminology must be clarified first. Strokes are either ischemic or hemorrhagic. An ischemic stroke is a cerebral infarction caused by an arterial occlusion in situ or by an embolic event. A hemorrhagic stroke is an intracerebral hematoma, intraventricular hemorrhage or a subarachnoid hemorrhage (SAH). Cerebrovascular accident

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https://doi.org/10.1007/978-3-319-95951-1_7

(CVA) is an unacceptable diagnostic term since it does not distinguish between infarction and hemorrhage. Nor is this event an accident, an inappropriate designation. Moreover, is a "right-sided CVA" a right cerebral infarction, a right cerebral hemorrhage, or a right hemiparesis? Does this label encompass brainstem infarctions or hemorrhage?

The anatomic source of ischemic stroke, extracranial and intracranial vascular disease or cardioembolism, determines treatment selection and should be part of the diagnosis.

The anatomic source of ischemic stroke, extracranial and intracranial vascular disease or cardioembolism, determines treatment selection and should be part of the diagnosis. The exception is tissue plasminogen activator (TPA) which is used within 4.5 h of the onset of an acute ischemic stroke irrespective of etiology. Ischemic stroke caused by extracranial atherosclerotic disease is nearly always, perhaps 95%, due to embolism. It has been estimated that a hemodynamic origin of stroke due to a carotid artery stenosis may only occur if the residual lumen is 2 mm or less. Hence a statement that a stroke is due to "thromboembolism," a not infrequently made diagnosis, is not sufficient to make a treatment recommendation.

Arterial atherosclerotic disease requires use of antiplatelet agents since the embolic material is a platelet/fibrin complex. Naturally, an endarterectomy or stenting are part of the treatment options. Apart from treating the underlying cardiac pathology cardioembolism is prevented by anticoagulation using warfarin, heparin or thrombin inhibitors as the embolic material comes from a red thrombus. Cholesterol embolism as a cause of stroke is rare. Hollenhorst plaques which are visible at retinal arteriole bifurcations are composed of cholesterol but are commonly found in asymptomatic patients. Lack of symptomatology may be due to their usual small size, flat shape and lack of significant interference with blood flow.

The vascular distribution of TIA or stroke must also be stipulated. Treatment selection is often determined by this information. For example, a TIA in the vertebrobasilar distribution is not treated by a carotid artery endarterectomy. Thus the history and neurologic examination supersedes the neuroimaging pathology.

Case 1 A 45-year-old man arrives in the Emergency Department with a history of slurred speech and right-sided weakness. He has coronary artery disease and smokes one pack of cigarettes per day. A fourth-year medical student on the cardiology service carefully questions the patient about his symptoms. For 5 min the patient's speech was barely intelligible according to witnesses. His words were spoken correctly but with marked slurring. Weakness was greater in the arm than the leg and walking was unstable. By the time the patient arrived in the Emergency Department he was normal.

A carotid Doppler showed a smooth 60% left internal carotid artery stenosis and a CT scan of the brain was normal. Bilateral carotid angiography confirmed the

pathology. Vascular surgery consultation was obtained and a left carotid endarterectomy was recommended. A neurologic consultation was then requested.

The neurology consultant queried the patient about specific additional neurologic symptoms. The patient had both auditory and visual symptomatology. He now recollects that he heard noises in one ear and saw colored spots in the left visual field for 1–2 min. An MRA (head and neck) was obtained and disclosed a severe basilar artery stenosis. This was not visualized on carotid angiography. The order should have stipulated four-vessel angiography or carotid and vertebral angiography. Many if not most neuroradiologists would have requested and performed a four-vessel study anyway. Nevertheless, a specific order is preferable and reinforces the principle that all vessels must be visualized when evaluating ischemic cerebrovascular disease.

Final diagnosis TIA in the vertebrobasilar distribution due to a basilar artery stenosis [1].

Lesson No. 1 Most TIAs last less than 5 min, rarely over 30 min.

Lesson No. 2 Dysarthria is a nonlocalizing symptom and must be distinguished from aphasia, a language disorder which presumes left cerebral hemisphere disease even if the patient is left-handed. A left-handed patient has only about a 50% chance that he or she is right hemisphere dominant.

> Dysarthria must be distinguished from aphasia. Dysarthria is nonlocalizing whereas aphasia indicates dominant hemisphere involvement.

Lesson No. 3 A neurologic history must include a complete review of all neurologic symptoms. Patients often need prompting to recall symptoms of diagnostic significance such as in this case.

> A complete review of all neurologic symptoms is essential in every neurologic evaluation.

Lesson No. 4 Hemiparesis is not a localizing symptom or finding other than usually indicating central nervous system but not peripheral nervous system disease.

Lesson No. 5 Auditory symptoms may occur with posterior circulation ischemic events but rarely with cerebral hemisphere ischemia.

Lesson No. 6 Seeing colored spots, unformed visual hallucinations, are characteristic of occipital lobe ischemia or neuronal dysfunction of nonvascular origin.

Lesson No. 7 The vascular supply of the occipital lobe is the posterior cerebral artery (PCA) which arises from the tip of the basilar artery. An infrequent exception is an anatomic variant whereby the PCA arises directly from the internal carotid artery.

Lesson No. 8 The left visual field location of the colored spots is contralateral to the right hemiparesis, thus ruling out a left internal carotid origin of the ischemic symptoms.

Neurovascular anatomy begins with the aortic arch and great vessels (see Figs. 7.1 and 7.2). Clearly, cardioembolism or embolism from the aortic arch (rare) are most likely to enter the carotid circulation, left more than right, because of the direct large vessel route. Approximately 70% of cardioembolic events occur in the carotid artery distribution. Of these, 60–65% are in the middle cerebral and about 6–8% in the

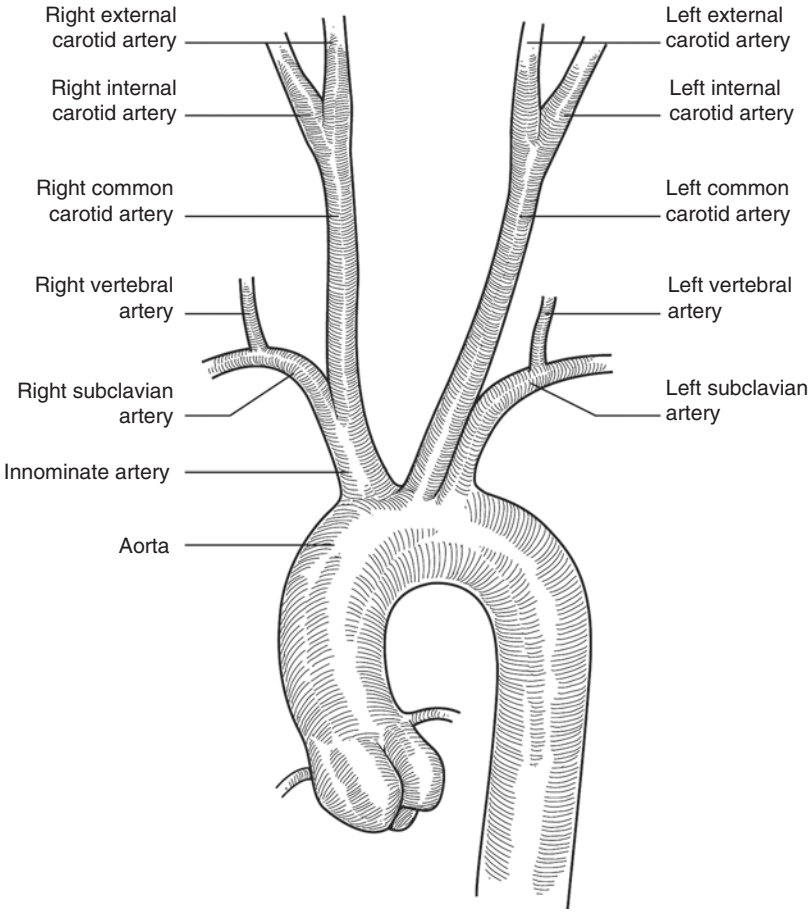


Fig. 7.1 Aortic arch and branches

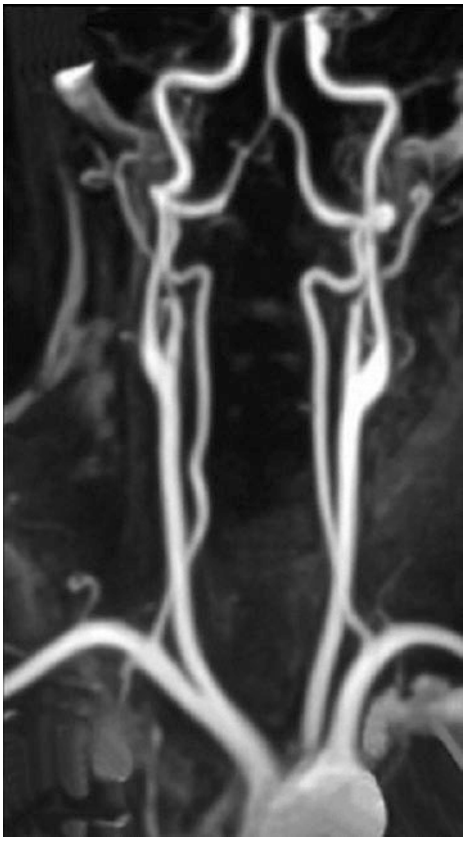


Fig. 7.2 Magnetic resonance angiography of the aortic arch and branches

anterior cerebral vascular systems. The vertebrobasilar circulation receives 23%, multiple areas 5% and watershed zones 2% of cardioembolic incidents.

The vertebral arteries arise from the subclavian arteries and, infrequently, the aortic arch. The right vertebral artery may originate from the innominate artery rather than the subclavian artery. The vertebral arteries are frequently asymmetric and the left is most often larger. The vertebral artery enters the transverse foramen at C6 and exits at C2 curving around the atlanto-occipital junction. It then enters the skull through the foramen magnum.

Vertebral arteries are frequently asymmetric and the left is most often larger.

The posterior inferior cerebellar artery (PICA) usually originates from the vertebral artery several millimeters above the foramen magnum, circles the medulla, and supplies the dorsolateral medulla. A medial trunk irrigates the cerebellar vermis and adjacent cerebellar hemisphere. A lateral trunk supplies the cortical surface of the cerebellar tonsils and inferior cerebellar hemisphere.

The posterior inferior cerebellar artery (PICA) usually originates from the vertebral artery above the foramen magnum and supplies the dorsolateral medulla. The medial trunk irrigates the cerebellar vermis and the lateral trunk supplies the cerebellar tonsils and inferior cerebellar hemisphere.

The anterior spinal artery is formed by an anastomosis of two branches derived from both intracranial vertebral arteries immediately below the origin of the basilar artery (Fig. 7.3). It extends from the medulla where it supplies its ventral surface, travels down the anterior sulcus of the spinal cord all the way to the conus medullaris and cauda equina. There are radicular arteries arising from the aorta at lower cervical and upper thoracic levels that provide additional vascular support. The anterior two-thirds of the spinal cord is supplied by the anterior spinal arteries and its branches.

The origin of the posterior spinal artery is usually the vertebral arteries and these supply the posterior one-third of the spinal cord. There are posterior radicular arteries which provide additional flow to the posterior spinal artery.

The thoracic cord between T3 and T8 has limited vascular supply and is particularly vulnerable to transient interruption of blood flow such as may occur with repair of a thoracic or abdominal aortic aneurysm. The artery of Adamkiewicz arises from the abdominal aorta and enters the spinal canal between T9 and L2. It is a large, major contributor to the anterior spinal artery vasculature. Its protection during abdominal surgery is essential to prevent paraplegia due to a thoracic spinal cord infarction.

The thoracic cord between T3 and T8 has a limited vascular supply and is particularly vulnerable to transient interruption of blood flow.

The two vertebral arteries merge and form the basilar artery at about the pontomedullary junction (see Figs. 7.3 and 7.4). The long lateral circumferential, short lateral circumferential, and median arteries arise from the basilar artery. The classical crossed syndromes such as Weber's and Benedikt's are, in most instances, due to pathology in the small, median, penetrating vessels arising from the basilar artery. These syndromes are defined in Chap. 13. The pathology in these arteries is either microatheroma or lipohyalinosis, the subintimal collection of hyaline material which stains for fat. The latter can lead to vessel occlusion and produce small infarctions (lacunes). These lacunar infarcts range from 0.2 mm to 15 mm in size and are commonly found in deep subcortical white matter.

The two vertebral arteries merge and form the basilar artery at about the pontomedullary junction.

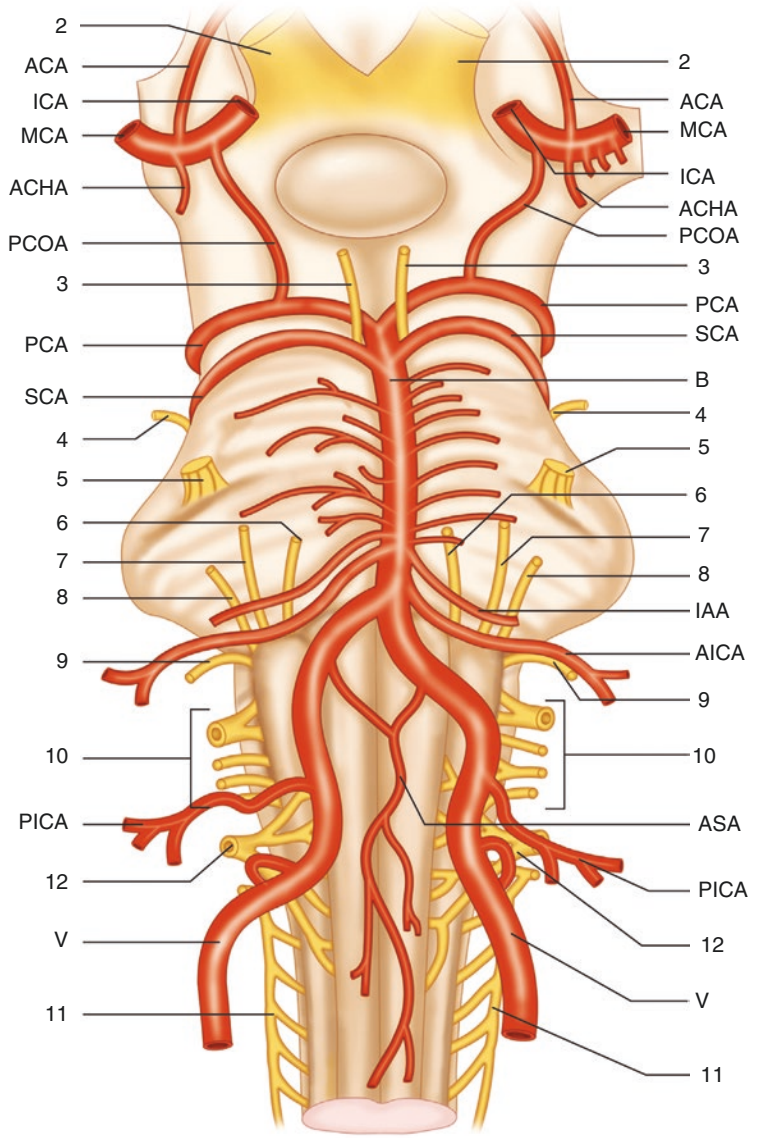
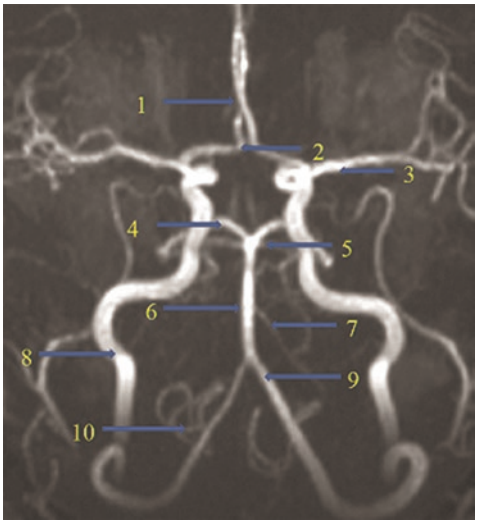


Fig. 7.3 Vertebrobasilar circulation with adjacent cranial nerves and a portion of the circle of Willis. ACA anterior cerebral artery, ACHA anterior choroidal artery, AICA anterior inferior cerebellar artery, ASA anterior spinal artery, B basilar artery, IAA internal auditory artery, ICA internal carotid artery, MCA middle cerebral artery, PCA posterior cerebral artery, PCOA posterior communicating artery, PICA posterior inferior cerebellar artery, SCA superior cerebellar artery, V vertebral artery. 2 optic nerve, 3 oculomotor nerve, 4 trochlear nerve, 5 trigeminal nerve, 6 abducens nerve, 7 facial nerve, 8 vestibulocochlear nerve, 9 glossopharyngeal nerve, 10 vagus nerve, 11 spinal accessory nerve, 12 hypoglossal nerve



1) Anterior Cerebral Artery
2) Anterior Communicating Artery
3) Middle Cerebral Artery
4) Posterior Cerebral Artery
5) Superior Cerebral Artery
6) Basilar Artery
7) Anterior Inferior Cerebellar Artery
8) Internal Carotid Artery
9) Vertebral Artery
10) Posterior Inferior Cerebellar Artery

Fig. 7.4 MRA of intracranial vasculature, anterior–posterior view

There are three long lateral circumferential arteries which arise from the basilar artery (see Fig. 7.3). From below upward they are the anterior inferior cerebellar artery (AICA), superior cerebellar artery (SCA), and posterior cerebral artery (PCA). A fourth, the internal auditory artery, arises from the basilar artery just above the origin of AICA or as a branch of AICA.

AICA courses around the pons, travels through the cerebellopontine angle, supplies the lateral tegmentum of the lower two-thirds of the pons, middle cerebellar peduncle (brachium pontis), and the ventrolateral cerebellum. The internal auditory artery supplies the cochlear and vestibular apparatus as well as the facial nerves.

The SCA arises from the distal portion of the basilar artery just below the basilar tip and close to the pontomesencephalic junction. It circles around the midbrain, supplies the upper pons and midbrain tegmentum, tentorial surface of the cerebellum, superior and lateral cerebellar hemispheres, and superior cerebellar peduncle (brachium conjunctivum).

The posterior cerebral artery originates from the basilar tip and, infrequently (14%), from the internal carotid artery. It supplies the occipital lobes, inferomedial portion of the temporal lobes, midbrain, thalamus, choroid plexus, and ependyma of the third and lateral ventricles. The first branches off the PCA are the small thalamoperforating arteries that supply the midbrain, thalamus, and lateral geniculate nucleus. The medial and lateral posterior choroidal arteries are the next branches which supply the thalamus in its posterior portion and the choroid plexus. The anterior portion of the PCA gives rise to the inferior temporal arteries which supply the inferior portion of the temporal lobe. Terminal branches of the PCA supply the parieto-occipital regions and, most importantly, give rise to the calcarine artery which supplies the visual cortex.

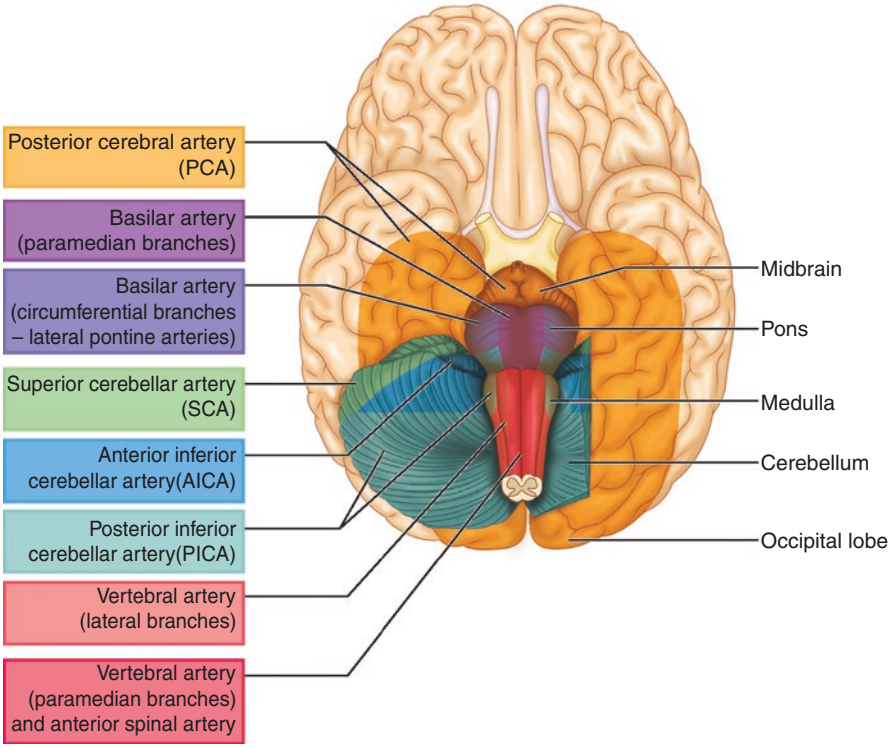


Fig. 7.5 Vascular distribution of posterior circulation

The vascular supply of the vertebrobasilar system and its relationship to cranial nerves is displayed in Fig. 7.3. The vascular irrigation patterns are shown in Fig. 7.5.

The common carotid arteries originate from the aortic arch on the left and usually the innominate artery on the right. The proximal common carotid artery is seldom the site of symptomatic atherosclerotic disease. It bifurcates into the internal and external carotid arteries.

> The common carotid arteries originate from the aortic arch on the left and usually the innominate artery on the right. It is seldom the site of symptomatic atherosclerotic disease.

The external carotid artery has several clinically important branches. It divides into the superficial temporal and internal maxillary artery. The superficial temporal artery begins within the parotid gland, ascends to just in front of the ear so that it is easily palpated, and extends to the forehead. Temporal arteritis frequently involves this vessel and the internal maxillary artery which supplies deep structures of the

face including the muscles of mastication. Hence headache and jaw claudication are common presenting symptoms. One branch of the internal maxillary artery is the middle meningeal artery which supplies the dura. Head trauma, especially associated with a skull fracture, may sever this artery which then results in an epidural hematoma. The occipital artery arises directly from the posterior part of the external carotid artery, supplies the posterior scalp and it may provide collaterals to the extracranial portion of the vertebral artery. Consequently, occipital pain may also occur with temporal arteritis, although infrequent.

The external carotid artery branches include the superficial temporal, internal maxillary and occipital arteries; the internal maxillary artery is the origin of the middle meningeal artery.

The lowest portion of the internal carotid artery is the usual site of atherosclerotic plaques. The high cervical internal carotid artery is often the diseased site in patients with fibromuscular dysplasia, internal carotid artery dissections, and those who have been treated with radiotherapy in that location. The other parts of the internal carotid artery are the petrous, cavernous, and supraclinoid portions. The internal carotid artery in the cavernous sinus is adjacent to cranial nerves 3, 4, $5_{1, 2}$, and 6. (Fig. 7.6).

The ophthalmic artery is the first major branch of the internal carotid artery in its supraclinoid portion. Its branches include the short posterior ciliary arteries which supply the optic nerve and the central retinal artery which irrigates the retina. The vascular supply to the optic nerve warrants special attention (see Fig. 7.7). The ophthalmic artery sends perforating branches to the intraorbital portion of the optic nerve. Branches of the short posterior ciliary arteries supply the optic nerve directly as well as anastomose to form the circle of Zinn-Haller. Branches from this circle also irrigate the optic nerve. Accordingly, the short posterior ciliary arteries are the

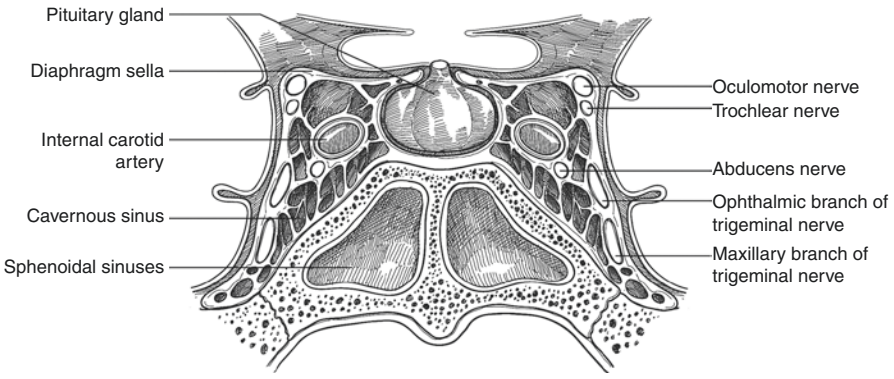


Fig. 7.6 Cavernous sinus anatomy

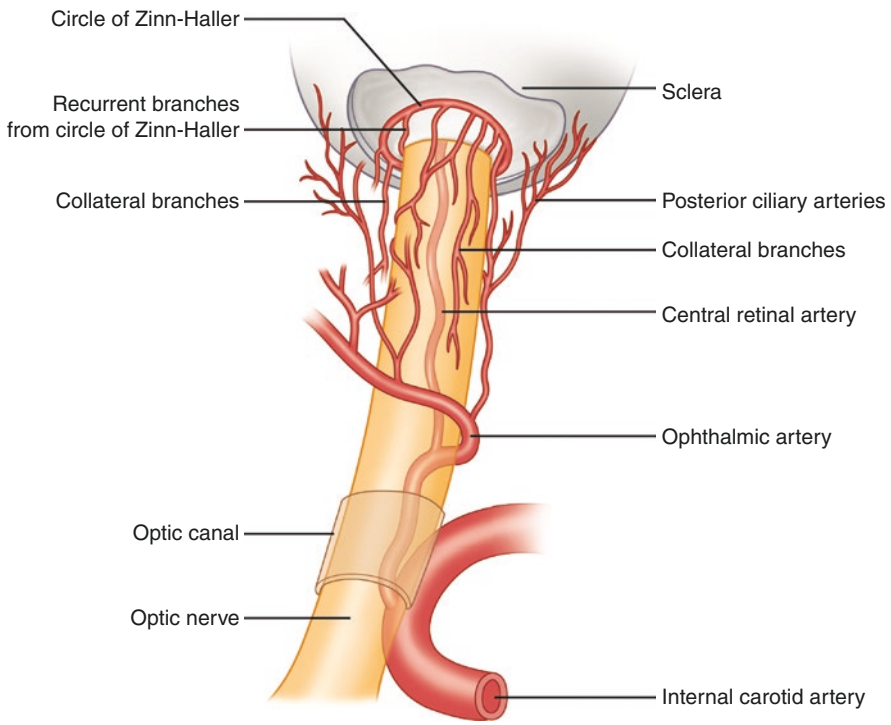


Fig. 7.7 Vascular supply of the globe. The ophthalmic artery, the first major branch of the internal carotid artery, supplies the globe. It provides collateral branches to the optic nerve. Its two major branches are the central retinal artery destined to supply only the inner surface of the retina and the posterior ciliary arteries which irrigate the choroid, optic nerve and the optic disk by means of an anastomotic channel of arterioles (the circle of Zinn-Haller). (Adapted from Digre and Corbett [2])

primary vascular supply of the optic nerve. The single central retinal artery supplies the entire retina. Thus an embolus to the central retinal artery causes blindness or severe visual loss but an embolus to one short posterior ciliary artery is usually asymptomatic because of the rich vascular anastomoses. Anterior ischemic optic neuropathy, both arteritic (temporal arteritis) and nonarteritic, is a result of vascular pathology affecting the short posterior ciliary arteries [3].

The ophthalmic artery, the first branch of the internal carotid artery, is the origin of the central retinal artery which supplies the retina and the short posterior ciliary arteries which supply the optic nerve.

The posterior communicating artery is the next branch of the internal carotid artery. It supplies the anterior and posterior hypothalamus, optic tract, posterior part of the optic chiasm and the anterior and ventral thalamic nuclei. The circle of Willis

connects the anterior circulation system (internal carotid artery) with the posterior circulation system (posterior cerebral artery) via the posterior communicating artery.

The anterior choroidal artery (Fig. 7.3) supplies the optic tract, lateral geniculate nucleus, hippocampus, optic radiations, and a large part of the posterior limb of the internal capsule. It is the most important supply of the internal capsule after the middle cerebral artery branches. Memory impairment and amnesia have been documented with anterior choroidal artery occlusions. Eventual recovery would be expected, however, because of only unilateral involvement. As mentioned previously severe memory loss occurs almost exclusively with bilateral cerebral disease.

The ACA (Fig. 7.4) arises from the bifurcation of the internal carotid artery. It is a midline vessel which supplies the medial surface of each cerebral hemisphere and the upper 2 cm of the frontal and parietal convexity. The ACA's A1 segment begins at the bifurcation of the internal carotid artery and ends at the level of the anterior communicating artery (ACoA) and ACA junction. The A2 segment begins at this junction and continues to the genu of the corpus callosum. Penetrating branches from the A1 segment supply the optic nerve, optic chiasm, optic tract, hypothalamus, inferior frontal lobe, and suprachiasmatic region. The A2 segment's penetrating branches supply the hypothalamus and anterior striatum. The artery of Heubner is commonly the first branch of the A2 segment and supplies the anterior limb of the internal capsule, anterior putamen, anterior globus pallidus, head of the caudate nucleus, hypothalamus, and olfactory regions.

The anterior cerebral artery (ACA) is a midline vessel which supplies the medial surface of each cerebral hemisphere and the upper border of the frontal and parietal lobes.

The two major branches of the ACA are the pericallosal and callosomarginal arteries. The pericallosal artery travels just over the corpus callosum and the callosomarginal, if present, runs near or in the cingulate sulcus; both are easily identified in most angiograms. These vessels supply the inferior frontal lobe, medial surface of the cerebral hemispheres, corpus callosum and the superior 2 cm of the lateral convexity, frontal and parietal regions.

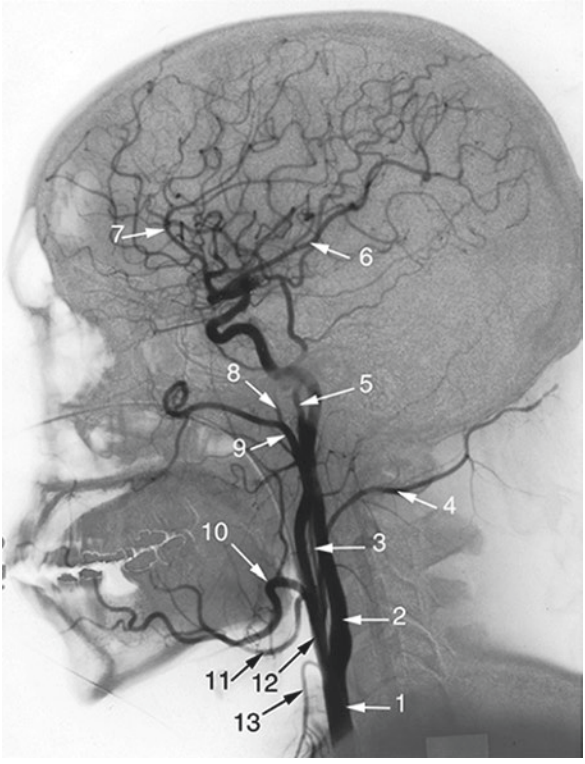
The very short ACoA which averages 4 mm in length and 1.5 mm in diameter supplies the suprachiasmatic region, dorsal optic chiasm, inferior frontal lobe, fornix, anterior portion of the corpus callosum, septal area, and anterior hypothalamus. Treatment of ACoA aneurysms is especially hazardous since ischemia or vasospasm in small branches of this artery may produce akinetic mutism.

The anterior communicating artery averages 1.5 mm in diameter and 4 mm in length.

The middle cerebral artery (see Figs. 7.4 and 7.8) irrigates the lateral surface of the cerebral hemispheres which include frontal, parietal, and temporal cortex along with the insula. The proximal portion (M1 segment) gives rise to the lenticulostriate vessels which supply the corona radiata, external capsule, putamen, portions of the globus pallidus, caudate, and most of the anterior and posterior internal capsules.

The middle cerebral artery irrigates the lateral surface of the cerebral hemispheres which include frontal, parietal, and temporal cortex including the insula.

There may be a bifurcation or trifurcation of the middle cerebral artery stem. The bifurcation pattern is most common and provides a superior and inferior division. The superior division gives rise to the orbitofrontal, precentral, central, and anterior parietal arteries. The inferior division gives off the posterior parietal, posterior



1) Common Carotid Artery
2) Internal Carotid Artery
3) Ascending Pharyngeal Artery
4) Occipital Artery
5) Superficial Temporal Artery
6) Middle Cerebral Artery
7) Anterior Cerebral Artery
8) Middle Meningeal Artery
9) Maxillary Artery
10) Facial Artery
11) Lingual Artery
12) External Carotid Artery
13) Superior Thyroid Artery

Fig. 7.8 Internal and external carotid system, lateral angiographic view. (With permission of Dr. Eric Bershad)

temporal, and angular arteries. The trifurcation pattern has an upper division which supplies much of the frontal lobe, a middle division which divides into the central, anterior parietal, and angular branch and an inferior division which supplies most of the temporal lobe and temporo-occipital region.

The lenticulostriate vessels arise from the M1 segment of the middle cerebral artery and supply most of the internal capsule. The stem of the middle cerebral artery has a bifurcation or trifurcation pattern.

Figure 7.8 illustrates the anatomy of the internal carotid system through a lateral angiographic view. Figures 7.9, 7.10, and 7.11 display the vascular supply of the internal carotid artery system.

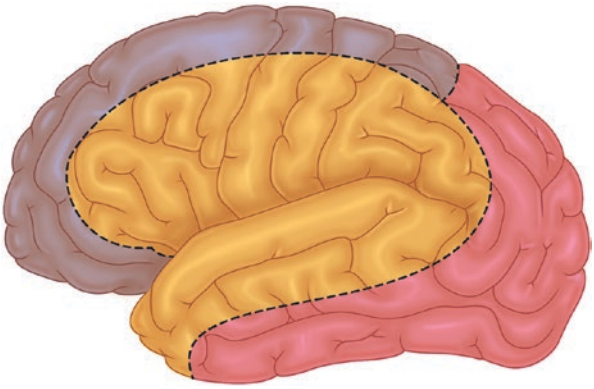


Fig. 7.9 Vascular supply of lateral portion of cerebral hemisphere. pink PCA distribution, yellow MCA distribution, gray ACA distribution

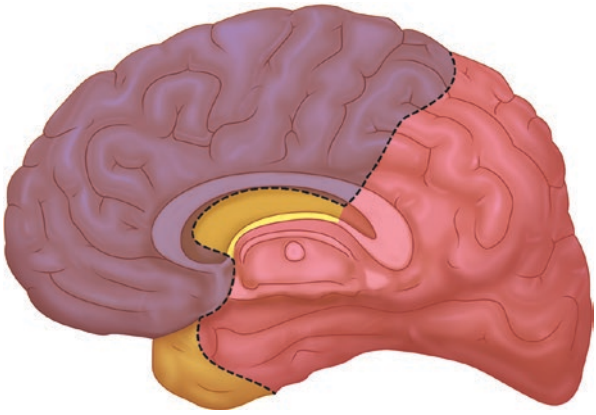


Fig. 7.10 Vascular supply of medial portion of cerebral hemisphere. pink PCA distribution, yellow MCA distribution, gray ACA distribution

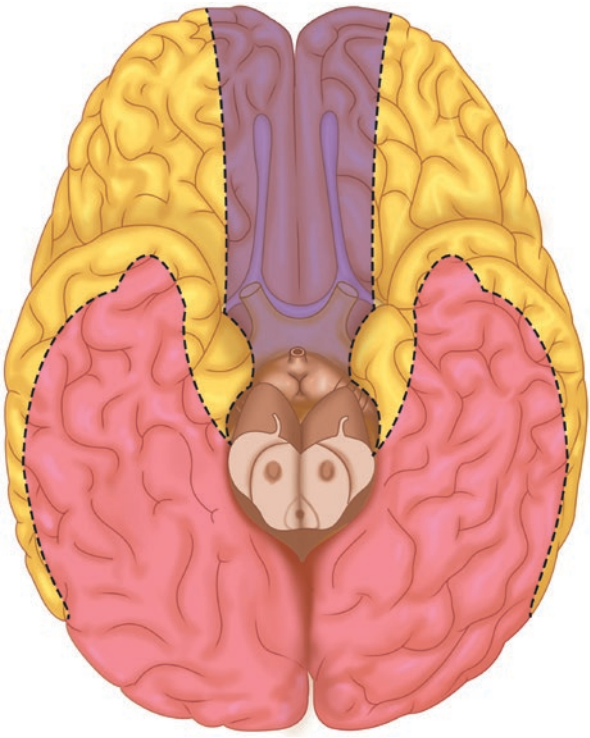


Fig. 7.11 Vascular supply of inferior portion of cerebral hemisphere. pink PCA distribution, yellow MCA distribution, gray ACA distribution

Summary

1. Major Branches of the Vertebrobasilar System.
   (a) Posterior inferior cerebellar artery. This vessel originates from the vertebral artery and supplies the dorsolateral medulla, cerebellar tonsils, inferior cerebellar hemisphere, inferior vermis and adjacent cerebellar hemisphere.
   (b) Anterior inferior cerebellar artery. This vessel arises from the most proximal section of the basilar artery and supplies the lateral and lower two-thirds of the pons, middle cerebellar peduncle (brachium pontis) and anterior inferior aspect of the cerebellar hemisphere. It travels through the cerebellopontine angle.
   (c) Internal auditory artery. This artery originates either from the AICA or directly from the basilar artery. If it is derived from the basilar artery it lies immediately rostral to the AICA. It supplies the vestibular and cochlear apparatus.
   (d) Superior cerebellar artery. This artery originates from the distal portion of the basilar artery irrigating the upper pons, midbrain tegmentum, quadrigeminal plate, superior cerebellar peduncle (brachium conjunctivum), superior medullary velum, superior vermis and the posterior part of the cerebellar hemispheres.

(e) Posterior cerebral artery. This vessel begins at the tip of the basilar artery or, infrequently (14%), from the internal carotid artery and supplies the midbrain, thalamus, lateral geniculate nucleus, inferior temporal lobe, parieto-occipital region, and occipital lobe.
(f) Anterior spinal artery. It is formed by an anastomosis of branches from both vertebral arteries. It irrigates the ventral medulla and anterior two-thirds of the spinal cord down to the cauda equina.

2. Major Branches of the Internal and External Carotid Arteries (Fig. 7.8).

(a) External carotid artery begins at the common carotid bifurcation. Its branches are:

- Superficial temporal artery. This vessel is palpable, located in front of the ear, and easily biopsied when temporal arteritis is suspected.
- Internal maxillary artery. It supplies the muscles of mastication.
- Middle meningeal artery. This vessel arises from the internal maxillary artery, supplies the dura mater and, especially, bone.
- Occipital artery. This artery supplies the posterior scalp.

(b) Internal carotid artery begins at the common carotid bifurcation. Its branches are:

- Ophthalmic artery. This is the first major branch of the internal carotid artery in its supraclinoid portion. It gives rise to the central retinal artery which irrigates the entire retina. The short posterior ciliary arteries anastomose to form the circle of Zinn-Haller. These arteries and collateral branches from the circle of Zinn-Haller supply the optic nerve (Fig. 7.7).
- Posterior communicating artery. This second offshoot from the intracranial portion of the internal carotid artery anastomoses with the PCA connecting the anterior and posterior circulation which completes the circle of Willis.
- Anterior choroidal artery. This is the third branch off the internal carotid artery and is the second most important vascular contribution to the internal capsule. Additionally, it supplies the optic tract, lateral geniculate nucleus, optic radiations, and hippocampus.

(c) Anterior cerebral artery. This large artery arises from the internal carotid artery bifurcation. It is a midline vessel which irrigates the medial surface of the cerebral hemispheres, corpus callosum, and the upper 2 cm of the frontal and parietal convexities. Other branches supply the optic chiasm, optic tract, and hypothalamus.

- Anterior communicating artery. This small artery averages 1.5 mm in diameter and 4 mm in length, connects both anterior cerebral arteries and supplies the chiasm, septal region, hypothalamus, and anterior parts of the fornix and corpus callosum.

(d) Middle cerebral artery. This large artery arises from the internal carotid artery bifurcation. It irrigates the lateral surface of the cerebral hemispheres including frontal, parietal, and temporal cortex as well as the insula. Lenticulostriate branches from the horizontal M1 segment supply most of the anterior and posterior limbs of the internal capsule and basal ganglia.

Case 2 A 77-year-old woman reports an episode of loss of vision of the right eye lasting 3 min. She describes a black curtain descending over the eye. Her past medical history includes severe chronic obstructive pulmonary disease (COPD) and a 60-pack year smoking habit. Medications are an Albuterol inhaler and prednisone 5 mg q.d.

Neurologic examination is normal other than bilateral carotid bruits heard only over the high cervical region just under the mandible.

Diagnosis Amaurosis fugax secondary to embolism from a right internal carotid artery stenosis/plaque.

Preliminary studies MRI (head) shows multiple T2 hyperintensities in subcortical white matter. Carotid Doppler studies disclose 50–79% stenoses of both internal carotid arteries. Cerebral angiography reveals a severe right internal carotid artery stenosis (90%) with ulcerated plaque in the right internal carotid artery 0.5 cm above the bifurcation.

The patient is successfully treated by a carotid stent since she is a high-risk surgical candidate because of severe COPD.

Clinical points

1. Amaurosis fugax is commonly due to platelet/fibrin emboli arising from the irregular surface of an ulcerated atherosclerotic plaque located near or at the common carotid bifurcation. Bruit location does not reliably predict stenosis location and, incidentally, may occur without significant stenosis.
2. The platelet/fibrin embolus passes through the ophthalmic artery, then the central retinal artery where it has been observed in retinal arterioles by ophthalmoscopy. It has a grayish coloration.
3. Smoking is a powerful risk factor for internal carotid artery stenosis. Hypertension and diabetes are additional major risk factors.
4. Carotid Doppler studies were unnecessary since, irrespective of the result, standard angiography or CT angiography were indicated. Moreover, they may be significantly inaccurate.
5. Subsequent medical treatment is antiplatelet therapy since emboli are of platelet/fibrin composition.
6. Extracranial internal carotid artery stenosis due to atherosclerosis accounts for approximately 10% of cerebral infarctions. The mechanism is primarily artery-to-artery embolism. Hemodynamic factors, impaired perfusion in the distribution of the severely stenotic vessel (greater than 90%), are likely responsible for less than 5% of ischemic strokes due to extracranial internal carotid stenoses. Although

this may seem surprising, internal carotid artery occlusions often occur without producing any neurologic symptoms. Good collateral circulation occurs via the circle of Willis or external carotid-intracranial arterial anastomoses which develop as a consequence of slowly progressive stenosis and eventual occlusion.

Smoking is a powerful risk factor for internal carotid artery stenosis.

Extracranial carotid artery stenosis accounts for about 10% of cerebral infarctions which are primarily due to artery-to-artery embolism.

Symptomatic carotid stenoses produce TIAs or ischemic infarctions most often in the distribution of the major middle cerebral artery branches. Small subcortical infarctions, however, are well-documented occurrences. Consequently, treatment selection will depend on the clinician's judgment as to whether an infarction is due to small vessel intracranial disease requiring medical management or extracranial stenosis for which surgery or stenting are commonly employed. This dilemma arises most often when the extracranial internal carotid artery stenosis is of borderline significance (60–70%) and without evidence of an ulcerated plaque.

Symptomatic carotid stenoses require stenting or endarterectomy.

Asymptomatic stenosis treatment decisions require an understanding of the natural history of this lesion. To the uninformed physician a severe internal carotid artery stenosis indicates a high incidence of sudden catastrophic ischemic stroke without warning. Careful investigations, however, have established that TIAs precede ischemic stroke due to extracranial internal carotid artery stenosis about 95–97% of the time. Thus, an alert, reasonably intelligent patient, well-educated about the usual symptoms of a TIA can be followed by careful observation awaiting a TIA before deciding on treatment. Another option is to repeat noninvasive testing such as serial carotid Doppler studies to observe for asymptomatic progression of a carotid stenosis before deciding on surgical treatment or stenting. Conversely, if the morbidity of the treatment by stent or endarterectomy is less than 3%, aggressive treatment may be warranted. At the date of this writing endarterectomy is the preferable treatment if the patient is a good surgical candidate. Morbidity varies from hospital to hospital and between surgeons or those physicians who perform stenting. Publication of results of treatment by individual vascular surgeons or neurointerventionists, which must include a neurologist's participation, is an ideal scenario but unlikely to occur for obvious reasons.

Transient ischemic attacks precede ischemic stroke due to extracranial internal carotid artery stenosis about 95–97% of the time.

Case 3 A 55-year-old man arrives in the Emergency Room at noon. On arising that morning he was unsteady and noted right leg weakness. The symptoms progressed in severity for 4 h prior to the Emergency Room examination. He has a 5-year history of well-controlled hypertension. His only medication is lisinopril.

Neurologic examination Blood pressure is 150/100 and the pulse is regular, 72 beats per minute. Abnormal findings are a right arm pronator drift and mild distal weakness of right arm and leg. He has a moderate right hemiataxia and right Babinski sign.

Diagnosis Left pons lacunar infarction disclosed by an MRI with diffusion-weighted imaging [4].

Clinical points

1. The patient manifests one of the characteristic syndromes of lacunar infarction, ataxic hemiparesis. The development over several hours is common.
2. Ataxia, in this case, is due to disruption of cerebellar pathways in the brainstem.
3. The presence of both weakness and Babinski signs indicates involvement of the corticospinal tract.
4. Although this patient has a pontine lacunar infarction, other possible locations of pathology which may cause ataxic hemiparesis include the posterior limb of the internal capsule and the midbrain in the region of the red nucleus.
5. Ataxia is not a pathognomonic sign of cerebellar hemisphere disease. Neither weakness nor Babinski signs occur with cerebellar pathology.

Lacunar infarctions range in size from 0.2 to 15 mm. They are primarily located in the basal ganglia, thalamus, internal capsule, pons, and infrequently in cortical or subcortical white matter such as the centrum semiovale or corona radiata. Most of them are in the distribution of the lenticulostriate vessels, thalamoperforating branches off the PCA, and paramedian branches of the basilar artery. The most common pathology is microatheroma or lipohyalinosis, the latter a subintimal collection of hyaline material which stains positive for fat.

Lacunar infarctions, 0.2 to 15 mm, are primarily located in basal ganglia, thalamus, internal capsule, and pons.

Table 7.1 Lacunar syndromes [7]

Name	Location
Pure motor stroke	Lesions of corona radiata, posterior limb of internal capsule, cerebral peduncle, pons, and medulla. Internal capsule lesions are most common.
Ataxic hemiparesis	Lesions in corona radiata, posterior limb of internal capsule, and pons.
Clumsy hand-dysarthria syndrome	Anterior limb of internal capsule and pons.
Pure sensory stroke	Thalamus and brainstem.
Sensorimotor stroke	Thalamic nuclei (VPL/VPM) and adjacent internal capsule.

VPL ventral posterolateral nucleus which receives sensory information from the contralateral arm, trunk, and leg, *VPM* ventral posteromedial nucleus which receives sensory information from the contralateral face

The classical syndromes of lacunar infarctions include pure motor stroke, pure sensory stroke, hemiparesis with homolateral ataxia (ataxic hemiparesis), clumsy hand-dysarthria syndrome, and sensorimotor stroke. (See Table 7.1).

Case 4 A 62-year-old woman is brought to the Emergency Room because of impaired vision. While singing in the shower she forgot the words to a favorite song. Her husband heard her misuse and mispronounce words. Simultaneously, she noted a bright glare and near total loss of vision. Her speech returned to normal in 1 min. Vision slowly improved but when looking straight ahead she could not see the floor.

Past Medical History Diabetes type II, hypertension and hypertriglyceridemia.

Medications losartan, metformin and gemfibrozil.

Neurologic Examination Neurologic examination is normal except for an inferior homonymous altitudinal hemianopsia.

Questions

1. What does the neurologic history indicate?
2. Is the examination helpful?
3. What type of pathology occurs abruptly and often resolves over a short time?
4. Is there a single artery that supplies both occipital cortices?
5. Why did the patient exhibit symptoms of aphasia?
6. What neuroimaging study visualizes this artery?
7. What medical disorder does the patient have that merits close lifetime attention?

Analysis

1. Misuse and mispronunciation of words are symptoms of aphasia, not dysarthria, and nearly always indicate left cerebral hemisphere dysfunction. Complete loss of vision, particularly with brightness or “glare” is a common symptom of occipital cortex ischemia or dysfunction. Darkness implies retinal hypoperfusion.

Brightness or "glare" is a common symptom of occipital cortex dysfunction.

2. The abnormal visual fields are most characteristic of bilateral, superior occipital cortex ischemia or infarction. Theoretically, lesions of the optic chiasm could be considered but this would be exceedingly rare, if ever described, as a vascular event.
3. Vascular disease.
4. Yes, the basilar artery. This artery usually gives rise to both posterior cerebral arteries at its tip, the distal termination.
5. Ischemia in the distribution of the inferotemporal branch of the left PCA.
6. Magnetic resonance angiography (MRA) will demonstrate the basilar artery and its branches as well as the vertebral arteries in the neck. Carotid Doppler studies are of no value.

When symptoms or signs indicate vertebrobasilar disease, an MRA is indicated, not carotid Dopplers.

7. Metabolic syndrome [5]. The metabolic syndrome has five criteria and is diagnosed when three of the risk factors are present. These are:
    1. Fasting plasma glucose >100 mg/dL or currently on treatment for diabetes.
    2. HDL cholesterol of 40 mg/dL or less in men and 50 mg/dL or less in women or receiving current treatment for low HDL.
    3. Triglyceride levels of more than 150 mg/dL or on treatment for hypertriglyceridemia.
    4. Waist circumference of 40 inches or more in men or 34.6 inches or more in women.
    5. Hypertension under treatment or blood pressure of more than 130/85.

The incidence of metabolic syndrome is approximately 22% of the U.S. population and it increases the risk of stroke 1.5 to 23 times in women and no risk to a sixfold risk in men for studies published up until 2013.

Test results The MRI shows bilateral occipital lobe infarctions involving the upper banks of the calcarine fissure. MRA (brain and neck) are normal. A transesophageal echocardiogram is normal. A 24-h Holter monitor discloses several prolonged bursts of atrial fibrillation [4].

Diagnosis Bilateral occipital lobe infarctions secondary to cardioembolism in the basilar artery-posterior cerebral artery distribution associated with paroxysmal atrial fibrillation.

Management Treatment is initiated with heparin and Cardiology is consulted.

Cardioembolism causes about 20–25% of cerebral infarctions. This is likely to be an underestimation since prolonged cardiac monitoring over 1 month has uncovered additional instances of paroxysmal atrial fibrillation. As previously noted, about 70% are in the carotid artery distribution and 23% in the vertebrobasilar system. The remainder are in watershed zones or multiple regions. There are numerous triggers for atrial fibrillation which include hyperthyroidism, valvular heart disease, coronary artery disease, cardiomyopathy, chronic obstructive pulmonary disease, heavy alcohol consumption, stress, obstructive sleep apnea, congestive heart failure and smoking.

Cardioembolism causes about 20–25% of cerebral infarctions and the most common etiology is atrial fibrillation.

The most common etiology of cardioembolism is atrial fibrillation, perhaps 45%. Other common sources of embolism are mural thrombus after an acute myocardial infarction, ventricular aneurysm, valvular heart disease, and prosthetic valves. There has been a keen interest in paradoxical embolism via a patent foramen ovale (PFO). The importance remains controversial. The simultaneous presence of an atrial septal aneurysm, however, does increase the risk of an embolic event. Other less common embolic sources include sick sinus syndrome, cardiomyopathy, atrial myxoma, marantic endocarditis, Libman-Sacks endocarditis (associated with systemic lupus erythematosus) and bacterial endocarditis.

It is important to note that perioperative stroke is nearly always cardioembolic in origin. It mandates a careful, thorough cardiac assessment including transesophageal echocardiogram, 24-h Holter monitor, and, if normal, an additional 1 month monitor for a cardiac arrhythmia. Atrial fibrillation is the most common etiology.

Perioperative stroke is nearly always cardioembolic and most often due to atrial fibrillation.

Case 5 A 68-year-old man complains of a 1-year history of frequent dizziness when standing up. It is a vague, lightheaded sensation sometimes accompanied by oblique double vision and facial tingling. Duration is 30–60 s.

Past medical history includes a two-pack per day smoking habit for 50 years and labile hypertension for 5 years. He takes no medication.

Neurologic examination Morning blood pressures taken by the resident are 106/64 supine, 95/60 sitting, 90/60 standing after 1 min, 88/48 after standing at 2 min and 94/60 after standing at 3 min. Pulses are 80, 84, 88, 86, and 80, respectively. Afternoon blood pressure taken by the nurse is 150/90 sitting. The heart rate is regular and the patient is asymptomatic. There are loud bruits over all neck vessels, no cardiac murmur, and the neurologic examination is normal.

Questions

1. Is there a diagnosis that can be made without neuroimaging?
2. What part of the medical examination should be reassessed in more detail?
3. What might it show?
4. If confirmed, what is the diagnosis?
5. What is the risk of stroke?
6. What is the treatment?

Answers

1. Yes.
2. Blood pressure should be taken in both arms. Both radial pulses should be palpated simultaneously.
3. Blood pressures reported by the resident were taken in the left arm. Blood pressure in the right arm reported by the nurse was 150/90. The patient's blood pressure was considered labile because it was taken in either right or left arm by the nurse without documentation of which side was taken. There is a pulse delay on the left side when both radial pulses are palpated simultaneously.
4. Diagnosis Subclavian steal syndrome.

   Cerebral angiography reveals an occlusion proximal to the origin of the dominant left vertebral artery, much larger than the right, a common anatomic variation. When the left arm is physically active or when the blood pressure drops, there is retrograde blood flow down the left vertebral artery to supply the needs of the left arm. This results in brainstem ischemia which, in this case, is manifested by diplopia and facial paresthesias.
5. Zero. Disabling TIAs are common.
6. Stenting can be performed for a stenosis, surgery for a subclavian occlusion. The surgical procedure is a left carotid-to-subclavian bypass, distal to the vertebral artery origin. If a patient is asymptomatic treatment is not required.

Case 6 A 48-year-old man is referred by an ophthalmologist because of blurred vision O.D. of presumed vascular origin. The patient reports an abrupt onset of painless loss of vision affecting his lower field of vision 3 days ago. He has mild type II diabetes, diet controlled, and takes no medicine.

Neurologic examination reveals a blood pressure of 150/110. The funduscopic examination O.D. discloses a swollen, pale optic disk with two flame-shaped hemorrhages at the disk margin. The retinal vasculature is normal. He has an inferonasal quadrant field loss and a relative afferent pupillary defect, O.D. The left eye is normal.

Questions

1. What other funduscopic finding could be discovered?
2. Where is the lesion?
3. What vascular supply is compromised?
4. What blood test should be ordered promptly?
5. What is the etiology and the primary differential diagnosis?

Answers

1. There is a small optic nerve head and a barely visible physiologic cup; thus the cup to disc ratio, which averages about 0.3, is much less.
2. Optic nerve. The unilateral quadrant visual field loss and a relative afferent pupillary defect indicate optic nerve disease. Pallid edema, hemorrhages at the disc margin, unilaterality and abrupt onset points to an ischemic event. Papilledema is bilateral and, when acute, has no major effect on vision other than enlarged blind spots.
3. Short posterior ciliary arteries. These are multiple vessels arising from the ophthalmic artery and provide circulation to the optic nerve. The central retinal artery supplies the retina but not the optic nerve. When occluded there is disc pallor, narrowed arterioles and boxcarring (segmented blood flow). (See Fig. 4.5)
4. ESR.
5. *Diagnosis:* Nonarteritic anterior ischemic optic neuropathy [3].

Temporal arteritis often produces the same findings on examination, but there are ordinarily additional symptoms such as headache, jaw pain with chewing due to internal maxillary artery involvement, or systemic symptoms such as fever, polymyalgia and polyarthralgia (Polymyalgia rheumatica).

Ischemic stroke due to intracranial small vessel disease, extracranial vascular disease, and cardioembolism has been briefly reviewed. There are numerous additional causes of ischemic stroke. In Chap. 12, Diagnostic Dilemmas, other etiologies will be discussed.

Venous Sinus Disease

Venous sinus disease is characterized by protean clinical manifestations [6]. There is often a baffling array of signs and symptoms. Thus the diagnosis depends on an alert physician who is aware of the predisposing illnesses. The three sinuses of greatest clinical importance are the superior sagittal sinus, transverse (lateral) sinus and the cavernous sinus (see Figs. 7.12 and 7.13).

The superior sagittal sinus drains the cerebral cortex and also the scalp by way of the emissary veins which pass through the skull. It contains most of the arachnoid granulations which absorb the cerebrospinal fluid. Hence papilledema is a relatively common presenting sign of superior sagittal sinus thrombosis along with headache, altered mental status, hemiparesis, and hemisensory syndromes. A classical but uncommon presentation is alternating hemiparesis. Seizures, tonic-clonic or partial, are frequent because infarctions are typically hemorrhagic. Hemorrhage is a cortical irritant. Multiple hemorrhagic cerebral infarctions point strongly to a superior sagittal sinus thrombosis.

Superior sagittal sinus thrombosis frequently causes hemorrhagic infarctions which are epileptogenic.

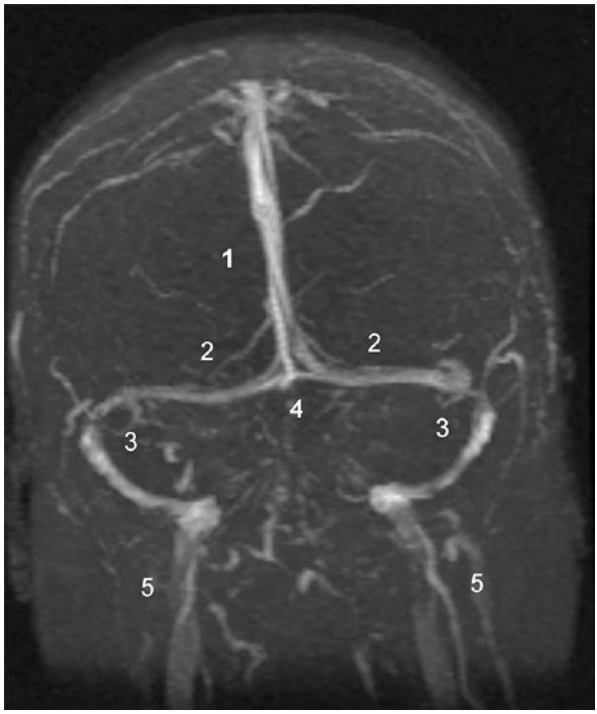


Fig. 7.12 Anterior-posterior view of cerebral veins. 1 superior sagittal sinus, 2 transverse sinus, 3 sigmoid sinus, 4 torcular Herophili, 5 internal jugular vein (with permission of Dr. Paul Gerson)

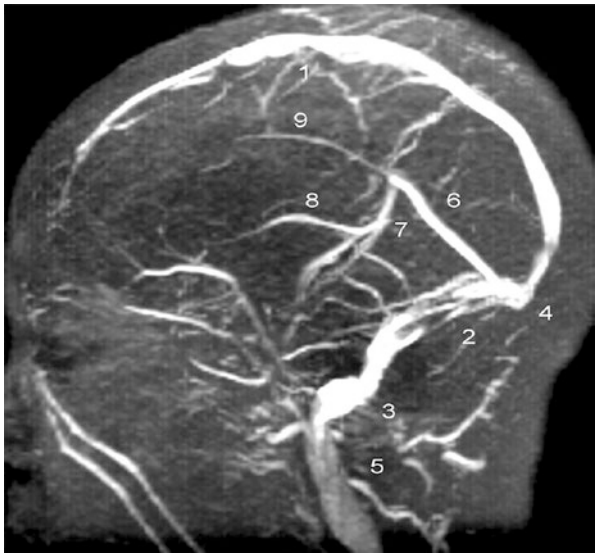


Fig. 7.13 Lateral view of cerebral veins: 1 superior sagittal sinus, 2 transverse sinus, 3 sigmoid sinus, 4 torcular Herophili, 5 internal jugular vein, 6 straight sinus, 7 vein of Galen, 8 internal cerebral vein, 9 inferior sagittal sinus (with permission of Dr. Paul Gerson)

The transverse (lateral) sinus drains the brainstem, cerebellum and posterior part of the cerebral hemisphere. The sigmoid section is adjacent to the mastoid process. Therefore, mastoiditis and otitis media may produce a septic thrombosis of this sinus and papilledema with its attendant manifestations of headache and transient visual obscurations, unilateral or bilateral, which often last just seconds. Horizontal diplopia, an occasional development, is most often due to a 6th nerve palsy, a non-specific feature associated with increased intracranial pressure. Thus all of the features of pseudotumor cerebri are produced.

Transverse sinus thrombosis is often septic and caused by mastoiditis or otitis media. It is one cause of pseudotumor cerebri.

The cavernous sinuses are located just lateral to the pituitary fossa (see Fig. 7.6). They drain the orbit and the base of the anterior parts of the brain. Its contents include the internal carotid artery in its medial portion. Adjacent, immediately below and lateral to it is the 6th nerve. Along the lateral wall, superior to inferior, are the 3rd nerve, 4th nerve, ophthalmic, and maxillary divisions of the trigeminal nerve. A cavernous sinus thrombosis produces unique clinical signs and is therefore more easily recognized. There is usually a unilateral ophthalmoplegia with variable involvement of the above-noted cranial nerves. Horner's syndrome may occur as the sympathetic fibers travel through the sheath of the internal carotid artery. Unilateral or bilateral proptosis and chemosis are frequent concomitant signs. The complex anatomy of structures within the cavernous sinus explains the wide array of clinical presentations.

Cranial nerves 3, 4, $5_{1,2}$, 6 and sympathetic fibers pass through the cavernous sinus.

The most important etiologic considerations of venous sinus disease are noted in the adjacent table (Table 7.2).

Intracerebral Hemorrhage

About 15% of all strokes are due to intracranial hemorrhage [7]. Intracerebral hematomas account for a little more than half of this number. The typical locations (frequencies) are putamen (40%), lobar (22%), thalamus (15%), pons (8%), cerebellum (8%), and caudate (8%).

The most common risk factor is hypertension which underlies 70–80% of hemorrhagic strokes. Additional, additive risk factors are age, low cholesterol level (less

Table 7.2 Venous sinus disease: most important etiologies

Disease category	Diseases
Sepsis	Otitis media; mastoiditis; facial, scalp, and dental infections; sinusitis; tuberculosis; bacterial endocarditis; meningitis; encephalitis; fungal-aspergillosis; parasitic-malaria and trichinosis; and viral diseases (especially human immunodeficiency virus)
Coagulopathies	Factor V Leiden; deficiencies of anti-thrombin 3, protein C and protein S; prothrombin gene mutation; disseminated intravascular coagulation; lupus anticoagulant; antiphospholipid antibodies; and heparin or heparinoid-induced thrombocytopenia
Other hematologic disorders	Polycythemia, sickle cell anemia, paroxysmal nocturnal hemoglobinuria, and thrombocythemia
Neoplasm	Meningiomas, metastases from any visceral carcinoma, lymphoma, leukemia, carcinoid, and glomus jugulare tumors
Gynecologic-obstetric	Oral contraceptives, puerperium, and pregnancy
Connective tissue diseases	Systemic lupus erythematosus, temporal arteritis, and Wegener's granulomatosus
Trauma	Neurosurgical procedures, head injury with or without fracture, and jugular vein catheters
Medical illnesses	
Cardiac	Congestive heart failure and congenital heart disease
Gastrointestinal	Cirrhosis, Crohn's disease, and ulcerative colitis
Medicines	Androgen, l-asparaginase
Miscellaneous	Dehydration of any etiology, Behcet's disease, nephrotic syndrome, and sarcoidosis

than 160 mg/dL), heavy alcohol use, smoking, and liver disease with thrombocytopenia. Pregnancy in the third trimester is a risk factor for hemorrhage but ordinarily this is associated with eclampsia and rupture of either an arteriovenous malformation (AVM) or aneurysm.

Hypertension is the predominant factor in 70–80% of intracerebral hematomas.

Chronic hypertension leads to fibrinoid necrosis with weakening of arterial walls and then aneurysmal development known as Charcot-Bouchard aneurysms. These are found in lenticulostriate vessels originating from both anterior and middle cerebral arteries, thalamogeniculate branches off the posterior cerebral arteries, thalamoperforating vessels arising from both posterior communicating and posterior cerebral arteries, and basilar perforating arteries.

Nonhypertensive etiologies include aneurysms which may rupture into cerebral parenchyma as well as the subarachnoid space, arteriovenous malformations (AVMs), amyloid angiopathy, coagulopathies, hemorrhage into an acute infarction,

hemorrhage into malignant neoplasms, rarely cavernous angiomas, and drugs. Warfarin and tissue plasminogen activator (TPA) are common offending medicines. Thrombin inhibitors are a less likely cause. Amphetamines and over-the-counter medicines such as phenylpropanolamine and pseudoephedrine can be the culprits.

Amyloid angiopathy is a relatively common etiology of hemorrhage in the elderly [8]. It comprises about 20% of intracerebral hematomas in patients over age 70. The hematomas are generally lobar and often recur in different locations. Infrequently, they may be multiple at first diagnosis. The differential diagnosis then includes venous sinus thrombosis, hemorrhagic metastases, and leukemia.

Amyloid angiopathy comprises about 20% of intracerebral hematomas in patients over age 70.

Complications of intracerebral hematomas include mass effect with a herniation syndrome, intraventricular rupture, and hydrocephalus. Seizures occur primarily with lobar hematomas. Because of extension of the hematoma or associated edema into adjacent structures a neat distinction into well-defined clinical syndromes is not possible. There are, however, some useful diagnostic patterns (see Table 7.3).

Table 7.3 Variable presenting manifestations of intracerebral hematomas

Location	Clinical presentations
Putamen (40%)	Aphasia (D), neglect-denial (ND), eye deviation, homonymous hemianopsia, apraxia, and hemiparesis (ND or D).
Lobar (22%)	*Frontal* – Abulia (ND or D), aphasia (D), denial or neglect (ND), hemiparesis and eye deviation (ND or D).
	Parietal – Aphasia (D), neglect-denial (ND), hemiparesis, hemisensory loss, apraxia, eye deviation, and homonymous hemianopsia (ND or D).
	Temporal – Aphasia (D), neglect-denial (ND), and homonymous hemianopsia (ND or D).
	Occipital – Homonymous hemianopsia (ND or D).
Thalamus (15%)	Hemisensory loss greater than hemiparesis, convergence-retractory nystagmus, downward eye deviation, paresis of upgaze, "wrong-way" eye deviation or gaze palsy, skew deviation, and light-near dissociation of pupillary responses.
Pons (8%)	Hemiparesis, quadriparesis, gaze palsy (unilateral or bilateral), skew deviation, decerebrate rigidity, locked-in-syndrome, pinpoint pupils, ocular bobbing or dipping, apneustic breathing, 1–1/2 syndrome (unilateral involvement of MLF and PPRF), ipsilateral or contralateral ataxia with contralateral hemiparesis, and hemisensory loss.
Cerebellum (8%)	Ipsilateral gaze preference with gaze paretic nystagmus, ipsilateral ataxia, but truncal ataxia is uncommon since hemorrhage in the vermis of the cerebellum is rare.
Caudate (8%)	Confusional state, transient gaze paresis, hemiparesis, hemisensory loss, and ipsilateral Horner's syndrome (ND or D).

D dominant hemisphere, *ND* non-dominant hemisphere

Case 7 A 57-year-old man is seen in a neurology clinic 2 days after suffering a severe occipital headache followed by feeling dizzy. He denies vertigo but says he was unsteady. The symptoms occurred toward the end of losing a tennis match. He has had similar symptoms in the past, mainly after a loss at tennis but this time his dizziness was more prolonged as it lasted the entire day. His headache resolved by the next morning. His past medical history is normal other than hypertension controlled with ramipril.

Neurologic examination reveals a blood pressure of 150/100, moderate right heel-to-shin ataxia and an unsteady tandem gait. There are no other abnormal findings.

Scenario 1 A stat noncontrast CT scan shows a 2 cm right cerebellar hemisphere hematoma. Routine blood chemistries, CBC with platelet count, PT, and PTT are normal. Because the hematoma is less than 3 cm and the abnormal neurologic findings are minimal, conservative management is selected. The patient is initially monitored in the Neurology ICU for 2 days. Hypertension is treated, serial neurologic examination discloses resolution of the ataxia after 1 week. During this time two additional CT scans of the brain show beginning resolution of the hematoma. The patient is discharged at 1 week.

Cerebellar hematomas, when less than 3 cm, often resolve spontaneously and do not require surgery.

Scenario 2 CT scan and laboratory data are as described above. Two days after admission the patient complains of dizziness. Examination shows paresis of upgaze and the pupils enlarge from 3 to 5 mm. The pupillary reactions to light are now 1+/4. The patient remains alert, oriented and has a normal screening mental status examination. An MRI discloses an enlarged hematoma with rostral displacement of the tip (iter) of the Sylvian aqueduct and the pons. Neurosurgical consultation is obtained. Immediately prior to surgery the patient is difficult to rouse. The hematoma is evacuated and postoperatively the patient is alert, pupils are 4 mm, equal and with a 3+/4 reaction to light. Upgaze is normal. The patient is able to perform tandem gait 3 days after surgery.

Scenario 1 analysis

Lesson No. 1

Right heel-to-shin ataxia is a discrete focal finding supporting the presence of a localized lesion. Only a complete neurologic examination would elicit this sole, abnormal sign.

Lesson No. 2

Cerebellar system lesions usually cause ipsilateral abnormal signs.

Lesson No. 3

Hemorrhages usually occur during physical activity. One-third are maximum at onset and two-thirds by 30 min. About one-third progress afterwards.

Lesson No. 4

Large lesions of the cerebellum often produce few abnormal signs.

Large lesions of the cerebellum often produce few abnormal signs.

Scenario 2 analysis

Lesson No. 1

Serial neurologic examinations which focus on the function of adjacent anatomic structures predict subsequent neurologic developments.

An enlarging cerebellar hematoma usually requires neurosurgical intervention.

Lesson No. 2

Upgaze paresis indicates posterior commissure compression and the large round sluggishly reacting pupils point to pretectal involvement.

Lesson No. 3

Lethargy implies dysfunction of the mesencephalic reticular formation. These findings occur with transtentorial upward herniation through the tentorial notch.

Lesson No. 4

Prompt evacuation of the hematoma and resection of a large amount of the cerebellar parenchyma may not interfere with a complete recovery. Cerebellar hematomas are amenable to surgical treatment.

Subarachnoid Hemorrhage [9]

Case 8 A 36-year-old woman arrives in the Emergency Room because of a severe, bilateral, pounding headache of 12 h duration. Associated symptoms include nausea, vomiting, photophobia, and phonophobia. She has had two similar headaches in the past 3 years prompting Emergency Room visits. Standard treatment for migraine on those occasions, ketorolac and metoclopramide I.V., terminated the headaches in 1 h.

The patient adds an additional history of transient loss of coordination of the right hand for 2–3 min about 2 months ago.

Her past medical history is negative. There is no history of migraine in the family.

General physical and neurologic examinations reveal a temperature of 100 °F, blood pressure 140/100, slight end nuchal rigidity, and positive Brudzinski's sign

(see section on neurologic examination for explanation). Pupils are 5 mm, equal and with 4+/4 reaction to light O.D. and 2+/4 O.S. Consensual responses are identical.

CT scan (head) is normal.

Questions

1. What common feature of migraine headache seldom occurs with SAH?
2. What physical signs do not occur with migraine?
3. The pupils show asymmetric reactivity to light. Is this due to a 3rd nerve or optic nerve lesion?
4. What is the differential diagnosis of acute headache, fever, and meningeal irritation?
5. What is the importance of the two prior headaches?
6. What may explain the episode of loss of coordination of the right hand for 2 min?
7. Does the pupillary abnormality have diagnostic significance?
8. Does a normal CT scan (head) rule out hemorrhage?

Answers

1. Unilateral headache, common in migraine, does not generally occur with SAH. Nausea and vomiting, photophobia, and phonophobia occur with both migraine and SAH. Absence of a positive family history for migraine is usual in patients with SAH but certainly this is not a diagnostic requirement since migraine is so common in the general population.
2. Low-grade fever is common with SAH but not migraine. A positive Brudzinski sign indicates meningeal irritation.
3. In optic nerve disease the pupils are equal in size but there is a decreased response to light on the involved side. In this case the pupils are equal in size but have a different reactivity to light. The direct and consensual responses are the same O.D. and hence the afferent loop O.S. is intact. The direct and consensual response O.S. is the same thus indicating a defect in pupillary constriction or a partial 3rd nerve lesion on the left side.
4. SAH or meningitis. Carcinomatous meningitis seldom begins acutely.
5. The prior headaches may have been "sentinel" headaches, minor leaks from an aneurysm which may precede SAH.
6. This is likely to have been a TIA which may occur in patients who have an aneurysm because of embolism from a clot within the aneurysm.
7. Yes. A 3rd nerve lesion suggests a posterior communicating aneurysm which frequently compresses this nerve.
8. No. CT scans are normal in 5–10% of patients with SAH.

The next step is a lumbar puncture.

The opening pressure is high at 230 mm H_2O, as the normal is equal to or less than 200 mm H_2O. The fluid is bloody and, after centrifuging, the supernatant is yellow (xanthochromic) indicating prior hemorrhage. Xanthochromia is a result of bilirubin which becomes apparent about 10–12 h after hemorrhage and may persist for 2–4 weeks. Testing for xanthochromia is the most reliable test for detecting

hemorrhage. Cerebrospinal fluid obtained within just a few hours is typically pink due to oxyhemoglobin but the supernatant is clear. The RBC count is 10,000 and wbc count is 1000, or a 10 to 1 ratio. Peripheral blood has a ratio of 700 to 1. Thus there is an increased wbc count, characteristic of an inflammatory response to hemorrhage. Counting red blood cells in the first and fourth tubes can be useful but is less reliable than testing for xanthochromia.

Followup examination Funduscopic examination is repeated on the night of admission and shows a subhyaloid hemorrhage O.S (Fig. 4.8). The hemorrhage has a half-moon appearance with a horizontal flat side located superiorly. There should be a careful search for this finding which is characteristic of SAH.

Angiography The patient has an 8 mm left posterior communicating artery aneurysm. Treatment is surgical or endovascular. The latter method is selected and is successful.

Diagnosis Subarachnoid hemorrhage secondary to rupture of left posterior communicating artery aneurysm.

Hospital course Four days after admission and 3 days after the aneurysm is coiled the patient is noted to misuse words. She is heard to say "ted" instead of "bed," "book" instead of "television"; thus she exhibits both phonemic and semantic paraphasias, respectively. Vasospasm involving the left middle cerebral artery is suspected and proven by transcranial Doppler study. The patient is treated by hypervolemia and induced hypertension. The following day language function returns to normal. The patient is discharged on the eighth hospital day feeling well.

> Vasospasm, which causes focal neurologic signs, and communicating hydrocephalus are common complications of subarachnoid hemorrhage.

Outpatient visit 1 month later The patient returns with a complaint of a tendency to fall backward. Two days prior to this visit she fell off a kitchen stool onto her back but suffered no injury. She has occasionally been incontinent of urine without awareness until she noted that she was wet. She complains of forgetfulness.

Neurologic examination The patient exhibits bradyphrenia (slowed thinking) and makes errors with short-term recall. When seated on the examining table she leans backward and requires support. She walks with a short stride, takes a few shuffling steps when turning, and has a positive pull test.

Analysis Truncal instability usually implies dysfunction in centrally located regions such as that which occurs with Parkinson's disease, lesions of the cerebellar vermis, hydrocephalus, and a mass lesion with midline shift. Her gait is apraxic and she has a history of urinary incontinence. Hence, she manifests the syndrome of normal pressure hydrocephalus (NPH), which is gait apraxia, memory loss, and urinary incontinence. She has communicating hydrocephalus due to obstruction of cerebrospinal

fluid flow around the convexities, a relatively common sequel of SAH and meningitis. Adhesions in the subarachnoid space or surrounding the arachnoid villae may be the cause. This is a well-known etiology of the NPH syndrome which usually begins with gait apraxia. In this case a ventriculo-peritoneal shunt returns the patient to normal.

SAH, due to ruptured cerebral aneurysms, accounts for 6–8% of all strokes [9]. Thirty-four percent arise from the AcoA, 30% from the internal carotid-posterior communicating arteries, 22% from the middle cerebral artery, and about 8% from the vertebrobasilar system. Multiple aneurysms have been found in 20–30% of patients with SAH. The remaining SAHs are due to coagulopathies such as thrombocytopenia, use of vitamin K or thrombin inhibitors, sympathomimetic drugs such as methamphetamines or cocaine as well as meningeal neoplasms and amyloid angiopathy.

Subarachnoid hemorrhage due to ruptured cerebral aneurysms accounts for 6–8% of all strokes.

The location of the aneurysm can sometimes be predicted by the neurologic examination. Clinical correlation [7] is noted in Table 7.4. A standard grading system of the severity of the hemorrhage is the Hunt and Hess Scale (Table 7.5).

Complications

1. Rebleeding (7%) occurs most often in the first 2 weeks.
2. Vasospasm is associated with delayed narrowing of large arteries usually between days 4 and 12. About 50% of these patients are symptomatic and, of these, about 50% suffer cerebral infarctions.
3. Hydrocephalus (20%) may occur any time after SAH.
4. Seizures (25%).
5. Increased intracranial pressure with or without 6th nerve palsy.
6. Hyponatremia (28%).
   (a) Syndrome of inappropriate ADH secretion (SIADH) which is associated with high intravascular volume.
   (b) Cerebral salt wasting which is associated with low intravascular volume.

Table 7.4 Clinical correlations

Location of aneurysm	Manifestations
Anterior communicating artery aneurysms	Abulia and leg weakness
Left middle cerebral artery aneurysm	Aphasia and right hemiparesis
Right middle cerebral artery aneurysm	Anosognosia/neglect and left hemiparesis
Posterior communicating-internal carotid artery aneurysm	3rd nerve palsy
Basilar artery aneurysm	Midbrain signs, much variability

Table 7.5 Hunt and Hess clinical grading scale

Group	Condition
0	Unruptured aneurysm
1	Asymptomatic or minimal headache and slight nuchal rigidity
2	Moderate or severe headache, nuchal rigidity and no neurologic deficit other than cranial nerve palsy
3	Drowsiness, confusion, or mild focal deficit
4	Stupor, moderate-to-severe hemiparesis
5	Deep coma, decerebrate posturing, and moribund appearance

7. Cardiac arrhythmias (35%).
8. Pulmonary edema (23%). This may be neurogenic or cardiogenic.

Epidemiology [10]

1. Aneurysms are present in 1–6% in large autopsy studies in adults.

Aneurysms are present in 1–6% in large autopsy studies in adults.

2. Aneurysms are incidentally discovered in 0.5–1% among adults undergoing angiography.
3. Each year 2% of patients with aneurysms develop new ones.
4. Annual rupture rates are 0.5–2% depending on aneurysm size. Aneurysms, 10 mm or larger, rupture at a higher rate.

Annual rupture rates are 0.5–2% depending on aneurysm size.

Genetic factors

1. Autosomal dominant polycystic kidney disease. Five to ten percent of patients have aneurysms on screening studies.
2. Marfan's syndrome.
3. Ehler-Danlos syndrome.
4. Neurofibromatosis type I.
5. Seven to twenty percent of patients with aneurysmal SAH have a first or second degree relative with a confirmed aneurysm.
6. Fibromuscular dysplasia.

Environmental predisposing factors

1. Smoking. This decreases the effectiveness of alpha-1 antitrypsin which inhibits proteases such as elastase.
2. Hypertension.

3. Hormones. Lack of hormone replacement in post-menopausal women.
4. Heavy ethanol consumption, especially binge drinking.

Case 9 A 24-year-old man requests an evaluation for acute, severe, unilateral, pounding headaches associated with nausea and photophobia. The last one occurred yesterday. He has had several headaches a year over the past 3 years. For a few minutes prior to the headache his right hand tingles and feels clumsy. These latter symptoms last from 3 to 4 h. He still has clumsiness of the right hand today. He has been diagnosed with the International Headache Society (HIS) classification of 1.2.3 or migraine with infarction. Past medical history includes rare tonic-clonic seizures with a postictal right arm paresis lasting 1 h. This was diagnosed as a Todd's phenomenon. They began at the age of 10 and have been well-controlled with valproate for the last 5 years because of good compliance, previously a problem.

Neurologic examination This is normal other than dysdiadochokinesis (impaired rapid alternating movements) affecting the right arm.

Questions

1. What part of the history indicates a focal lesion? What is the most likely location?
2. Does the examination support the same localization?
3. Where is the lesion and why?
4. What findings by history and examination suggest the underlying pathology?

Answers

1. The headache history is typical of migraine. Paresthesias are part of the classical migraine spectrum, migraine with aura. The prototypical sensory phenomenon is a "march of paresthesias" beginning in the hand, then arm and face. It usually lasts between 5 and 60 min, the same duration as the typical visual aura of migraine. Clumsiness is not common with migraine. It is a red flag indicating focal dysfunction and a possible lesion in the anterior portion of the left cerebral hemisphere. Migraine and clumsiness in one hand would be an unlikely manifestation of a brainstem or cerebellar lesion.
2. Yes. Impaired rapid alternating movements may occur with lesions involving any of the three motor systems, corticospinal, extrapyramidal, and cerebellar.
3. A postictal right arm paresis or Todd's phenomenon indicates left cerebral hemisphere pathology. Seizures are pathognomonic of cerebral hemisphere disease. Thus the patient has evidence of a left cerebral hemisphere lesion, probably frontal lobe.
4. The triad of migraine, seizures, and focal findings is a common presentation with arteriovenous malformations (AVMs).

Diagnosis AVM, left frontal lobe

Seizures, migraine, and focal findings are the hallmark manifestations of an arteriovenous malformation.

Table 7.6 Spetzler-Martin grading scale

Feature	Score
Maximum dimension	
<3 cm	1
3–6 cm	2
>6 cm	3
Location	
Non-eloquent	0
In or adjacent to eloquent cortex	1
Venous drainage	
Superficial only	0
Deep	1

AVMs are congenital lesions of focal collections of dilated arteries and veins connected by one or more fistulas [11, 12]. The arteries do not have a smooth muscle layer. They are located within brain parenchyma and may cause both intracerebral and SAH. Complications are hemorrhage (2% of all strokes), seizures, migraine, and hypoperfusion (ischemic steal) of adjacent structures. Anatomic features of the AVM are best analyzed by the Spetzler-Martin Grading Scale (Table 7.6).

Epidemiology and natural history Risk of hemorrhage in patients who present without stroke is 2–4% per year and the highest incidence of hemorrhage is between ages 20 and 40. The annual risk of recurrent hemorrhage in those treated conservatively is 5.9%. Arterial aneurysms are often present within the malformation. Predictors of high risk for recurrent hemorrhage include prior hemorrhage, deep venous drainage, and deep location [10].

Arteriovenous malformations carry a 2–4% per year risk of hemorrhage.

The sum of the scores, using the Spetzler-Martin scale, equals the grade. Grades 1–3 are considered treatable by embolization, surgical resection, or radiosurgery. Details of treatment are beyond the scope of this text.

Questions (True or False)

1. Seizures are a frequent occurrence with superior sagittal sinus thrombosis.
2. The posterior inferior cerebellar artery arises from the basilar artery.
3. A major supply of the anterior spinal artery is the artery of Adamkiewicz.
4. Acute vertigo may occur with occlusion of the anterior inferior cerebellar artery.

5. The posterior cerebral artery supplies the occipital cortex but not deep nuclear structures.
6. Epidural hematomas can be caused by traumatic injury to the middle cerebral artery.
7. The first branch of the internal carotid artery is the ophthalmic artery which takes off from its supraclinoid portion.
8. The anterior communicating artery is a large diameter vessel that connects the two anterior cerebral arteries.
9. Pure sensory stroke may occur from an infarction in the thalamus.
10. Carotid atherosclerotic disease is the most common cause of perioperative stroke after coronary bypass surgery.
11. High-grade extracranial internal carotid artery stenosis usually causes stroke by embolism.
12. Embolism associated with atherosclerotic disease at the origin of the common carotid artery is the most common source of cerebral infarction.
13. The posterior cerebral arteries provide important vascular supply to the temporal lobes.
14. Ischemia associated with anterior communicating artery aneurysms may produce abulia.
15. Crohn's disease has been associated with venous sinus disease.
16. Lobar intracerebral hematomas are the most amenable to surgical treatment.
17. Arteriovenous malformations commonly cause seizures.
18. Intracerebral hematomas most likely to cause seizures are thalamic.
19. The most reliable cerebrospinal fluid test for hemorrhage is xanthochromia of the supernatant in a centrifuged CSF sample.
20. A single episode of migraine aura lasting 10 h does not require neuroimaging.
21. The most common sign of increased intracranial pressure is a 3rd nerve palsy.
22. The lenticulostriate arteries arise from the M2 segment of the middle cerebral artery.
23. The clumsy hand-dysarthria syndrome is specific for a pontine infarction.
24. A common cause of a basilar artery occlusion at its termination is cardioembolism.
25. When a patient is heard to say "fled" instead of "bed" after successful clipping of a left middle cerebral artery aneurysm, vasospasm may be occurring and causing left temporal lobe ischemia.

Answers

1. T
2. F

3. T
4. T
5. F
6. F
7. T
8. F
9. T
10. F
11. T
12. F
13. T
14. T
15. T
16. F
17. T
18. F
19. T
20. F
21. F
22. F
23. F
24. T
25. T

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Chapter 8
Autonomic Nervous System Anatomy with Clinical Correlation

Familiarity with the anatomy of the autonomic nervous system is critically important for the diagnosis of numerous neurologic diseases. Abnormalities of the pupil, blood pressure, bladder, bowel, and sexual function are frequent concomitants of neurologic disorders and may provide the sole clue for solving diagnostic puzzles. The most clinically useful elements of the autonomic nervous system will be reviewed in this chapter.

Pupil

In the absence of ophthalmologic pathology or prior surgery, there are just three possible explanations for pupillary asymmetry [1]. These are a sympathetic system lesion on the side of the small pupil, a parasympathetic system lesion on the side of the large pupil, and physiologic (central) anisocoria.

> There are only three explanations for a pupillary asymmetry in the absence of ocular pathology or prior surgery, a sympathetic or parasympathetic system lesion and normal variation.

1. The parasympathetic pathway (see Fig. 8.1) is a three neuron arc which mediates the light reflex. The light reflex proceeds from retinal ganglion cells to the optic nerve, optic chiasm, optic tract, brachium of the superior colliculus, pretectum, Edinger-Westphal nucleus of the third cranial nerve and then the third nerve which exits the brainstem. The third nerve travels between the posterior cerebral and superior cerebellar arteries, under the medial aspect of the uncus of the temporal lobe, into the cavernous sinus and exits through the superior orbital fissure.

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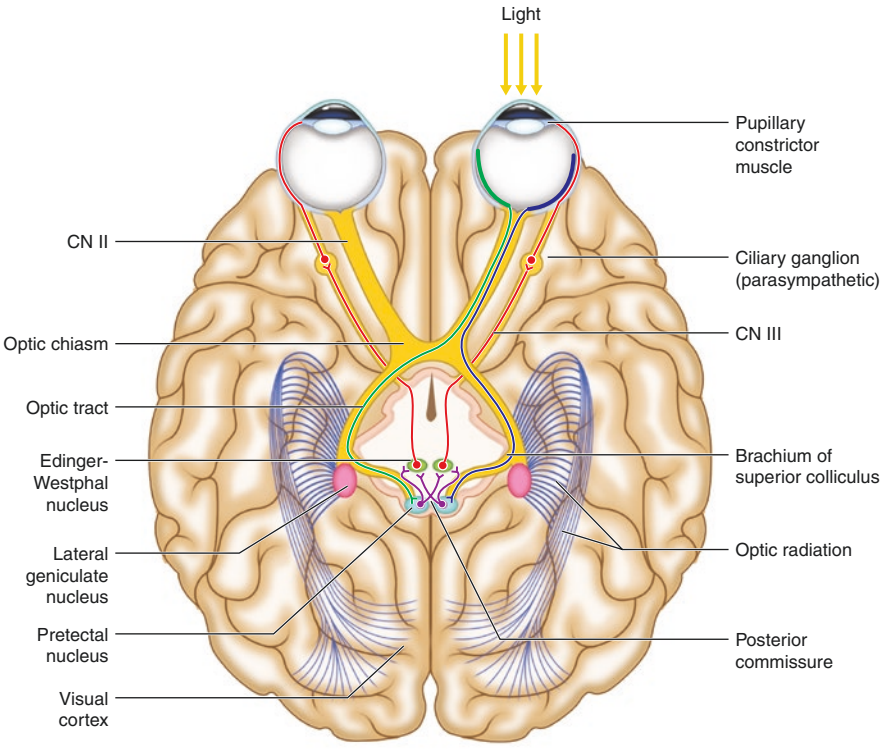

Fig. 8.1 Parasympathetic pathway of the light reflex. (Adapted from: Blumenfeld [2])

Fibers then synapse at the ciliary ganglion in the orbit. Small ciliary fibers extend from the ciliary ganglion to innervate the sphincter pupillae.

The three neurons in the parasympathetic pathway are located in the pretectum, Edinger-Westphal nucleus and ciliary ganglion.

The pretectum is the pupillary center and is the location of the first of three synapses. The second synapse is at the Edinger-Westphal nucleus and the third is in the ciliary ganglion. Interference with the parasympathetic outflow, beginning with the pretectum, causes a large, ipsilateral, poorly or nonreactive pupil. Pretectal involvement usually results in bilateral, round 5–6 mm nonreactive pupils. Involvement of the Edinger-Westphal nuclei and adjacent midbrain structures ordinarily result in bilateral nonreactive, 4–5 mm, irregular pupils. A unilateral third nerve or nucleus lesion produces a large pupil of variable size which is poorly reactive or nonreactive to light. A lesion affecting the ciliary ganglion or short ciliary nerve fibers causes Adie's syndrome (tonic pupil).

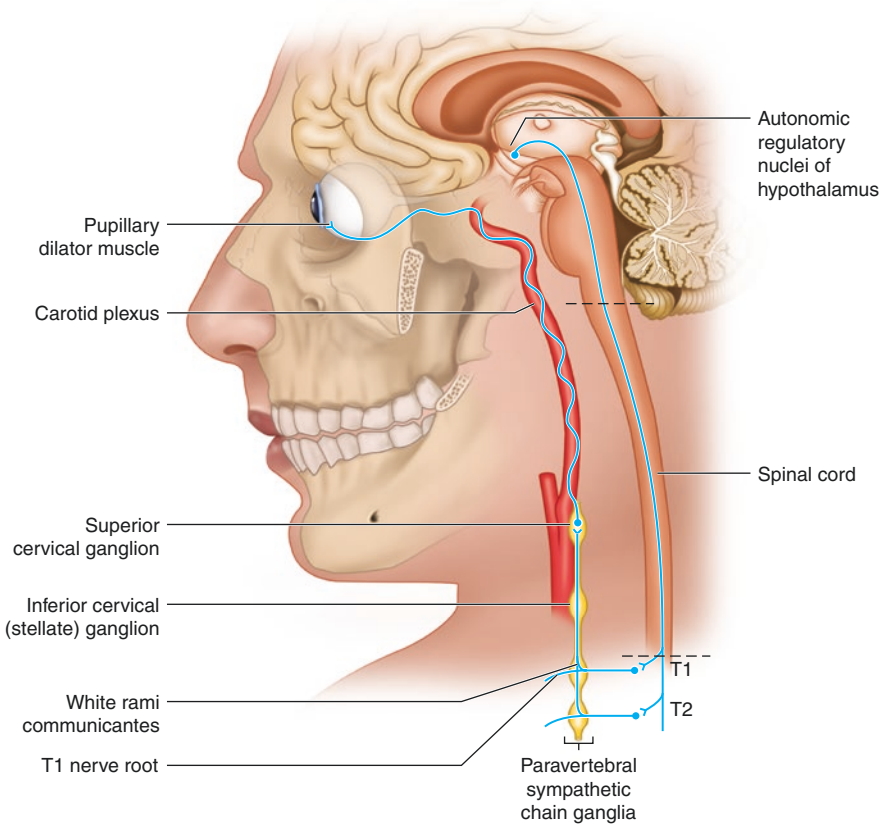

Fig. 8.2 The sympathetic pathway for innervation of the pupil. (Adapted from Blumenfeld [2])

2. The sympathetic pathway contains three neurons and two synapses (see Fig. 8.2). A lesion causes a Horner's syndrome which is miosis, ptosis, occasionally inverse ptosis with elevation of the lower lid and anhidrosis primarily of the forehead. Ptosis of sympathetic origin is due to a weak Müller's muscle (superior tarsal muscle) and occasionally there is inverse ptosis, with elevation of the lower lid due to a weak inferior tarsal muscle. Involvement of both of these muscles leads to an impression of enophthalmos.

   The location and severity of the involvement of the sympathetic system will determine whether all or just one or two of these findings are present. The first-order neuron is in the hypothalamus and its axons descend diffusely through the ipsilateral midbrain and pons; but they eventually merge into a discrete bundle in the dorsolateral medulla. They pass into the spinal cord to synapse in the intermediolateral cell column at T1-T2, also called the ciliospinal center of Budge. The preganglionic sympathetic fibers exit with the T1-T2 roots, arch over the apex of the lung and then ascend in the cervical sympathetic chain to synapse in the superior cervical ganglia which is adjacent to the carotid artery bifurcation. Most of

the postganglionic axons exiting the ganglion enter the sheath of the internal carotid artery. A smaller number of fibers, the sudomotor fibers, enter the sheath of the external carotid artery to supply the sweat glands on the face. A large majority of the sympathetic fibers remain in the internal carotid artery sheath as it passes through the cavernous sinus; then they exit with the first division of the trigeminal nerve forming the long ciliary fibers to innervate Müller's muscle in the upper lid, the inferior tarsal muscle in the lower lid and the dilator pupillae.

Horner's syndrome may be associated with heterochromia iridis, iris pallor with different colors, which can be complete or sectoral, acquired, congenital or genetic (autosomal dominant). The etiology is deficient sympathetic activity which interferes with melanin pigmentation of melanocytes in superficial stroma of the iris. It nearly always occurs before age 2 and may be associated with several conditions including agenesis of the internal carotid artery, Parry-Romberg syndrome (progressive hemifacial atrophy), neurofibromatosis, Sturge-Weber disease and traction on the head during delivery.

The three neurons of the sympathetic pathway are located in the hypothalamus, intermediolateral cell column in the spinal cord at T1-T2 and the superior cervical ganglion.

3. Physiologic or central anisocoria is generally less than 0.5 mm. In the normal population 15–30% will exceed this limit and careful examination for ancillary neurologic signs is required. The diagnosis is best made through looking at old pictures of the patient. Many patients have the same asymmetry and further detailed assessment is required only if there is clinical relevance.

Physiologic (central) anisocoria is generally less than 0.5 mm.

The most practical bedside method of diagnosing Horner's syndrome is to turn off the lights and see if the pupillary asymmetry increases after 5 s and before 15 s have elapsed. This is because of the lag in pupillary dilatation for several seconds in the presence of a sympathetic lesion. If, for example, a 0.5 mm asymmetry in light becomes a 1 mm asymmetry in dark at 5 s, the smaller pupil is evidently unable to dilate well and hence a sympathetic system lesion, Horner's syndrome, must be suspected. With a Horner's syndrome the pupils respond briskly to light, with both direct and consensual testing. Conversely, if a bright light shown on each eye independently produces a slower response on only one side, both direct and consensual, then a parasympathetic lesion usually involving the third nerve is the etiology.

When Horner's syndrome is suspected the pupils should be examined in the dark after 5–15 seconds have elapsed.

4. Light-near dissociation (retinomesencephalic-occipitomesencephalic dissociation). This is the comparison between the response to light and response to near. This discrepancy can be easily missed if one simply looks for a contraction to light rather than a disparity between the two reactions. A suspicion of light-near dissociation begins with an assessment of the pupillary reaction to light. If it is 2 + /4, for example, then testing a near reaction is the next step. A suspicion of syphilis or midbrain disease would also prompt such testing. Visual loss due to severe optic nerve or chiasm pathology may result in light-near dissociation. Even the blind individual can imagine his own finger approaching his face which provokes the near-synkinesis (lens accommodation, convergence of the eyes and pupillary constriction), a response which is independent of the visual system.

Severe optic chiasm, optic nerve and also midbrain lesions may result in light-near dissociation.

The prototypical patient with light-near dissociation is the patient who has neurosyphilis. These are Argyll-Robertson pupils [3]. They are bilateral, miotic, irregular and associated with iris atrophy. This diagnosis assumes normal vision since, as noted above, optic chiasm or bilateral optic nerve disease will interfere with the light reflex and result in better pupillary constriction with the near response. Moreover, any midbrain lesion may produce light-near dissociation.

Argyll-Robertson pupils are bilateral, miotic, and irregular.

Adie's pupil (tonic pupil) occurs typically in young women ages 20–40, begins with mydriasis, is unilateral and due to pathology in the ciliary ganglion or short ciliary nerve fibers. It is often asymptomatic and discovered incidentally by an acquaintance or when putting on makeup. Ankle or knee reflexes are usually absent. A comparison of Adie's and Argyll-Robertson pupils is reviewed in Table 8.1.

5. A relative afferent pupillary defect (RAPD) must be distinguished from parasympathetic pathway disruption. An RAPD is diagnostic of an optic nerve lesion. In this case the direct response of the involved eye to light is suboptimal, but the consensual response to light is normal because the third nerve innervating the involved eye is usually intact. In an uncertain case, a light is held on the involved eye for 2–3 s, then the intact eye for 2–3 s, then back to the involved eye. There may be an inability of the involved eye to constrict on this second attempt or a third attempt and, consequently, an RAPD is present which is diagnostic of optic nerve disease. Another method of detecting an RAPD is to simply shine a light directly on the pupil and measure the time it takes for the pupil to begin to dilate. The pupil which dilates more quickly has the RAPD. The older term for an RAPD is Marcus-Gunn pupil.

Table 8.1 comparison of Adie's and Argyll-Robertson pupils

	Argyll-Robertson pupil	Adie's pupil (tonic pupil)
Laterality	Bilateral, usually	Unilateral, initially, but becomes bilateral at a rate of approximately 4%/year
Size	Miotic, 1–3 mm commonly	Mydriatic, 5–7 mm commonly
Reactivity to light	Nil to minimal	Nil to minimal
Response to dark	Dilates poorly	Dilates poorly
Reactivity to near	Good	Slow constriction to prolonged near effort and slow redilation
Vision	Normal	Normal
Iris	Variable degrees of atrophy	Vermiform movement of the border region best seen with slit-lamp exam
Reflexes	Commonly absent at ankles since tabes dorsalis is frequently present	Commonly absent at the ankles and occasionally at the knees
Lesion location	Probably midbrain	Ciliary ganglion or short ciliary nerves
Pharmacologic testing	None	Supersensitivity response to either pilocarpine 0.125 or 2.5% methacholine (Mecholyl)
RPR, FTA-ABS	Positive	Negative

A relative afferent pupillary defect (RAPD) occurs when the consensual pupillary response is better than the direct one.

6. Chemical testing. For a questionable sympathetic lesion (Horner's syndrome), apraclonidine 0.5% is useful. [4] Apraclonidine is an alpha receptor agonist which has been used to reduce elevated intraocular pressure. Installation of one drop of a 0.5% solution in both eyes usually affects only the involved eye restoring its pupil to normal size. Ptosis may also be reversed. The eyes are examined 1 h after installation. The basis for the pharmacological response is denervation supersensitivity of alpha 1 receptors in the iris dilator and in Müller's muscles. The test is useful for lesions of the first, second and third order neurons.

A 0.5% apraclonidine solution is used to confirm a Horner's syndrome. The older standard method uses 10% cocaine.

The cocaine 10% eyedrop test is the older standard method. Cocaine will prevent the reuptake of norepinephrine and the increased amount of norepinephrine in the synapse results in maximal pupillary dilatation in normal eyes. Depletion of norepinephrine in the synapse, which occurs in patients with sympathetic system denervation, results in a poor response.

The hydroxyamphetamine test is diagnostic of a third-order neuron lesion. A third-order lesion results in decreased norepinephrine within the presynaptic terminal. Since hydroxyamphetamine stimulates release of norepinephrine from the presynaptic terminal, the involved eye does not dilate as well as the normal eye. Hydroxyamphetamine is difficult to obtain and is rarely used.

7. Unexplained mydriasis. Patients who have transient enlargement of the pupil are occasionally seen, a puzzling clinical observation. Transient mydriasis has been described in patients with migraine. Intermittent isolated mydriasis associated with vague sensations in the eye and normal neuroimaging has been called the "springing pupil" and generally is also attributed to migraine. In the unresponsive patient who is brought to the Emergency Room, uncal herniation causing a "Hutchinson pupil" must be suspected. When neuroimaging studies (MRI/MRA) are obtained, the frequent absence of pathology is vexing for the attending physician. Generalized tonic-clonic seizures have rarely been noted to produce transient unilateral mydriasis and, consequently, this diagnosis must be remembered in perplexing cases.

Transient mydriasis has rarely been observed in patients with migraine and during or immediately after a generalized tonic-clonic seizure.

Case Reports

Case 1 A 55-year-old man sees his internist because of a chronic cough producing yellowish-white sputum every morning for the last 3 months. He has chronic bronchitis and smokes two packs of cigarettes per day.

Physical Examination Physical examination by his internist discloses asymmetric pupils, 4 mm on the right and 3 mm on the left with brisk equal reactions. Palpebral fissures are slightly asymmetric with the right greater than the left. In a darkened room the right pupil is 5.5 mm and the left is 4 mm. There is no anhidrosis. Chest examination reveals scattered rhonchi and wheezes.

Laboratory Tests The chest X-ray with apical lordotic views and a CT scan of the chest disclose findings of emphysema. An MRI (brain) and MRA (head and neck) are normal. Neurologic consultation is requested.

Neurologic Examination The neurologist does a complete review of neurologic symptomatology. Twenty years ago the patient recollects severe, unilateral, excruciating, left-sided headaches lasting 20 min to 1 h. They occurred roughly three times a day occasionally awakening him at night during a period of 1 month. When they occurred he was forced to pace the floor because of severe pain, a crucial distinction from migraine patients who prefer to lie down in a dark, quiet environment.

Diagnosis Cluster headache associated with a partial Horner's syndrome.

Cluster headache is often associated with Horner's syndrome.

Main Clinical Points

1. The absence of facial anhidrosis supports a third-order Horner's syndrome which implies involvement of the sympathetic chain in the internal carotid artery sheath. In patients who have cluster headache, angiography has demonstrated changes in the carotid siphon manifested by distention of the carotid artery wall thus possibly compressing the sympathetic nerve fibers lying within it.
2. The cardinal manifestations of cluster headache are its short duration and the behavior of the patient who often paces back and forth.
3. Although neuroimaging is essential, a complete history yields the diagnosis and is more relevant. A limited review of systems is always inadequate.

Case 2 A 20-year-old woman complains of difficulty running. She is on her college volleyball team and has been unable to compete effectively for the last 3 months.

Neurologic Examination There is a pupillary asymmetry with the right pupil 4.5 mm and the left 4.0 mm. In the dark the right pupil is 5.5 mm and the left 4.5 mm. There is questionable anhidrosis on the left face; this is tested by checking the temperature on the face just under the eye and on the forehead using the dorsal part of the hand or fingers which are less moist. The palpebral fissures are equal. There is mild spasticity of the left leg. Plantar responses are neutral on the right and extensor on the left.

What optional test can be performed to confirm the cause of the miosis and the lesion location? What single neuroimaging study should then be ordered?

A cocaine test is performed using a 10% solution. Two drops are placed in each eye. The right pupil dilates to 6.5 mm and the left to 5 mm. Consequently, this patient has a partial left Horner's syndrome since there is no ptosis. An MRI (cervical) is obtained and discloses an intramedullary cyst within the lower cervical and upper thoracic cord on the left side.

Diagnosis Cervical myelopathy secondary to syringomyelia.

Main Clinical Points

1. The left Babinski sign and mild spasticity of the left leg indicate involvement of the left corticospinal tract below the pyramidal decussation or the right corticospinal tract above the decussation.
2. The presence of a partial Horner's syndrome is confirmed by the cocaine eye drop test. This test is optional since the increased pupillary asymmetry in the dark is convincing for a sympathetic system lesion. The term "partial" is used because of the absence of ptosis.

3. A partial Horner's syndrome on the left side fits neatly with a left corticospinal tract lesion indicating pathology within the left side of the cervical spinal cord. A crossed syndrome, right Horner's and left Babinski would indicate a brainstem lesion.

> Spinal cord lesions which produce Horner's syndrome are most often intramedullary.

4. An MRI scan of the cervical cord reveals a syrinx with maximum involvement at the C8-T1 level.

Case 3 A 47-year-old man requests an evaluation because of an episode of severe vertigo 5 days prior to his appointment. One month ago he was in a motor vehicle accident. His car was struck from behind when he was stopped at a red light. Because of constant neck pain he sought chiropractic treatment. One hour after his second treatment he had an acute episode of vertigo associated with nausea and vomiting which lasted 5 min. This was followed by a staggering gait for 1/2 h.

Neurologic Examination The key abnormal findings relate to the pupils. The right pupil is 5 mm with a 4+/4 reaction. The left is 4.5 mm with a 4+/4 reaction. The right face is slightly moist and cool and the left face is dry, warm and there is no ptosis. After 5 s in a darkened room, the right pupil is 6 mm and the left is 5 mm proving a partial left Horner's syndrome.

An MRI (brain) reveals a small infarction in the left dorsolateral medulla. An MRA discloses a left vertebral artery dissection which is likely to be a complication of chiropractic manipulation of the neck.

Diagnosis Brainstem infarction, left dorsolateral medulla, secondary to a left vertebral artery dissection.

Main Clinical Points

1. Vertigo is the prototypical symptom of vestibular dysfunction, central or peripheral.

> Vertigo and a Horner's syndrome indicate a brainstem lesion.

2. The vestibular system includes the peripheral vestibular apparatus (semicircular canals and otolith organs), 8th nerve and the vestibular nuclei. There are additional pathways from the vestibular nuclei to other brainstem nuclei and cerebellum.
3. A partial left Horner's syndrome with a history of vertigo points to involvement of the sympathetic pathway and vestibular nuclei. They are close to each other in the left dorsolateral medulla. The vascular supply of this region is the left vertebral and posterior inferior cerebellar artery.

Case 4 A 50-year-old woman is referred by her internist because of fluctuating pupillary size. Seven years ago, when on a European trip, she developed acute, painless double vision on up, down and right lateral gaze. She was told that her left pupil was slightly larger than the right but reacted well. She does not recall what studies were done nor does she have any reports. Complete recovery was reached in about 3 months.

Past medical history is remarkable for insulin-dependent diabetes mellitus and hypertension, both well-controlled.

Neurologic Examination Neurologic examination includes a suspected left lateral rectus paresis. Red glass testing confirms the clinical impression since the white image is lateral on gaze left when the red glass covers the right eye. (See Chap. 4). On gaze right the left pupil constricts from 4 mm to 3 mm and returns to 4 mm on direct forward gaze.

Questions

1. What mechanism explains the pupillary constriction on gaze to the right?
2. Where is the lesion and why?
3. What is the differential diagnosis and does it depend on the anatomic site?
4. Why is diabetes a remote consideration?
5. What is the diagnosis?

Answers

1. Aberrant third nerve regeneration explains the pupillary constriction O.S. as fibers intended for medial rectus innervation are misdirected to the pupillary parasympathetic pathway. Consequently, use of the medial rectus muscle simultaneously causes the pupil to constrict.
2. Only a lesion in the cavernous sinus could easily explain these abnormalities since the patient has both a left sixth nerve palsy confirmed by red glass testing and left third nerve involvement by history and pupillary findings. (Fig. 7.6).
3. As the lesion is in the cavernous sinus it is most likely to be a mass. The probable etiologies would be an aneurysm or neoplasm such as meningioma or pituitary tumor. Aneurysms usually involve the superior division of the third nerve (LPS and SR). Trauma, congenital lesions, syphilis and ophthalmoplegic migraine have also been reported etiologies.
4. Diabetes almost invariably causes an extremely painful, pupil sparing third nerve palsy and there are rare reported cases of aberrant third nerve regeneration due to ischemic etiologies. An MRI (sella) with and without contrast reveals a parasellar meningioma.
5. *Diagnosis:* Parasellar meningioma invading the cavernous sinus.

Other causes of fluctuating pupillary size, episodic unilateral mydriasis, include migraine, epilepsy, cyclic oculomotor spasm and hippus. The latter is a brief oscillation of pupillary size that can be a reaction to a light stimulus and is considered normal. Hippus has also been seen in midbrain lesions.

Blood Pressure

An essential element of every neurologic examination is measurement of pulse and blood pressure. The absence of a history of hypertension even in a 30-year-old patient with footdrop does not obviate an obligation to participate in preventive care. Furthermore, hypotension or hypertension is often relevant to many neurologic disorders.

> Blood pressure and pulse should be taken in every patient irrespective of the chief complaint.

There are manifold symptoms of hypotension which commonly demand neurologic attention. Most are obvious and include brief or prolonged dizziness when standing up, blurred vision, fatigue, and weakness. Blurry vision is bilateral and is most often described as "darkening" or "graying out" due to impaired blood supply to both retinas. Much less often is absence of vision or such complaints as opaque vision, brightness, or simply blindness. These observations suggest occipital lobe ischemia. Infrequent complaints are neck and shoulder pain due to ischemia of neck musculature. Orthostatic dyspnea may occur presumably caused by impaired vascular supply to the apices of the lungs. Lastly, slowed mentation may accompany one of the above-noted symptoms although it is rarely an isolated complaint. Clearly, the review of neurologic symptoms, a critical step in taking a history, is likely to yield additional information.

A brief review of the physiology of blood pressure control, through the baroreceptor reflex [5], will be elaborated. Baroreceptors are located in the carotid sinus and aortic arch. These are innervated by the glossopharyngeal and vagus nerves, respectively. A drop in blood pressure provokes a decrease in afferent neural discharges from these regions. The afferent nerve fibers of the 9th and 10th cranial nerves enter the dorsomedial medulla to make up part of the nucleus of the tractus solitarius. The decrease in afferent input through this pathway results in decreased output from the nucleus ambiguus which contains nuclei of the 9th, 10th and 11th cranial nerves. The sinus node receives decreased vagal input which causes compensatory increased heart rate. There is an increased sympathetic output mediated by fibers from the nucleus tractus solitarius to the caudal ventrolateral medulla, which is an excitatory pathway. Noradrenergic connections from this area innervate the paraventricular nucleus and supraoptic nucleus of the hypothalamus. This stimulates vasopressin release from the vasopressin-synthesizing neurons located in these structures. Vasopressin causes smooth muscle constriction in arterial walls resulting in an increased blood pressure. Sympathetic fibers also descend from the medulla down to the intermediolateral cell column in the spinal cord where they synapse between T1 and L2. The preganglionic fibers then exit at their respective levels to form the sympathetic chain which is between T1 and L2. T1 through T4 supply the arms and heart, T5 through T12 supply the adrenal medulla, and T11 through L2 the genitourinary system.

Baroreceptors are located in the carotid sinus and aortic arch. These are innervated by the 9th and 10th cranial nerves, respectively.

Hypotension provokes a decrease in afferent neural discharges from the carotid sinus and aortic arch.

The result is to increase sympathetic output from the caudal ventrolateral medulla and decrease vagal innervation to the sinus node. An increase in blood pressure and heart rate results.

Norepinephrine is released from postganglionic axons and, as noted above, from central nervous system noradrenergic axons. Catecholamines are released from the adrenal medulla into the circulation through the adrenal vein. Vasoconstriction by these secretions results in a compensatory return of blood pressure to normal levels.

Case 5 A 68-year-old retired male engineer complains of an episode of loss of vision associated with shortness of breath. He was playing with his grandchild on the floor for approximately 10 min, stood up and was immediately short of breath. Simultaneously, he lost his vision. He describes the room turning black. He lay down on the sofa and recovered over 2 min. On further specific questioning the patient reports an unsteady gait and mild memory impairment developing over the past year.

Examination Blood pressure when supine is 140/90 with a regular pulse of 80. Sitting blood pressure is 134/86 with a pulse of 82. Blood pressure upon standing, taken at 1 min, is 122/82 with a pulse of 84 and regular. After standing for 3 min the patient feels faint, the blood pressure is 80/60 and the pulse remains 84. The neurologic examination discloses impaired short-term memory as he recalls 1 of 3 words after 2 min have elapsed. He is unable to add 14 + 19 or reverse 5-letter words. He walks with a wide base and is unable to perform tandem gait. He exhibits moderate heel-to-shin ataxia.

Diagnosis Multiple system atrophy (MSA).

Main Clinical Points

1. The room turning black indicates retinal ischemia. When unilateral and brief it is called amaurosis fugax, a typical TIA associated with an internal carotid artery stenosis with embolism to the central retinal artery; when bilateral, hypotension is the likely etiology.
2. Dyspnea suggests ischemia to the apices of the lungs.
3. The blood pressure must be taken supine, sitting and standing after 1, 2 and 3 min have elapsed unless there is a major drop of blood pressure in the interim. The

definition of "orthostatic hypotension" is a reduction in systolic blood pressure of at least 20 mmHg or a reduction in diastolic blood pressure of at least 10 mmHg during the first 3 min of standing. This is a classic finding of sympathetic failure of vasoconstriction. The lack of a compensatory increase in heart rate is common. The estimated incidence of orthostatic hypotension among elderly people living in long-term care facilities is reported to be between 54 and 68% [6]. Dehydration,

Orthostatic hypotension is defined as a systolic blood pressure reduction of ≥20 mmHg or diastolic blood pressure reduction of ≥10 mmHg during the first 3 min of standing.

Orthostatic hypotension among elderly people living in long-term care facilities is very common with a reported incidence of 54 to 68%.

medications and deconditioning are the most likely etiologies.

4. Orthostatic hypotension is a common manifestation of neurologic diseases with autonomic dysfunction such as multiple system atrophy, Lewy body dementia, Parkinson's disease and pure autonomic failure. Multiple system atrophy encompasses diseases previously described separately in the past, olivopontocerebellar atrophy, Shy–Drager syndrome, and striatonigral degeneration.
5. The patient exhibits mild cognitive impairment and cerebellar ataxia.

Comment: This patient has a combination of cognitive, autonomic and cerebellar system involvement characteristic of MSA. Two or more dysfunctional systems must be present to establish this diagnosis.

Case 6 A 50-year-old woman complains of shortness of breath when getting up from a squatting position. This is sometimes accompanied by blurred vision which she describes as brightness associated with multicolored spots. When that happens she has no functional vision. These symptoms last less than 30 s and have been increasing in frequency over the last 3 months. She denies other neurologic complaints. On thorough questioning, however, she acknowledges symptoms of burning and prickly sensations in both feet.

Neurologic Examination Neurologic examination reveals a blood pressure of 140/80 in the supine position with a heart rate of 80 and blood pressure immediately on standing is 100/74 with a heart rate of 82. The patient complains of being slightly dizzy, but after 2 min the blood pressure rises to 120/80 with a heart rate of 84 and she feels well. Nevertheless, a final blood pressure is taken at 3 min at which time the patient complains of shortness of breath and brightness of her vision. Her blood pressure is 85/60 and heart rate is 88.

Neurologic examination discloses absent ankle reflexes, absent vibratory perception at toes and ankles and distal sensory loss to pin in all extremities. This is apparent in the hands up to the wrist and in the feet up to the ankles.

An MRA (brain and neck) and MRI (brain) performed because of the atypical visual symptoms were normal.

Impression Autonomic neuropathy associated with a sensory neuropathy. Diabetes is suspected and proven.

Main Clinical Points

1. Brightness of vision plus seeing multicolored spots indicates occipital lobe ischemia. This is unusual for most patients with orthostatic hypotension. Hence neuroimaging was performed to exclude underlying basilar artery or posterior cerebral artery disease.
2. The history of burning paresthesias in the feet is common with neuropathy. The addition of orthostatic hypotension strongly suggests an autonomic neuropathy.
3. The blood pressure must be taken after 3 min have elapsed if earlier blood pressures are nondiagnostic. In this instance both the initial and final drops in blood pressure confirm that orthostatic hypotension was the cause of her symptoms.

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4. The most common etiology of orthostatic hypotension due to an autonomic neuropathy is diabetes; but orthostatic hypotension occurs more commonly as an adverse effect of antihypertensive medication. Amyloidosis is a rare but well-documented cause of an autonomic neuropathy.

Case 7 A 20-year-old female college student has been referred because of chronic fatigue. A general medical evaluation has disclosed no organic pathology. The student is under considerable stress trying to excel in her premedical courses at the university. She reluctantly acknowledges being chronically anxious since her symptoms have been repeatedly dismissed as psychogenic. Treatment with alprazolam and fluoxetine has been ineffective.

Examination Blood pressures are 110/80 supine, 108/82 sitting, 106/80 standing at 1 min, and 105/85 standing at 3 min. Heart rates are 90, 94, 100 and 110, respectively. The patient is then requested to walk up and down the corridor for 3 min after which she becomes fatigued. Her blood pressure is 100/60 and her heart rate is 136 and regular. She complains of anxiety. The remainder of the neurologic examination is normal.

Impression Postural orthostatic tachycardia syndrome (POTS) [7].

Main Clinical Points

1. One must never assume psychiatric explanations for a patient's symptoms without a thorough examination.
2. POTS is a well-established cause of chronic fatigue and is manifested by tachycardia, with minimal exertion, of at least 30 points higher than the resting rate.

POTS is a well-established cause of chronic fatigue and is manifested by tachycardia, with minimal exertion, of at least 30 points higher than the resting rate.

3. Deconditioning may be a significant factor in its development. Consequently, this is a treatable form of chronic fatigue. An exercise program, probably best in a sitting position such as using a stationary bicycle, and a low-dose beta blocker are often very helpful.

Genitourinary System

Anatomic and Physiologic Overview

Control of bladder function, which is primarily inhibitory, is a complex interplay of parasympathetic, sympathetic and voluntary muscle function [8]. Cerebral control of micturition originates in the superomedial frontal lobe, anterior cingulate gyrus and genu of the corpus callosum. The pathway descends to the pontine micturition center (PMC), also known as Barrington's nucleus, while collecting numerous inputs from the limbic system, thalamus, substantia nigra, red nucleus, hypothalamus, subthalamic nucleus and cerebellum. Efferents from the PMC descend with the reticulospinal tract in the anterior funiculus of the spinal cord to terminate in the detrusor motor neurons in the intermediolateral cell column of the sacral gray matter (S2–S4). Efferents from cortical and subcortical micturition centers pass through the PMC and travel via the corticospinal tract to synapse in the pudendal nuclei (Onuf's nucleus) located in the ventral horn of the S2–S3 segments of the sacral spinal cord. Additionally, sympathetic input travels from the PMC down the lateral funiculus to modulate thoracolumbar sympathetic outflow. The nerves which mediate parasympathetic, sympathetic and somatic function are described below.

1. Pelvic Nerves
   These are parasympathetic and carry both afferent and efferent fibers. The former carry impulses from stretch receptors in the bladder which synapse in sacral segments (S2–S4) of the spinal cord. Efferent fibers emerge from those segments and activate detrusor muscles to contract the bladder and expel urine.

2. Hypogastric Nerve
   This nerve mediates sympathetic control which relaxes the bladder detrusor muscle and contracts the internal sphincter which is composed of smooth muscle. This function promotes retention of urine.
3. Pudendal Nerve
   The pudendal nerve contains somatic, voluntary fibers which assist in controlling the external sphincter. This sphincter, which is composed of striated muscle, will contract or relax depending on whether voiding is desired. The input from the cerebral cortex (frontal lobe) passes through the PMC and descends with the corticospinal tract to Onuf's nucleus located mainly in the ventral horn of the sacral spinal cord (S2–S3). S2–S4 segments are the source of the pudendal nerve.

Voiding begins with a full bladder, 300 or more cc's of urine. Stretch receptors in the bladder wall increase impulses in afferent fibers of the pelvic nerves (parasympathetic) which synapse in sacral segments of the spinal cord. Information is then relayed to the thoracolumbar cord which sends impulses through the hypogastric nerve (sympathetic) to relax the internal sphincter and inhibit relaxation of the detrusor muscle. The neural pathway ascends to the periaqueductal gray and PMC and then continues to the cerebral cortex where a decision is made about whether voiding is appropriate. If not, then the cerebral cortex sends a message to the pudendal nerve via Onuf's nucleus in the sacral cord to contract the external sphincter. Additionally, there will be inhibition of the parasympathetic detrusor function to the sacral cord and excitation of sympathetic function in the thoracolumbar cord. Otherwise, the PMC is activated, sends messages through the lateral funiculus of the spinal cord to inhibit thoracolumbar sympathetics, promote coordinated activation of sacral parasympathetic neurons to contract the bladder detrusor muscle via the pelvic nerves (parasympathetic) and inhibit motor neurons in Onuf's nucleus to relax the external sphincter.

Neurogenic Bladder with Clinical Correlation [9]

1. *Hyperreflexic* (*spastic*) *neurogenic bladder*. This is caused by detrusor-sphincter dyssynergia, i.e., uncoordinated function. The internal sphincter becomes hypertonic but not sufficient to withstand the detrusor contraction thus resulting in urinary incontinence. The bladder capacity is reduced and there are frequent uninhibited contractions. This may occur with any chronic central nervous system disorder affecting the cerebral hemispheres, brainstem, or spinal cord. Correlative symptoms are urgency, frequency and incontinence.
2. *Flaccid neurogenic bladder*. This is an areflexic atonic bladder which results in overflow incontinence and/or stress incontinence. The bladder capacity is markedly increased and the voiding stream is poor. This is usually due to disease affecting dorsal roots, cauda equina and the lumbosacral plexus. Acute CNS lesions such as large cerebral hemisphere or brainstem infarctions and spinal cord trauma may temporarily cause this syndrome.

3. *Uninhibited neurogenic bladder.* This disorder may be acquired or congenital and is caused by a lesion or underdeveloped function between medial frontal lobe and the pontine micturition center. Normal inhibitory control of detrusor muscle is impaired and thus there is intermittent precipitant voiding. Correlative symptoms may be urgency, frequency, incontinence, enuresis and frequent urinary tract infections.

Sexual Function

Sexual arousal occurs through multiple sensory modalities including psychogenic factors. Three neural pathways innervate the genital organs. These are the sacral parasympathetics (pelvic nerves), thoracolumbar sympathetics (hypogastric and thoracolumbar sympathetic chain), and somatic nerves (pudendal nerve).

> Sacral parasympathetic nerves are primarily responsible for erection (tumescence).

Sacral parasympathetic nerves are primarily responsible for erection by eliciting vasodilation of penile or clitoral arteries and relaxation of venous sinusoids in erectile tissue resulting in tumescence as the corpora cavernosa of the penis fills with blood. The mediator is nitric oxide. The conus medullaris is the reflex center for erection and the pelvic nerves via the pelvic plexus provide the parasympathetic input. Sympathetic input is primarily anti-erectile but there are descending pathways which can mediate erectile function.

Descending pathways which originate in the cerebral hemispheres, travel through the lateral columns of the spinal cord, exit at T12 and pass to the genitalia via the hypogastric (sympathetic) nerves. This intact sympathetic pathway can inhibit norepinephrine release and thus prevent vasoconstriction which can thereby enhance erection. Preserved synapses with postganglionic parasympathetic and somatic nerves allow for nitric acid and acetylcholine release, respectively. Consequently, despite sacral cord lesions which interrupt the reflex pathway, psychogenic erection, although weak, is possible.

In females parasympathetics cause secretion of mucus by Bartholin's glands. They also produce swelling and engorgement of external genitalia and clitoral erection. The sympathetic system has a less potent role with regard to secretions, but it does increase vaginal blood flow. It is likely to participate in sexual arousal. Sympathetic activation accompanies orgasm. Somatic fibers mediate rhythmic perineal contractions in females during orgasm.

Ejaculation is mediated by the sympathetic system at T12-L1 and the somatic nerves. Semen is emitted into the urethra by sympathetically mediated smooth muscle contraction in the seminal vesicles, vas deferens, prostate and bladder neck.

The somatic nerves originate in the anterior horn cell in Onuf's nuclei in the S2–S4 spinal cord segments. These fibers travel in the pudendal nerves and provide excitatory input to striated muscles, bulbocavernosus and bulbospongiosus muscles in the male, which are responsible for ejaculation.

Ejaculation and detumescence are mediated by both sympathetic and somatic nerves.

Sexual functions are governed centrally by regions in the hypothalamus which act as integration centers for sexual responses. These areas are likely to be involved in sexual preference and gender identity. As expected they receive input from cortical and subcortical structures concerned with memory and emotion.

Bowel Function

The anal sphincter mechanism includes the internal anal sphincter, external anal sphincter, and puborectalis muscles. The internal anal sphincter is supplied by sympathetic fibers arising from the superior rectal and hypogastric plexus. The external anal sphincter and puborectalis muscles act as the voluntary sphincter as they are innervated by pudendal nerves (somatic). Receptors in the pelvic floor detect the presence of stool. Some neuropathies, especially diabetic, may cause diarrhea with fecal incontinence. A lax anal sphincter implies lesions of sensory roots, conus medullaris, motor roots (S3–4), or peripheral nerves.

A lax anal sphincter implies lesions of sensory roots, conus medullaris, motor roots (S3–4) or peripheral nerves.

Questions (True or False)

1. The pupillary center is the Edinger-Westphal nucleus.
2. The pathway for pupillary constriction includes the ciliary ganglion neurons where the third synapse of the sympathetic system is located.
3. Intramedullary lesions of the spinal cord may cause Horner's syndrome.
4. Physiologic anisocoria can measure up to 2 mm.
5. The best method of testing the pupil for a parasympathetic lesion is a brightly lit room.

6. Light-near dissociation findings may be present in patients who have midbrain lesions.
7. Argyll-Robertson pupils are mydriatic.
8. Symmetrical pupils occur with severe unilateral optic nerve lesions.
9. There is depletion of norepinephrine in both the synapse and presynaptic terminal irrespective of the lesion site in patients with Horner's syndrome.
10. Horner's syndrome can be associated with cluster headache.
11. Sympathetic fibers to the pupil remain unilateral.
12. Horner's syndrome may occur with lesions of the dorsolateral medulla.
13. Pupillary fibers are located in the center of the third nerve.
14. Shortness of breath and neck pain may occur with hypotension.
15. Baroreceptors are located in the carotid sinus and are innervated by the vagus nerve.
16. The thalamus is critically involved in blood pressure control.
17. Darkening of vision in both eyes is called amaurosis fugax.
18. An acute frontal lobe lesion may produce an atonic bladder.
19. Sacral sympathetic fibers are responsible for erections.
20. Diabetic neuropathies may cause diarrhea with fecal incontinence.

Answers

1. F
2. F
3. T
4. F
5. T
6. T
7. F
8. T
9. F
10. T
11. T
12. T
13. F
14. T
15. F
16. F
17. F
18. T
19. F
20. T

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Chapter 9
Neuromuscular Diseases: Neuroanatomic and Differential Diagnoses

Neuromuscular diseases can be defined as those which affect the lower motor neuron or anterior horn cell (AHC), roots and root ganglia, plexus, nerves, neuromuscular junction and muscle. This covers an immense array of illnesses: degenerative, genetic, immune, infectious, metabolic, neoplastic, nutritional, paraneoplastic, traumatic, toxic, and vasculitic. Clearly, a thorough review is neither possible nor intended. An approach to patients with these disorders will be outlined with the major emphasis placed on the history and neurologic examination. The method used herein will be case presentations followed by case analysis.

The first task for the physician is to distinguish between central nervous system and neuromuscular disease. There is an overlap at the AHC and pathology which affects these lower motor neurons will be included. This first hurdle is a familiar one, often simple, but occasionally baffling even to seasoned neurologists. Careful attention is always required for this first step. The second task is to select the site of pathology within the neuromuscular system. An accurate selection will allow for a well-reasoned differential diagnosis.

Neuropathies will be examined in a special manner. Several distinctions must be made. Is the neuropathy acute or chronic, primarily motor or sensory, acquired or genetic, part of a systemic disorder, and is there concomitant autonomic nervous system involvement? An additional piece of information may also be vital, the results of electromyography and nerve conduction studies (EMG-NCV). Since analysis of this physiologic study is beyond the scope of this text, accommodations will be made for the absence of data derived from this examination or its interpretation will be provided.

Myopathies can be subdivided into several categories which include the dystrophies (genetic), inflammatory, metabolic and endocrine, infectious, nutritional, paraneoplastic, toxic, and vasculitic. Differentiating between these disorders can be an arduous task. The anatomic distribution of weakness commonly provides the diagnostic clue and this element will be emphasized.

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Discussion of muscular dystrophies (genetic muscular diseases) will be a rudimentary foray into a complex, huge, burgeoning field. The purpose of the discussions is merely to acquaint the student or physician with the most common dystrophies and pique the interests of some to investigate this disease category in more depth. Several dystrophies will be reviewed primarily about their clinical presentation and differential diagnosis. Brief commentaries on genetic and protein abnormalities will be added. The incidence of these disorders approaches 1/1000 of the general population, far exceeding expectations since most neurology practices see few of them. Surprisingly, the totality of these diseases approximates the frequency of multiple sclerosis. Most of these patients will ultimately be referred to a neuromuscular disease center where a precise diagnosis can be made, newest treatments offered and long-term care planned.

Motor neuron, root and root ganglia, plexus and neuromuscular junction diseases make up the remainder of the illnesses to be discussed. Their characteristic features will be reviewed.

There will be 40 case presentations followed by a case analysis. At the end of the chapter, the case numbers of each anatomic site will be listed to facilitate a review of all reports pertaining to that disease location.

Case Reports

Case 1 A 55-year-old woman complains of left arm pain for 2 weeks. She describes an intermittent, severe ache affecting the upper arm and forearm muscles reaching an intensity of 8/10. It can be provoked by working on a computer and is aggravated at night. When queried about her sleeping position, she reports that she sleeps on her back with a neck support which she has used for years to prevent neck strains.

Neurologic Examination Blood pressure is 120/70; pulse is 80 and regular.

There is 4+/5 strength of left triceps. Extension of the head for 50 s while seated provokes pain in the left triceps muscle. Isolated arm movement produces no pain.

Questions

1. Why is the pain provoked when the patient works on her computer? Why is it worse at night?
2. Why does head extension produce pain?
3. Where is the lesion?
4. Is the character and location of the pain typical for this condition? What is the differential diagnosis? What test should be ordered?

Case 1 Analysis

1. Working on a computer commonly involves leaning forward which extends the head. The patient's neck support has the same effect.

2. Head extension narrows the intervertebral foramina aggravating any compression of the exiting nerve root.
3. Cervical root, probably at C6–C7 because the triceps muscle is primarily innervated by the C7 root.
4. Yes. The differential diagnosis is primarily a herniated disk or spondylosis. Neoplasm is rare. Cervical spine films with oblique views may disclose focal narrowing of an intervertebral foramen due to spondylosis and should be ordered.

Diagnosis Cervical radiculopathy, left, due to spondylosis at C6–C7.

Comment An MRI scan should only follow failure of conservative treatment for a minimum of 2 weeks. Exceptions are progressive or severe arm weakness, uncontrollable pain and development of myelopathic symptoms or signs such as leg weakness, sustained ankle clonus, asymmetric leg reflexes, spasticity, Babinski signs and a sensory level.

An EMG is utilized for radiculopathy primarily for localization purposes or when the anatomic diagnosis is unclear. It is commonly normal in radiculopathies and should be performed, if necessary, after at least 2 weeks and preferably 3 weeks have elapsed from the onset of symptoms as signs of denervation are not found earlier. It is not indicated for this patient.

Case 2 A 77-year-old man complains of the rapid onset over 2 days of unprovoked, severe, right thigh and hip pain. As a result he has fallen three times and requires assistance to walk. He denies weakness and attributes all of his falls to pain. He has a history of hypertension and coronary artery disease.

Neurologic Examination Blood pressure is 140/80; pulse is 64 and regular.

Strength of right iliopsoas is 3/5, quadriceps and extensor hallucis longus 4/5. The right knee jerk is absent. There is hypesthesia to pin over the right medial calf.

Questions

1. Where is the lesion?
2. What is the differential diagnosis?
3. What specific test is indicated?
4. What is the diagnosis and prognosis?

Case 2 Analysis

1. The lumbosacral plexus. A herniated disk at L3–L4 does not affect the extensor hallucis longus (L5 root) nor does it commonly cause medial calf numbness. The numbness is due to involvement of the saphenous nerve, a branch of the femoral nerve.
2. Diabetes mellitus is the primary consideration as this may be its first manifestation. Most often the etiology is unknown. Additional possibilities are malignant pelvic neoplasm, radiation plexopathy, psoas hemorrhage, and an immune or viral origin.

3. Hemoglobin A1C and 2-h glucose tolerance test. The hemoglobin A1C is 7.5% and a 2-h postprandial glucose is 200 mg%. An EMG-NCV could be useful after 3 weeks have elapsed if the diagnosis remains questionable. Clinical judgment will determine whether a pelvic or possibly a lumbar MRI is indicated.
4. *Diagnosis*: Lumbosacral plexopathy secondary to diabetes [17].

Comment The prognosis is excellent for recovery over 6 months if it is of diabetic origin or idiopathic, the most usual clinical scenarios. Speculation about the idiopathic variety includes viral, immune, and microvasculitic pathogenesis.

Case 3 A 35-year-old man complains of rapid progression of his diabetic neuropathy. He was diagnosed with type I diabetes at age 24 and has a 5-year history of burning pain with paresthesias affecting feet greater than hands. Over the last 3–4 weeks he has become fatigued, drowsy, developed a hoarse voice and notes progressive weakness of both feet. Paresthesias in both hands have markedly increased and are especially troublesome at night. His diabetic control is excellent.

Neurologic Examination Blood pressure is 130/90; pulse is 100 and regular.

The patient is obese (BMI = 31), lethargic, and he has a hoarse voice. Strength of anterior tibialis is 4/5 bilaterally and gastrocnemius 4 + /5 bilaterally. Reflexes are absent in the legs and "slow" at brachioradialis, bilaterally. Vibration perception is absent at the toes, ankles, and knees. Position sense is absent at the toes. There is subjective distal sensory loss to pin and temperature in all extremities. The Romberg test is positive.

Questions

1. Are all the symptoms, signs, and progression compatible with a diabetic neuropathy? What features are unexpected?
2. What part of the reflex examination should be clarified?
3. Is a positive Romberg unusual in these circumstances? Is it usual to find severe vibration sense loss and only mild position sense impairment?
4. Why are paresthesias in the hands much more severe?
5. Should a new diagnosis be considered?

Case 3 Analysis

1. No. Fatigue, drowsiness, hoarseness, and rapid progression are red flags. Well-controlled diabetes is not compatible with rapid neurologic deterioration.
2. The brachioradialis reflex has a slow relaxing phase, common with hypothyroidism.
3. No. A positive Romberg is common when there is position sense loss. Loss of vibration perception exceeds position sense loss in patients with neuropathy. Depending on evaluation of position sense alone leads to serious errors.
4. Nocturnal paresthesias suggest superimposed carpal tunnel syndromes.
5. Yes. This patient has hypothyroid neuropathy superimposed on his diabetic neuropathy and bilateral carpal tunnel syndromes, common with hypothyroidism.

The symptoms of fatigue, drowsiness, and hoarseness indicate additional pathology best explained by this disease.

Diagnoses

1. Diabetic neuropathy [17].
2. Hypothyroid neuropathy [14].
3. Carpal tunnel syndromes, bilateral.

Comment In the patient who has a neuropathy that explodes with unexpected progression an intensive search for a new disease must be initiated.

Case 4 A 78-year-old woman complains of difficulty climbing stairs. She has noticed progressive leg weakness during the past 2 years. This last year she has become aware of weakness of both hands. She has lost her "equilibrium" in the shower when washing her hair and has fallen twice.

History Analysis

1. Weakness climbing stairs usually indicates proximal leg weakness, primarily quadriceps and iliopsoas muscles. This could indicate a myopathy or neuromuscular junction disorder, i.e., myasthenia gravis.
2. Distal weakness manifested by weak intrinsic hand muscles militates against myopathy but not necessarily the neuromuscular junction, neuropathy or myelopathy.
3. Washing one's hair is usually done with eyes closed. Losing her balance while washing her hair implies eye closure and thus she depends on visual cues to maintain balance. When vision is required to maintain balance there is usually vestibular dysfunction or a proprioceptive abnormality which is most common with neuropathy and occasionally seen in myelopathy.
4. Weakness does not occur with vestibular disease. Hence, the patient must have significant sensory loss. Furthermore, myopathy and a disorder of the neuromuscular junction are not likely since neither are accompanied by poor equilibrium with eye closure. Neuropathy and myelopathy are the prime considerations.

Neurologic Examination Blood pressure is 110/60; pulse is 72 and regular.

The patient has a quadriparesis with mild proximal and moderate distal weakness. Head flexion is moderately weak. Reflexes are unobtainable except for 1 + triceps and 1 + knee jerks, the latter only with reinforcement. Vibration perception is absent at the toes, ankles, and knees. Position sense is absent at the toes and a few errors are made at the ankles. Mild pinprick stimulation evokes severe pain, much more than expected. The Romberg test is positive.

Questions

1. Where is the lesion? Could this patient have a myelopathy?
2. Does the finding of proximal weakness, especially involving head flexion, help with the diagnosis?

3. Is a positive Romberg test a precisely localizing finding?
4. Does the disparity between vibration and position sense loss have value in the differential diagnosis? What is the name of the exaggerated response to pin?
5. What is the diagnosis and what laboratory findings confirm it?

Case 4 Analysis

1. This patient has a neuropathy not a myelopathy. The absence of reflexes supports this diagnosis. Hyperreflexia and Babinski signs are characteristic of myelopathy. Pure AHC pathology is ruled out by sensory loss. Polyradiculopathy is a consideration but it ordinarily produces severe, spontaneous pain.
2. Most neuropathies produce distal weakness. Proximal weakness indicates nonselective pathology such as an immune disorder or vasculitis. As a rule myelopathies do not cause weakness of head movements.
3. No. Positive Romberg tests are primarily due to a proprioceptive or vestibular disorder, the former most often due to neuropathy, rarely myelopathy. Midline cerebellar disease affecting vestibulocerebellar fibers can probably cause a positive Romberg. This is a controversial topic.
4. No. Vibration loss nearly always exceeds position sense loss with lesions of the central or peripheral nervous system with the exception of cerebral disease. The disparity between these modalities is expected and, consequently, not especially helpful. An exaggerated response to mild pinprick stimulation is called hyperpathia.
5. *Diagnosis* Chronic inflammatory demyelinating polyneuropathy [13].

Comment The diagnosis is confirmed by examining the CSF and performing an EMG-NCV. The CSF usually shows a marked increase in protein and a normal or slightly elevated white blood cell count. This is called albuminocytologic dissociation a common finding in many neurologic diseases and therefore not useful for diagnostic purposes unless the protein is remarkably increased, such as more than twice the high normal level. The EMG-NCV primarily demonstrates a demyelinating neuropathy and is usually diagnostic.

Case 5 A 65-year-old retired watchman complains of tingling in both arms and hands for 6 months. Occasionally, there is associated chest pain. Initially the tingling was intermittent, lasting just minutes, and affecting either arm independently. Now it is constant with periodic exacerbations occasionally awakening him at night with or without chest pain. The hands are particularly affected and have become weak.

Past medical history includes osteoarthritis and hypertension. His only medicine is hydrochlorothiazide.

Neurologic Examination Blood pressure is 140/90; pulse is 78 with an occasional irregular beat.

There is atrophy of the right thenar eminence. Strength of right opponens pollicis (OP) and left abductor pollicis brevis (APB) is 4/5. Leg strength is normal. Reflexes

are normal at 2+ and symmetrical. Sensory examination is normal. There are deformities of the proximal interphalangeal joints.

Questions

1. What additional bedside tests would be useful to make a diagnosis?
2. Could tingling in both arms and hands be an early sign of neuropathy? What is the significance of nocturnal paresthesias? Why are myelopathy and radiculopathy unlikely?
3. What could explain the patient's chest pain?
4. What is the diagnosis and the likely etiology?

Case 5 Analysis

1. Prolonged head extension, for up to 1 min, often aggravates cervical root pain. The test is negative. Phalen's maneuver (forced flexion at the wrist) is performed and provokes paresthesias after maintaining the position for 30 s. Tinel's sign is present as paresthesias are produced on the 2nd–fourth fingers of both hands, palmar surface. A Tinel's sign is elicited by tapping the volar surface of the wrist over the median nerve. These positive signs support but do not confirm the diagnosis. Tingling in both arms and hands may indicate a compressive neuropathy and nocturnal paresthesias are virtually diagnostic of carpal tunnel syndrome. Presumably, this is due to wrist flexion when the patient lies on his side, a spontaneous Phalen's sign.
2. Not likely. Polyneuropathy begins in the legs and thus it can be rejected as the etiology. Examination shows no signs of a myelopathy such as a sensory level, asymmetric hyperreflexia, spasticity, or Babinski signs. Muscular atrophy may occur with AHC disease, radiculopathy or neuropathy. Cervical radiculopathy is a consideration but the typical findings of radicular pain and asymmetric reflexes are not present. Sensory symptoms exclude AHC disease.
3. Chest pain may occur with cervical radiculopathy and, in rare instances, carpal tunnel syndromes.
4. *Diagnosis*: Bilateral carpal tunnel syndromes [16], possibly secondary to rheumatoid arthritis.

Comment Prior repetitive provoking activities such as typing or sewing are not required for the diagnosis. Additionally, there is a high incidence of carpal tunnel syndrome in patients with rheumatoid arthritis. This patient has arthritis affecting proximal interphalangeal joints; thus rheumatoid arthritis is a consideration as it may cause carpal tunnel syndromes. Other unusual specific etiologies include hypothyroidism, acromegaly, and amyloidosis.

Case 6 A 45-year-old retired professional basketball player complains of progressive leg weakness over 3 years. For the past year he has not been able to run or play basketball with his two sons because he has been dragging his feet. For 6 months he has had difficulty making his overhead shots at the three-point line as they are falling short of the basket. Morning and evening strength is the same. Climbing stairs

requires extreme effort. Over the last few weeks swallowing has been difficult especially with large pieces of meat.

History Analysis Dragging his feet implies weak anterior tibialis musculature. Wrist flexor weakness is suspected since making overhead shots requires good strength of these muscles. Inability to climb stairs signifies quadriceps/iliopsoas weakness and raising the arms requires good deltoid strength. Thus the illness begins with symptomatic distal weakness but eventually spreads to proximal leg muscles and affects the swallowing mechanism.

Neurologic Examination Blood pressure is 140/82; pulse is 90 and regular.

The palate elevates in the midline. The gag reflex is present and tongue movements are normal. Strength of deltoids, triceps, wrist flexors, and arm pronation is 4/5 in both arms but the right side is slightly weaker. Right iliopsoas, quadriceps, and anterior tibialis are 3/5, 4/5, and 4 + /5, respectively. The left side is 3 + /5, 4 + /5, and 4/5, respectively. The patient walks with a short stride and bilateral footdrop. Reflexes are 1+ and symmetrical, plantars are flexor and sensory testing is normal.

Questions

1. Where is the lesion?
2. What may cause the patient's dysphagia?
3. What is the differential diagnosis?
4. What is the diagnosis and what findings confirm it?

Case 6 Analysis

1. The patient has a painless, pure motor system disorder. He does not have concomitant signs of cerebral disease such as aphasia, impaired cognition, visual field defects or a history of seizures. There are no signs of brainstem pathology such as crossed findings or eye movement abnormalities. Furthermore, since palate movements are normal, the dysphagia must be due to pathology located elsewhere. Typical findings of myelopathy such as spasticity, asymmetric hyperreflexia, and Babinski signs are not present. The cardinal symptom of polyradiculopathy, pain, is absent. There are no sensory symptoms or signs which usually accompany neuropathy. Thus, the lesion is either in the neuromuscular junction or muscle. The former ordinarily involves the soft palate and liquids are typically not tolerated. A purely motor neuropathy is a remote consideration. Thus muscular pathology is probable.
2. Videofluoroscopy was performed and demonstrated cricopharyngeal sphincter dysfunction. This is caused by inflammatory involvement of the cricopharyngeal muscle.
3. The differential diagnosis must take into account the duration of the illness, the tempo of progression and, particularly, the anatomic distribution of the pathology.

The initial diagnostic considerations are inclusion body myositis (IBM), dermatomyositis (DM), polymyositis (PM), muscular dystrophy (limb-girdle), and multifocal motor neuropathy with conduction block. Myasthenia gravis is a remote possibility since fluctuating strength especially related to time of day is not present and dysphagia only for solids are atypical. Additionally, a steadily progressive course is not expected.

4. *Diagnosis*: Inclusion body myositis (IBM). (Fig. 9.1) [5].
   The diagnostic features include the distribution of weakness, proximal and distal, which are characteristic of IBM. Swallowing is often impaired and is due to inflammatory involvement of the cricopharyngeal muscle. The CK is moderately elevated to 800 U/L which rules out a motor neuropathy and myasthenia gravis. The EMG shows signs of an inflammatory myopathy and repetitive nerve stimulation is normal. The muscle biopsy is diagnostic of inclusion body myositis.

Brief Review DM [10]. Weakness is proximal and especially involves neck musculature. The CK is elevated up to 50 times normal. It may be associated with malignancy (six-fold expected rate), vasculitis, cardiac involvement or interstitial lung

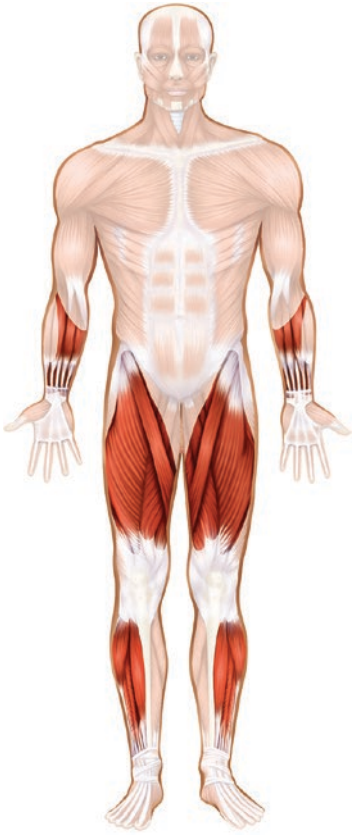

Fig. 9.1 Inclusion body myositis

disease. Dysphagia, fever, and rash occur. The rash is a "heliotrope" rash with periorbital edema, purplish discoloration of eyelids, sun sensitive rash, and papular erythematous lesions over the knuckles.

PM. Weakness is proximal and especially involves neck musculature. There is no rash or other associated dermatologic disorder. There is an increased risk of malignancy (two-fold expected rate). Dysphagia is common and polyarthritis may occur. The CK is markedly elevated up to 50 times normal.

Vasculitis can occur with either DM or PM and the disorders include Sjögren's disease, scleroderma, rheumatoid arthritis, systemic lupus erythematosus (SLE), and mixed connective tissue disease.

Case 7 A 77-year-old man complains of severe right calf pain after walking one block. This has developed gradually over 6 weeks. There is no weakness but he has paresthesias in both feet. He has no calf pain when sitting or lying down.

Past medical history: The patient has a 50 pack-year history of smoking, hypertension, and type II diabetes. Current medications are metformin and lisinopril.

Neurologic Examination Blood pressure is 130/86; pulse is 78 and regular. General physical examination is normal including good peripheral pulses.

Ankle reflexes are absent. Vibration perception is absent at the toes and diminished at the ankles. When testing vibration the patient perceives it as pain. There is decreased perception of pin up to the ankles bilaterally. He makes errors with light touch on the toes. Straight leg raising is negative.

Questions

1. Is peripheral vascular disease the cause of his pain?
2. Where is the lesion causing his pain?
3. Can diabetes be the only underlying pathology? What word is used to explain the patient's perception of a vibration stimulus as painful? With what disease is it associated. Can the sensory signs (not symptoms) be caused by lumbar radiculopathy?
4. Can one neurologic disease explain all of the findings?

Case 7 Analysis

1. No. The patient has normal peripheral pulses. Importantly, paresthesias are not caused by vascular disease. There is no swelling, tenderness, warmth or redness to suggest deep venous thrombosis.
2. Unilateral calf pain suggests lumbar radiculopathy and does not occur with neuropathy. Neuropathy typically causes bilateral foot discomfort such as paresthesias and burning sensations. Lumbar radiculopathy due to a herniated disk usually causes asymmetric leg pain which is aggravated by prolonged sitting. When root pain is provoked by walking, the term applied is neurogenic claudication and it is characteristic of lumbar spinal stenosis. Normal straight leg raising is commonly present with patients who have this disorder.
3. No. Allodynia. This word is used to explain the elicitation of pain with a nonpainful stimulus. Allodynia is most often associated with neuropathy. Sensory

signs, especially impaired vibration perception, are caused by neuropathy not lumbar radiculopathy.
4. No. The MRI shows severe lumbar spinal stenosis at L4–L5, right greater than left. This explains the calf pain with exercise.

Diagnoses

1. Lumbar spinal stenosis with right L5 radiculopathy and neurogenic claudication.
2. Diabetic neuropathy [17].

Comment Despite the valid principle of the parsimony of diagnosis, a second illness must not be overlooked.

Case 8 A 47-year-old man complains of a 1-year history of loss of balance and a burning, itchy sensation affecting both feet. The sensory symptoms awaken him at night, but during the day he gets some relief with gabapentin.

Three months ago he noted mild blurring of vision affecting the right eye. An optometrist found slight blurring of the temporal margin of the right optic disk. Visual acuity was 20/25 O.D. and 20/20 O.S. A follow-up visit was scheduled in 1 month but the patient was out of town on a business trip and canceled the appointment. Since then he has noticed progressive loss of vision O.D., especially the last 2 weeks.

Past medical history: The patient had lymphoma 5 years ago and responded well to chemotherapy but had an adverse effect from vincristine which caused painful paresthesias and weak feet. There was partial recovery after the medication was discontinued. Two years ago he had atrial fibrillation and tachycardia which was refractory until treatment with amiodarone was initiated. He has hypercholesterolemia, coronary artery disease and required stents 4 years ago. He has a 3-year history of diabetes and hypertension.

Current medications are amiodarone, simvastatin, metformin, and ramipril.

Neurologic Examination Blood pressure is 150/94; pulse is 80 and regular.

There is a large central scotoma O.D. with a visual acuity of 20/200. A relative afferent pupillary defect (RAPD) is present. Funduscopic examination reveals a blurred right optic disk margin and two splinter hemorrhages at the disk margin. There is a generous cup-to-disc ratio O.S. There is bilateral moderate-to-severe finger-to-nose and heel-to-shin ataxia. Failure of check is noted in both arms. He is unable to perform tandem gait. Strength of anterior tibialis is 4/5 bilaterally. Vibration perception is absent at the toes, ankles, knees, and fingers. A few position sense errors are made at the toes and there is distal sensory loss to pin and temperature in all extremities. Reflexes are 1+ except for absent ankle jerks.

Questions

1. Where are the lesions? Does this patient have papilledema?
2. Can the ataxia be due to sensory loss?
3. Is there one etiology? What is the differential diagnosis?

4. What are the main considerations and the most likely etiology?

Case 8 Analysis

1. This patient has optic nerve disease, cerebellar system dysfunction, and neuropathy. Unilateral funduscopic abnormalities, central scotoma, decreased visual acuity, and a RAPD all indicate an optic neuritis. A generous cup-to-disc ratio in the contralateral eye makes a nonarteritic anterior ischemic optic neuropathy (AION) unlikely. This is not papilledema which is bilateral and associated with normal vision and pupils. Limb ataxia, inability to perform tandem gait, and failure of check signal cerebellar system dysfunction. Distal sensory loss, absent ankle jerks, and distal weakness are signs of neuropathy.
2. Not in this case. Severe position sense loss can cause heel-to-shin ataxia but the amount of proprioceptive loss is minimal, affects only the toes and therefore cerebellar system pathology must explain the ataxia.
3. No. It is unlikely since the patient did not fully recover from a neuropathy probably due to vincristine toxicity. The differential diagnosis includes:

   (a) Toxic factors.
   (b) Diabetes.
   (c) Vasculitis.
   (d) Paraneoplastic syndrome.

4. Diabetes causes neuropathy and predisposes to an anterior ischemic optic neuropathy (AION), but does not cause cerebellar ataxia unless there is an associated stroke involving the cerebellar system. The signs would then be focal.

Vasculitis may cause an optic neuritis and neuropathy but not cerebellar ataxia without focality which is expected with an ischemic complication. Paraneoplastic syndromes may cause neuropathy and cerebellar dysfunction but rarely a simultaneous optic neuropathy.

Simvastatin may rarely produce neuropathy but neither optic neuropathy nor cerebellar system dysfunction. Vincristine commonly causes neuropathy but not the other findings, and was discontinued years ago. Amiodarone is well-known to cause an optic neuritis, cerebellar dysfunction, and neuropathy. The insidious onset of optic nerve disease and generous cup-to-disc ratio in the contralateral eye makes a nonarteritic anterior ischemic optic neuropathy very unlikely. Amiodarone toxicity is the unifying diagnosis but it does not include contributing factors of vincristine toxicity and possibly diabetes.

Diagnosis Optic neuritis, cerebellar dysfunction, and neuropathy secondary to amiodarone toxicity [3].

Comment Drug toxicity can cause a multitude of symptoms and signs which can easily be overlooked.

Case 9 A 36-year-old woman complains of severe pain on the left lateral thigh. The pain is intermittent, sharp, and often worse with movement. The severity is 8/10. It

occurs several times per hour and each pain lasts 5–10 min. She has had low back pain for many years but without any definite radiation down the legs.

Neurologic Examination The patient is 5 ft. 4 in. and weighs 213 lb. Blood pressure is 140/90, pulse is 86 and regular.

The only neurologic abnormality is hypesthesia to pin and light touch on a well-defined region over the anterolateral portion of the left thigh. Straight leg raising elicits low back pain at 80° bilaterally.

MRI (lumbar) discloses two large herniated disks, L3–L4 and L4–L5.

Questions

1. Where is the lesion?
2. Do the MRI findings help with regard to the diagnosis?
3. What causes the pain?

Case 9 Analysis

1. The presence of unilateral leg pain suggests radiculopathy. The neurologic deficit, however, is in the distribution of the lateral femoral cutaneous nerve of the thigh and loss of perception of light touch is rarely found with radiculopathy, certainly not in such a well-outlined form.
2. No. The test was unnecessary and resulted in needless expense, unfortunately.
3. This is due to compression of the lateral femoral cutaneous nerve of the thigh as it passes under the inguinal ligament. Obesity may be a predisposing factor.

Diagnosis Meralgia paresthetica [16].

Comment Abnormal MRI findings commonly lead to incorrect diagnoses and even unnecessary major surgery.

Case 10 A 22-year-old college student requests an evaluation for weakness of both hands. The weakness has been slowly progressive since his teen years. Over the last few years his eyelids have tended to droop. He has had difficulty swallowing over the past year associated with occasional choking spells. His grades have declined despite putting forth maximum effort. He complains of daytime drowsiness.

Past medical history is remarkable for three episodes of momentary loss of consciousness causing an abrupt fall. Afterwards he is cold, sweaty, and nauseated. The patient is adopted. He does not smoke or use alcohol.

Neurologic Examination Blood pressure is 120/60; pulse is 88 with frequent irregular beats.

The patient has a receding hairline and sunken cheeks giving him a gaunt appearance. He exhibits bradyphrenia but he has a Mini-Mental State Exam score of 30/30. He has mild bilateral ptosis, severe weakness of eye closure and is unable to smile. There is early cataract formation. His mouth is slightly ajar and there is wasting of

temporalis musculature. Palate and tongue movements are normal. Head flexion is 4/5, intrinsic hand musculature 4/5 except for finger flexors 3+/5 and anterior tibialis is 4+/5. His gait is normal other than difficulty with heel-walk. Reflexes and sensory examinations are normal.

Questions

1. What muscles of the eyes, face, and neck are weak?
2. Can a disorder of the neuromuscular junction explain the clinical findings?
3. Where is the primary pathology?
4. Is there another neuroanatomic site affected?
5. What bedside test is diagnostic?
6. What is the diagnosis and the etiology?
7. What physiologic systems are commonly involved in this disorder?
8. What is the differential diagnosis?
9. What laboratory tests are indicated?
10. What consultation should be requested promptly?

Case 10 Analysis

1. Ptosis without pupillary abnormalities usually indicates weakness of levator palpebrae superioris rather than sympathetic or parasympathetic nerve involvement. Masseter and temporalis muscle weakness and atrophy results in the partially open mouth and contributes to the gaunt appearance. Orbicularis oculi and oris weakness is evident because of weak eye closure and inability to smile. Weak head flexion indicates weak sternocleidomastoid muscles. Dysphagia is likely due to pharyngeal and/or esophageal pathology as palate and tongue movements are normal.
2. No. Similar weakness occurs but impaired cognition does not, nor does muscular atrophy or syncope.
3. Muscle.
4. Cerebrum in view of the history of cognitive dysfunction.
5. The diagnostic bedside tests are grip and percussion myotonia. The patient is requested to grip two fingers of the examiner's hand for several seconds and then quickly release them, which the patient is unable to do. Percussion myotonia is detected by tapping the thenar eminence with a reflex hammer. The thumb remains flexed at the metacarpal-phalangeal joint for a few seconds. Tongue myotonia can occasionally be demonstrated by placing the edge of the tongue blade on the midline of the tongue and tapping the upper edge gently.

   Differential diagnosis of myotonia includes hyperkalemic periodic paralysis, paramyotonia congenita, Schwartz-Jampel syndrome and Isaac's syndrome (neuromyotonia).

6. *Diagnosis*: Myotonic dystrophy DM1. (Fig. 9.2) [7].

Comment This is an autosomal dominant disorder associated with a defective gene on chromosome 19. There is an unstable trinucleotide repeat sequence, cytosine,

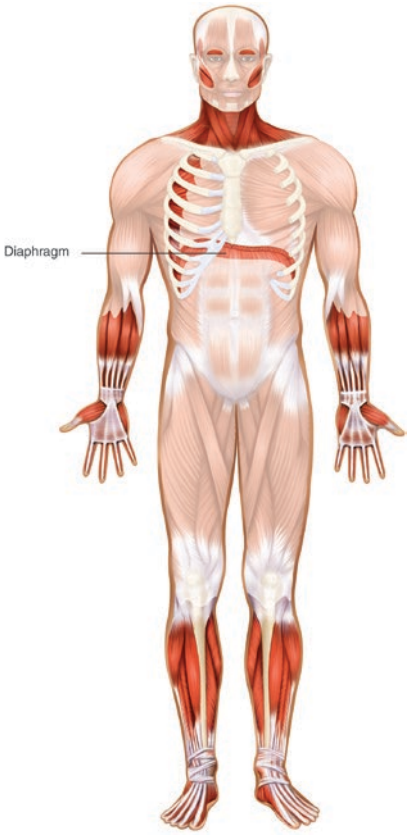

Fig. 9.2 Myotonic dystrophy DM1

thymine, and guanine (CTG). The severity of the symptoms is proportional to the number of excess repeats. Progression is slow and longevity may not be affected.

7. Endocrine disorders are common such as testicular atrophy, glucose intolerance and thyroid disease. There are cardiac conduction defects and gastrointestinal motility problems due to smooth muscle involvement. Additional manifestations, some of which are noted in the case report, include frontal baldness, cognitive impairment, respiratory insufficiency because of diaphragmatic and intercostal muscle weakness and excessive daytime somnolence. The latter is probably due to nocturnal hypoventilation. Cataracts are nearly universal.
8. The main differential diagnosis includes:

   (a) Myotonia congenita (Thomsen's disease). This is an autosomal dominant painless disease. Patients have generalized myotonia associated with well-developed and occasionally hypertrophic muscles in the legs with myotonia provoked by exertion after rest. The other manifestations of myotonic dystrophy are not present.

(b) Myotonic dystrophy DM2. This proximal myotonic myopathy is due to an unstable CCTG repeat expansion on chromosome 3 and is autosomal dominant. It commonly begins with grip myotonia which is less severe than in DM1. Pain is often severe, affects the abdomen, musculoskeletal system and is exercise-related. Weakness affects the face, proximal muscles of all limbs and is milder than DM1. Cataracts are frequent; glucose intolerance and hypogonadism may be present. Cognitive disorders and cardiac conduction defects are milder. Repeat expansion numbers are not proportional to the clinical presentation as they are with DM1.

9. CK, Holter monitor, and EMG. The CK is normal and the Holter monitor may reveal both atrial and ventricular arrhythmias. The EMG discloses characteristic features of myotonia.
10. Cardiology. The patient has already had three syncopal events most likely secondary to a serious ventricular arrhythmia. Ninety percent of patients have conduction defects.

Case 11 A 56-year-old woman complains of neck, right shoulder, and upper arm pain of 2 months duration. She finds that the pain radiates from the neck down to the posterior part of the right upper arm. The pain is aggravated when lying on her right side and she is awakened by it frequently. Her right arm feels weak.

Past medical history: The patient has type II diabetes. Medication is metformin.

Neurologic Examination Blood pressure is 115/80; pulse is 106 and irregularly irregular.

The neurologic examination is normal except that pain interferes with testing the strength of the right arm.

MRI (cervical). There are narrowed intervertebral foramina bilaterally at C5–C6 and on the right side at C6–C7.

Questions

1. What symptom suggests the source of the pain?
2. What bedside tests are diagnostic?
3. How is the MRI scan helpful?
4. What part of this entire examination is most important?
5. What is the diagnosis?

Case 11 Analysis

1. Pain when lying on the right side suggests that the pathology is in the right shoulder.
2. Abduction of the arm and pressure placed at the biceps insertion causes pain and thus the pathology is local.
3. It isn't. It is an expensive unnecessary test.
4. The vital signs. These must be taken on every visit. The patient has atrial fibrillation and is promptly referred back to her internist.

5. *Diagnosis*: Biceps tendonitis.

Comment This diagnosis is often misconstrued as cervical radiculopathy prompting inappropriate treatment. The patient will be referred to an orthopedic surgeon after her atrial fibrillation is treated and cardiac status is stabilized. A local steroid injection should be helpful.

Case 12 A 52-year-old man complains of a 3-year history of fatigue and a 2-year history of leg weakness. For the past year he has been troubled by dry mouth, constipation, impotence, and paresthesias.

Past medical history includes chronic obstructive pulmonary disease associated with a 40 pack-year history of smoking.

Neurologic Examination Blood pressure is 130/92; pulse is 96 and regular.

Pupils are 3 mm with a 1+/4 reaction to light. Strength of deltoids, infraspinatus, iliopsoas, and quadriceps is 4/5. When deltoid strength is repeatedly examined several times over a period of 15 s, its strength increases to 4+/5. Reflexes are 1+ except for absent ankle jerks. Sensory examination is normal.

Questions

1. What symptoms and signs are major clues to the diagnosis?
2. What bedside test may be diagnostic?
3. Where is the lesion and what is the diagnosis?
4. Why does weakness occur?
5. What additional investigations are indicated?

Case 12 Analysis

1. There is evidence of autonomic nervous system dysfunction because the patient's symptoms include impotence, dry mouth, and constipation. The poor pupillary light reaction is a sign of autonomic nervous system dysfunction, parasympathetic in this case.
2. Repetitive use of weak muscles paradoxically increases their strength.
3. The lesion is at the neuromuscular junction.

Diagnosis Lambert–Eaton syndrome [15].

4. This is a presynaptic disorder with decreased quantal release of acetylcholine due to autoantibodies against neuronal voltage-gated calcium channels, P–Q type. Impairment of calcium channel function leads to the reduced quantal release of acetylcholine.
5. An EMG with rapid repetitive stimulation results in a markedly facilitated response, just the opposite of myasthenia gravis. There is a blood test to measure the level of autoantibodies. About 50% of patients have an occult malignancy, primarily small cell lung cancer. Consequently, an intensive investigation for underlying malignancy is required. This patient's CT scan of the chest disclosed lung cancer in the right middle lobe.

Case 13 A 28-year-old man requests an evaluation because of progressive, painless weakness of all extremities over 4 years. He has particular difficulty raising his arms to reach for objects over his head. For the last 4 months he has been unable to climb stairs. He now needs assistance to get out of a chair.

Past medical history is remarkable for insulin-dependent diabetes mellitus since his teens. He has always had good control of his diabetes. There is no family history of muscular disease.

Neurologic Examination Blood pressure is 120/70; pulse is 80 and regular.

There is wasting and atrophy of shoulder and thigh muscles. There is symmetrical 4/5 strength of deltoids, triceps, infraspinatus and supraspinatus. Strength of gluteus maximus, iliopsoas, and quadriceps musculature is 4+/5 on the right side and 4/5 on the left. Fasciculations are frequent in triceps, deltoid, and quadriceps muscles. Reflexes are barely elicitable and sensory testing is normal.

Questions

1. Where is the lesion?
2. What specific finding localizes the lesion?
3. If Babinski signs were present, what would be the presumptive diagnosis? If fasciculations were not present what diagnosis would be considered?
4. What test confirms the diagnosis?
5. What is the name of the disease and its variations?

Case 13 Analysis

1. The lesion is in the anterior horn cell (AHC) , the lower motor neuron.
2. The prototypical sign is the fasciculation. Localized fasciculations are often found with radiculopathies but, if widespread, AHC disease is nearly certain. Plexus and nerve pathology rarely cause fasciculations. Neuromuscular junction and muscle diseases do not cause fasciculations. Weakness and atrophy are common with diseases affecting the AHC.
3. If a Babinski sign is found, amyotrophic lateral sclerosis (ALS) would be the presumptive diagnosis because of concomitant upper and lower motor neuron signs. Limb girdle muscular dystrophy would be considered in the absence of fasciculations.
4. EMG-NCV.
5. *Diagnosis*: Spinal muscular atrophy [7].

Comment This is an inherited disorder with numerous variations occurring in adults over age 20. The inheritance can be autosomal recessive, autosomal dominant or X-linked recessive. Spinal muscular atrophy occurring in patients ages 2–20 is called Kugelberg–Welander disease. In infancy the name given is Werdnig–Hoffman's disease. The prognosis for Werdnig–Hoffman's disease in infancy is less than 2 years; Kugelberg–Welander in childhood is 2–40 years; spinal muscular atrophy in adults is compatible with a normal life span. Gene therapy is now being studied and shows promise as a future treatment.

Case 14 A 54-year-old woman complains of unsteadiness for 3 months. This has been steadily progressing in severity. She adds a history of painful burning and prickly sensations in both feet. She has fallen a few times when entering a dark room. Her hands feel clumsy but strength is unimpaired. She has no other illnesses and prides herself on taking no medications. She has never had surgery.

Recent laboratory data includes a normal CBC, FBS, liver functions, TSH, BUN, creatinine, electrolytes, calcium, phosphorus, ANA, ESR, B12 level, serum protein electrophoresis and immunofixation.

Neurologic Examination Blood pressure is 95/60; pulse is 88 and regular.

There is 4+/5 strength of interossei and iliopsoas musculature. She has moderate heel-to-shin ataxia and mild finger-to-nose ataxia. Gait is slightly wide-based and she has a positive Romberg. Reflexes are 1+ and symmetrical except for absent biceps and ankle reflexes. Plantars are flexor. Sensory examination discloses absent vibratory perception at toes, ankles, fingers, and wrists. Vibration is perceived as painful at elbows and knees. Position sense is absent at toes, ankles, and fingers.

A lumbar puncture reveals a CSF protein of 107 mg/dl and 14 lymphocytes/cu mm. Blood tests were obtained and the patient refused follow-up care.

The patient expired 1 year later and an autopsy was obtained.

Questions

1. Where is the lesion?
2. How can limb ataxia be explained?
3. What is the name for a vibration stimulus perceived as painful?
4. Why does the patient fall in the dark and why are her hands clumsy? Are there other reasons for falling in darkness if this is the only symptom?
5. Does the rapid progression suggest the diagnosis?
6. What could be the diagnosis and what additional tests might have been performed and been diagnostic? Could treatment have been helpful?

Case 14 Analysis

1. Neuropathy. Reduced reflexes and distal sensory loss support this localization.
2. Limb ataxia is commonly observed in patients with severe position sense loss.
3. Allodynia is the term used when a usually painless stimulus is painful.
4. Vision is necessary to maintain balance when patients have position sense loss. Impaired proprioception in the fingers interferes with dexterity. Vestibular dysfunction will also cause instability in darkness. Vision suppresses nystagmus of peripheral vestibular origin and compensates for instability when the vestibular system is dysfunctional. Pure cerebellar disease rarely produces a positive Romberg. This is a controversial topic. When it occurs it is most likely due to interruption of vestibulocerebellar pathways.
5. Yes. The rapid development with primarily sensory features suggests a paraneoplastic sensory neuropathy.
6. *Diagnosis*: Paraneoplastic sensory neuropathy [3].

Comment In this case a paraneoplastic panel was performed prior to loss of follow-up care and revealed an anti-Hu antibody, a neuronal antinuclear antibody. There is a strong association with an occult malignancy, probably 90%, and often this neuropathy precedes the discovery of cancer by 1–2 years. A paraneoplastic panel for neuropathy should be obtained, followed by a search for an occult malignancy. Surgical resection of the malignancy can ameliorate the symptoms.

This patient expired from metastatic carcinoma of the breast. Small cell lung cancer is the most common etiology. Others include lymphoma, ovarian and prostate carcinomas. Pathologic studies disclosed inflammation in the dorsal root ganglia.

Case 15 A 42-year-old male truck driver requests an evaluation for left hand weakness which has been progressive over 6 months. He also has occasional tingling sensations affecting the left fifth finger. He does mainly long distance hauling.

Neurologic Examination Blood pressure is 140/86; pulse is 88 and regular.

There is atrophy between the thumb and the index finger as well as the hypothenar eminence of the left hand. He has mild weakness of extension of the terminal phalanx of the left fourth and fifth fingers, moderate weakness of abduction and adduction of the 2nd–fifth fingers. There is mild weakness of wrist flexion medially and of thumb adduction. There is mild hypesthesia to pin over the fourth and fifth fingers.

Questions

1. What muscles are involved?
2. What questions should be asked of the patient to establish the precise etiology of the weakness?
3. What is the anatomic differential diagnosis?
4. What movement can be an aggravating factor?
5. What is the diagnosis?

Case 15 Analysis

1. Adductor pollicis, palmar and dorsal interossei (adduction and abduction, respectively), third and fourth lumbricales, flexor carpi ulnaris.
2. Over the last 6 months has there been any change in your work habits? “Yes, I lost the air conditioning in my truck and have to leave the windows open.” Where is your left arm? “I lean it on the window ledge.”
3. Ulnar nerve vs. medial cord of the brachial plexus vs. C8T1 radiculopathy.
4. Frequent flexion at the elbow aggravates the neuropathy because it tightens the flexor carpi ulnaris aponeurosis thus reducing the size of the cubital tunnel.
5. *Diagnosis*: Ulnar neuropathy due to compression of the nerve at the cubital tunnel [16].

Comment An EMG-NCV confirms the diagnosis. A careful review of the history of prior injuries is also necessary. An old elbow fracture with bony overgrowth compressing the ulnar nerve (tardy ulnar palsy) is always a diagnostic consideration.

Case 16 A 60-year-old man requests an evaluation for a droopy left eyelid. He denies any other problems. On review of neurologic symptoms he acknowledges that he has been "aging" by which he means that his strength has decreased. He is a paralegal and often has to retrieve large volumes of tax laws from shelves above his head. He now requires assistance to do this. He used to climb five flights of stairs to his office for exercise but now manages just one flight and then takes the elevator. He is easily fatigued and short of breath with minimal exertion.

Past medical history is remarkable for hypertension for which he takes atenolol.

Neurologic Examination Blood pressure is 146/96; pulse is 112 and regular.

He has moderate left ptosis, 4/5 strength of head flexion, deltoids, triceps, and infraspinatus bilaterally. Iliopsoas is 4+/5 on the right and 4/5 on the left. Reflexes are 1+ with flexor plantar responses. Sensory examination is normal.

Laboratory data: FBS is 115 mg/dl. Vital capacity is 1.5 L. Arterial blood gases are normal.

An edrophonium test restores eyelid function to normal and vital capacity increases to 3 L but muscle strength is unchanged. A neostigmine test is performed later and muscle strength remains unchanged.

Questions

1. Is there more than one lesion site?
2. What are the major risks of edrophonium? Why was a neostigmine test performed?
3. If there is no edrophonium or neostigmine available or if the patient refuses an injection is there another diagnostic test that could be useful?
4. Is it common to have normal arterial blood gases yet a decreased vital capacity?
5. What are the major diagnostic clues for another disease process?
6. What workup is indicated?
7. What is the diagnosis or what are the diagnoses?

Case 16 Analysis

1. Yes. The patient clearly has myasthenia gravis, a neuromuscular junction disorder. The lack of response to either edrophonium or neostigmine regarding muscle strength suggests an additional disease process. Proximal weakness without fasciculations, reflex, or sensory abnormalities is compatible with a myopathy.
2. The edrophonium test is especially helpful for patients with ptosis or eye movement weakness. Its major, infrequent complications include bradycardia and hypotension because it inhibits destruction of acetylcholine by cholinesterase and thus augments cholinergic responses. Performance of this test with the patient supine is safest. A neostigmine test is especially useful to assess muscular strength since the patient can be examined more carefully every 30 min up to 2 h.

3. Yes.
   (a) The ice pack test. Ice covered with a light cloth applied to the affected eye for 2–5 min may alleviate ptosis. A 2 mm or more elevation is considered a positive test. Ice will not help other muscles and therefore it is not useful for diplopia. The presumed mechanism is cooling of skeletal muscles which inhibits activity of cholinesterase.
   (b) Evaluate for Cogan's lid-twitch sign. During refixation from downgaze to direct forward gaze the upper eyelid will twitch upward and briefly expose the sclera.
4. Yes. Testing the vital capacity is a direct assessment of chest musculature integrity. Arterial blood gases are not reliable markers for evaluating this neuromuscular weakness. They are often normal immediately prior to a respiratory arrest due to muscle fatigue.
5. The patient has hypertension and tachycardia despite treatment with a beta blocker, atenolol. Furthermore, he has proximal muscle weakness unimproved with anticholinesterase agents.
6. Workup includes a CK, TSH, free T-4, ESR, ANA, CT chest with and without contrast, and an EMG with repetitive nerve stimulation. The CK is 60 U/L, TSH is 0.2 μU/ml. (normal 0.5–5.0 μU/ml.), free T-4 is 3.8 ng/dl (normal 0.8–2.4 ng/dl), ESR is 10 mm/h and ANA is negative. The TSH and free T-4 values indicate hyperthyroidism, a well-known associated disorder in patients with myasthenia gravis. CT of the chest shows no thymoma which is present in about 15% of patients with myasthenia gravis. It should be noted that hypothyroidism may also be present in myasthenic patients. The EMG shows typical fatigue with repetitive nerve stimulation and is diagnostic of myasthenia gravis.
7. *Final Diagnosis*
   (a) Myasthenia gravis [6].
   (b) Hyperthyroidism with myopathy [14].

Comment It is essential to search for a second diagnosis when the symptoms or signs, even if minor, are not compatible with the primary diagnosis.

Case 17 A 72-year-old man complains of burning feet and "passing out." Over the past 5 years the patient has had intermittent, prickly sensations on the soles of both feet. He ignored them up until 3 months ago when they became painful. When taking his usual 1-h walk in the park he has found it necessary to sit down nearly every 10 min, due to pain and feeling faint. Intense pain usually precedes the sensation of faintness. On two occasions over the last 2 weeks he felt faint with only minor pain. He also had the sudden onset of feeling cold, clammy, nauseated and then fell. On these occasions there was complete loss of consciousness for several seconds without subsequent confusion.

Past medical history: The patient has asthma but currently takes no medications.

Neurologic Examination Blood pressure: supine 120/72, sitting 115/72, standing at 1 min 110/66, standing at 3 min 106/60, and standing at 5 min 100/56. The heart rates are 72, 76, 78, 80, and 80, respectively.

Strength of anterior tibialis is 4+/5 bilaterally and ankle reflexes are absent. Vibration perception is absent at toes and ankles and a few position sense errors are made at the toes bilaterally. There is distal sensory loss to pin and temperature in all extremities.

Questions

1. What is the most likely cause of this patient's syncope?
2. What part of the examination is incomplete?
3. What is the single anatomic diagnosis?
4. What is the most likely etiology and what tests confirm it?
5. What is the differential diagnosis of neuropathy with autonomic involvement?

Case 17 Analysis

1. Delayed orthostatic hypotension. The etiology of syncope is usually a cardiac arrhythmia or severe hypotension. The former diagnosis is sporadic. The latter is more likely to be uniform with regard to the time it occurs after assuming an upright posture. This is consistent with the patient's history.
2. The patient's blood pressure was dropping consistently over 5 min. Although the patient can be diagnosed with orthostatic hypotension because the diastolic pressure dropped 16 points between being supine and at 5 min he was not symptomatic. (A drop greater than 10 points is abnormal). Thus the readings should have been continued until a minimum of 10–12 min had elapsed since he reports being symptomatic only after walking for 10 min. A 10-min walk disclosed a blood pressure of 80/55 and the patient became symptomatic, an additional confirmation of the diagnosis.
3. *Diagnosis*: Neuropathy plus autonomic neuropathy [17].
4. Diabetes mellitus. Standard accepted tests are hemoglobin A1C and a 2-h glucose tolerance test. The hemoglobin A1C is 7.5%. The FBS is 102 mg/dl and the 2-h glucose level is 220 mg/dl.
5. Amyloidosis, paraneoplastic syndromes, Guillain–Barré disease, porphyria, HIV, and pandysautonomia. Additional considerations include toxic drugs, especially vincristine, amiodarone, and cisplatin as well as toxic substances such as thallium, N-hexane, arsenic and mercury. Hereditary sensory and autonomic neuropathies are rare etiologies.

Case 18 A 27-year-old man complains of severe, "searing," right arm pain and weakness. The pain began 1 week ago and, after 4 days had elapsed, he noted weakness around the right shoulder. The pain began in the upper part of the shoulder blade, extended up to the neck and radiated down the outer aspect of the upper arm. The severity was 8/10. Since the weakness developed, the pain has dropped to a level of 5/10. Movement aggravates the pain.

Past medical history: Asthma and recurrent bronchitis.

Neurologic Examination Blood pressure is 120/70; pulse is 88 and regular.

The strength of right deltoid, infraspinatus, and supraspinatus is 3/5. Strength of right biceps and brachioradialis is 4/5. There is winging of the right scapula. Right biceps and brachioradialis reflexes are absent. There is decreased perception of pin in a small round patch on the outer aspect of the right upper arm in the distribution of the axillary nerve.

Questions

1. Where is the lesion? Why? What nerves innervate these muscles?
2. What is the significance, if any, of the motor signs far exceeding any sensory loss?
3. What is the most common etiology? Is it ever bilateral?
4. What is the differential diagnosis?
5. What is the diagnosis?

Case 18 Analysis

1. Brachial plexus, upper trunk and the long thoracic nerve. The pathology affects several nerves, the axillary, long thoracic, suprascapular, radial, and musculocutaneous. These innervate, respectively, the deltoid, serratus anterior, infra- and supraspinatus, brachioradialis, and biceps muscles. The long thoracic nerve is formed proximal to the trunk and is composed of C5–C7 roots
2. This is characteristic of brachial plexopathies.
3. A post-infectious disorder is the most common etiology in an outpatient practice. It has been called Parsonage–Turner syndrome and it can rarely be bilateral.
4. Associated diseases are diabetes, polyarteritis nodosa and systemic lupus erythematosus (SLE).

   Other etiologies are:

(a) Post-vaccinal. Tetanus, influenza, typhoid-paratyphoid, and DPT.
(b) Post-infectious. Epstein–Barr, cytomegalic inclusion virus, influenza, diphtheria, typhoid, and typhus.
(c) Trauma. Causes include stretching, compression, traction, direct injury, surgical positioning, and intravenous drug abuse.
(d) Neoplasm. The etiology may be infiltration of a malignant neoplasm originating from the apex of the lung (Pancoast's tumor).
(e) Complication of radiotherapy.

5. *Diagnosis*: Brachial plexopathy (Parsonage-Turner syndrome), postinfectious.

Comment Clues to the diagnosis are the excruciating pain aggravated by arm movement. The initial diagnosis is cervical root compression but this condition typically causes pain with head movement, primarily extension, and focal weakness. Moreover, brachial plexus lesions are ordinarily manifested by diffuse weakness.

Case 19 A 32-year-old woman complains of pain in the left forearm for 4 years. Over the last 10 months she has noticed intermittent tingling of the left fourth and fifth fingers. Over recent weeks the strength of her left grasp has decreased.

Past medical history is remarkable for insulin-dependent diabetes mellitus.

Neurologic Examination Blood pressure is 100/60; pulse is 64 and regular.

There is wasting of the muscles in the left thenar eminence. Strength of abductor pollicis brevis, opponens pollicis, flexor pollicis longus, and flexor digitorum profundus (second and third digits) is 4/5, all median innervated muscles. First palmar and dorsal interossei, adductor pollicis and flexor carpi ulnaris are 4+/5, all ulnar innervated muscles. There is decreased perception of pinprick over the dorsal and palmar surfaces of the fourth and fifth fingers, ulnar nerve distribution, as well as the medial forearm (medial antebrachial nerve) which arises from the medial cord. Additionally, there is hypesthesia to pinprick over the palmar surface of the hand medial to the fourth and fifth fingers, the median nerve distribution.

Questions

1. Where is the lesion?
2. Is the history of insulin-dependent diabetes mellitus pertinent?
3. What part of the history determines the seriousness of the diagnosis?
4. What is the differential diagnosis?
5. What is the diagnosis?

Case 19 Analysis

1. This lesion affects both median and ulnar nerve innervated muscles. The sensory loss is primarily in the ulnar and median nerve distributions. The medial forearm is supplied by the medial antebrachial nerve which originates from the medial cord. The anatomic diagnosis is brachial plexopathy, lower trunk.
2. No.
3. The duration of 4 years indicates a benign process.
4. The differential diagnosis includes neoplastic infiltration, complication of radiotherapy, repetitive trauma, and the neurogenic thoracic outlet syndrome which is usually due to a cervical rib. Diabetes, vasculitis, post-infectious and post-vaccinal etiologies are excluded because of the slow focal progressive course.
5. *Diagnosis*: Neurogenic thoracic outlet syndrome secondary to a cervical rib [4].

Comment This is most often due to a rudimentary cervical rib with an elongated transverse process of the C7 vertebra. A fibrous band arises from the tip of this rib, attaches to the first thoracic rib, and compresses the lower trunk of the brachial plexus.

The syndrome is an extremely rare disorder and initial diagnoses are seldom accurate. Wasting occurs and is most often prominent in median nerve innervated muscles and sensory symptoms are often present in the ulnar nerve distribution. The diagnosis of this disorder due to sensory symptoms alone is frequently made and

rarely accurate. Numerous first thoracic ribs have been removed without amelioration of symptoms.

There is a vascular thoracic outlet syndrome, equally rare, due to compression of the subclavian artery by a fully developed cervical rib; this may result in poststenotic dilatation of the subclavian artery with thrombus formation and distal embolization.

Finally, there are instances of combined vascular and neurologic symptomatology without definite signs, a nebulous concept. It may occur in female patients with droopy shoulders and long necks which cause stretching of the brachial plexus.

Case 20 A 33-year-old man complains of left foot weakness after spending an evening gambling in Las Vegas 5 days previously. He noticed the weakness after getting up from the poker table where he had been sitting for 3 straight hours. He now has a dropped left foot.

Last night, after several cocktails, he fell asleep next to his girlfriend. Today he complains of inability to raise his right hand.

Past medical history: Several years ago, the patient was diagnosed with a "dropped foot" and recovered without residual weakness after 3 months. He is not certain which foot was involved.

Neurologic Examination Blood pressure is 138/88; pulse is 76 and regular.

Dorsiflexion of the left foot is 2/5. Dorsiflexion of the left big toe is 2/5. Dorsiflexion of the 2nd–fifth toes is 3/5. Eversion of the left foot is 2/5. Reflexes are normal and there is decreased perception of pin over the left lateral calf and dorsum of the foot.

Right elbow extension is 2/5. Flexion at the elbow with the forearm between the pronated and supinated position is 2/5. Extension of the wrist to the radial side is 2/5. Extension of the distal phalanx of the thumb is 1/5. Extensors of the fingers at the metacarpal-phalangeal joints is 1/5. Reflexes are 2+ except for absent brachioradialis and triceps on the right side. There is decreased perception of pin on the dorsum of the thumb, index, and third fingers as well as the proximal portion of the adjacent hand.

Questions

1. What muscles and nerves are involved?
2. What additional diagnostic information may be obtainable?
3. What is the likely diagnosis?

Case 20 Analysis

1. Dorsiflexion of the foot is anterior tibialis, dorsiflexion of the big toe is extensor hallucis longus, and dorsiflexion of the 2nd–5th toes is extensor digitorum longus and brevis. These are all innervated by the deep peroneal nerve. Eversion of the foot is peroneus longus and brevis and decreased perception of pin, as described, are both mediated by the superficial peroneal nerve. The reflex at the ankle is intact since the efferent response is mediated by the posterior tibial nerve which supplies the spared gastrocnemius.

The following muscles and sensory loss are all radial nerve supplied. Elbow extension is triceps muscle, right elbow flexion midway between pronation and supination is brachioradialis, extension of wrist to radial side is extensor carpi radialis longus, extension of distal phalanx of thumb is extensor pollicis longus, and loss of reflexes are those of the triceps and brachioradialis. The decreased perception of pin over the dorsum of the thumb, index, and middle fingers as well as proximal adjacent hand is via the superficial radial branch.

2. How does he sit at the card table? "I cross my legs." Was his girlfriend on his right or left side and where was her head? "Her head was on my right shoulder." Does anyone in the family have similar problems? "Yes, my father."
3. *Diagnosis*: Hereditary neuropathy with liability to pressure palsies, with right radial and left common peroneal neuropathies [8].

Comment This is an autosomal dominant trait causing a defect in peripheral myelin which increases susceptibility to pressure. The disorder resulted in common peroneal and radial neuropathies. Genetic testing for this illness is available.

Case 21 An 88-year-old male, retired, philosophy professor complains of difficulty swallowing liquids for 4 months. The dysphagia began abruptly and has persisted. It is unchanged throughout the day. Over the last month he has had difficulty climbing stairs and replacing heavy books on shelves overhead.

His past medical history includes rheumatoid arthritis, symptomatic for 15 years with early morning stiffness and migrating polyarthralgia. This was diagnosed 1 year ago. After therapeutic trials with several medicines, he was placed on prednisone 2 years ago and has improved with a dose of 12 mg per day. He has hypercholesterolemia and hypertension. Current medicines are atorvastatin and losartan.

Neurologic Examination Blood pressure is 135/85; pulse is 60 and regular.

Palate movements are sluggish but gag is intact. Repeated checks of deltoid strength yield 4/5 strength bilaterally on the 12th try. Iliopsoas and quadriceps are 4+/5. Reflex and sensory examinations are normal. There are scattered ecchymoses on both arms.

Questions

1. What is the neuroanatomic diagnosis and the differential diagnosis?
2. Why must examination of the palate be done carefully?
3. What tests are performed?
4. What treatment is initiated?

First Follow-Up Visit 1 Month Later

The patient is pleased with his new treatment regimen because of normal swallowing and the return of arm strength to normal. He has, however, increasing difficulty climbing and descending steps although he can still manage one flight of stairs. Examination is normal except for 4/5 strength of iliopsoas and quadriceps. The treatment regimen is readjusted.

Second Follow-Up Visit 3 Months Later

One month ago the patient tripped and fractured his left hip which was pinned. Osteoporosis was diagnosed at that time. He can no longer climb a flight of stairs. Examination reveals mottled skin with several ecchymoses. There is 4+/5 strength of iliopsoas and quadriceps muscles.

Questions

5. What were the test results? Which were abnormal?
6. What conditions support the diagnosis?

Case 21 Analysis

1. The anatomic differential diagnosis related to dysphagia is a brainstem lesion (medulla-nucleus ambiguus), motor neuron disease, neuromuscular junction disorder, and myopathy. The sudden onset raises a suspicion of a vascular event affecting the brainstem. But there is no single artery which supplies both right and left nucleus ambiguus which contain neurons of the 9th and 10th cranial nerves. Motor neuron disease is not of sudden onset and usually declares itself with fasciculations. Myasthenia gravis seldom begins abruptly but dysphagia is often an early symptom. Although it often worsens later in the day this is not required for the diagnosis. Myopathies such as oculopharyngeal dystrophy will not develop acutely. Myasthenia gravis must be the suspected diagnosis.
2. If the patient has myasthenia gravis there should be an intact gag reflex because of normal sensation but the palate may not move in response to the stimulus.
3. CK, antiacetylcholine receptor antibodies, thyroid functions and EMG with repetitive nerve stimulation.
4. The patient is treated with pyridostigmine 60 mg. 1 h ac t.i.d. and prednisone 60 mg. q. a.m.
5. The antiacetylcholine receptor antibodies were elevated and the EMG disclosed scattered myopathic units plus a decremental response to repetitive nerve stimulation. The increased antibody levels and the response to repetitive nerve stimulation indicate myasthenia gravis. The myopathic units in proximal muscles indicates a myopathy. The normal CK rules out statin myositis.
6. The patient's skin is fragile resulting in scattered ecchymoses and he now has osteoporosis. Both of these developments are complications of long-term treatment with prednisone, usually with doses greater than 10 mg/day. Many neurologists prefer every other day treatment which has less risk for prednisone complications.

Diagnoses

1. Myasthenia gravis.
2. Steroid myopathy.

Comment Steroid myopathy is another instance of treatment-induced complications. A new anatomic diagnosis, myopathy, prompts a search for a second illness.

Case 22 A 54-year-old male retired baseball player is admitted to the hospital with fever, productive cough, and cachexia. He was diagnosed with carcinoma of the tongue 6 months ago and treated by hemiglossectomy and node resection. He has been anorectic since then and dropped 40 lb. from 170 to 130.

Past medical history is remarkable for a 30-year history of using chewing tobacco daily.

Neurologic Examination Temperature 101.5 ° F blood pressure is 140/100; pulse is 110.

The patient is dehydrated, has a supple neck and there are rales, dullness to percussion and decreased fremitus at the right base. The heart is enlarged. The liver is 4 cm below the right costal margin on deep inspiration and there is 3+ pedal edema. Neurologic examination is normal.

Laboratory data shows a white count of 22,000/cu mm with 92% neutrophils. Gram stain of sputum reveals Gram-positive diplococci.

The patient is admitted to the Intensive Care Unit. After rehydration and treatment for pneumococcal pneumonia he recovers over 1 week. An additional diagnosis of congestive heart failure is made and he is transferred to a rehabilitation unit because of cachexia, malnutrition, and dyspnea on exertion. On the rehabilitation unit he complains of poor balance and falls in the shower while washing his hair.

Examination reveals moderately severe heel-to-shin ataxia, inability to perform tandem gait and a positive Romberg. He has absent position sense at toes and ankles, absent vibration sense from the knees down and at the fingers. There is distal sensory loss to pin and temperature in all extremities and impaired light touch over the toes. Reflexes in the legs are absent.

Questions

1. Where is the lesion?
2. Are all the neurologic abnormalities consistent with this lesion location?
3. What is the cause of the acute disorder?
4. What routine blood tests and medical disorder provide support for this diagnosis?
5. What is the diagnosis and what treatment restores the patient to normal in 1 month?

Case 22 Analysis

1. The patient has a neuropathy because of distal sensory loss to all modalities and absent reflexes in the legs.
2. Yes. Heel-to-shin ataxia and poor tandem gait are commonly present in patients with large fiber neuropathies causing impaired vibration, position sense, and touch. Cerebellar system involvement remains a consideration, however.
3. This patient was malnourished, cachectic, and given intravenous fluids without vitamins. This further depleted his already deficient stores of vitamins. He could

be assumed to have vitamin B_1 deficiency as he has signs of beriberi syndrome manifested by congestive heart failure, hepatomegaly and polyneuropathy.
4. A subsequent review of his laboratory data is significant for macrocytic blood indices with an MCV of 105 fL and MCH of 35 pg/cell. The differential diagnosis of macrocytosis includes deficiencies of vitamins B_1, $B_{12,}$ and folate often associated with alcohol abuse as well as hypothyroidism, myelodysplasias and drug toxicity e.g. phenytoin and azathioprine.
5. *Diagnosis*: Neuropathy, nutritional, associated with beriberi syndrome.

Comment The etiology is thiamin (vitamin B_1) deficiency due to anorexia and malnutrition associated with carcinoma of the tongue. There is rapid improvement after treatment with thiamin and other B vitamins.

Case 23 A 37-year-old woman complains of numbness, tingling, and pain in both feet and the fingertips for 1 year. The pain has a needle-like quality. Three months ago she noted dimming of vision with the right eye alone. Color perception was impaired. She has difficulty closing the right eye. For 2 months she has had tenderness and weakness of her shoulder muscles and joint pain involving knees, elbows, and wrists.

Past medical history includes a diagnosis of arthritis for the past 8 years, the etiology of which is unknown.

General physical examination reveals a blood pressure of 130/80 and a regular pulse of 72. There is cervical adenopathy, an enlarged liver which is 3 cm below the right costal margin and splenomegaly.

Neurologic Examination The patient has a central scotoma O.D. to small red targets and a visual acuity of 20/25. The optic disk margin is blurred O.D. with two splinter hemorrhages at the disk border. There is a relative afferent pupillary defect and weakness of orbicularis oculi O.D. Deltoids are weak with strength of 4−/5 on the right and 4+/5 on the left along with localized tenderness on the right side. Anterior tibialis strength is 4/5 bilaterally. Ankle, brachioradialis and biceps reflexes are absent. Vibration perception is absent at the toes and diminished at ankles and fingers. Pinprick and temperature perception are diminished distally in all extremities.

Questions

1. Where are the lesions?
2. What physical findings are especially helpful in making the diagnosis?
3. What is the differential diagnosis?
4. What tests should be ordered?
5. What is the diagnosis and what are the other manifestations of this disease?

Case 23 Analysis

1. The patient has an optic neuritis because of a blurred disk margin, splinter hemorrhages, and a central scotoma associated with a relative afferent pupillary defect, O.D. It is not papilledema which is bilateral and does not affect central

vision. Weakness of orbicularis oculi indicates seventh nerve involvement. Tenderness and weakness of deltoids indicates a myopathy. Moreover, she has a sensorimotor neuropathy because of distal weakness and impaired perception of vibration, pin, and temperature.

2. Cervical adenopathy, hepatomegaly and splenomegaly raise consideration of sarcoidosis and lymphoma since both disorders could give rise to optic neuropathies, cranial neuropathies, neuropathy and myopathy.
3. This is a multisystem disorder suggesting several diagnoses. These include HIV, lymphoma, Lyme disease, sarcoidosis, and vasculitis such as systemic lupus erythematosus, polyarteritis nodosa, and Sjögren's syndrome.
4. A screening workup will be extensive and include CBC, ESR, RA factor, ANA, SSA, SSB, serum protein electrophoresis, CK, renal and liver functions, electrolytes, angiotensin converting enzyme level (for sarcoidosis), calcium, HIV serology, and Lyme disease screening. A chest X-ray is essential.

   There is an increased alkaline phosphatase of 250 U/L, increased gamma globulins, elevated CK of 300 U/L, increased ALT, AST to 60 and 70 U/L, and an abnormal chest X-ray which reveals prominent hilar adenopathy. An EMG-NCV discloses findings of neuropathy and myopathy. An MRI (brain and orbits) is normal. A lymph node biopsy reveals noncaseating granulomas.
5. *Diagnosis*: Optic neuropathy, facial neuropathy, polyneuropathy, and myopathy due to sarcoidosis.

Comment Sarcoidosis is often manifested by a plethora of medical and neurologic symptoms and signs. Facial nerve involvement is typical but certainly not pathognomonic. A chest x-ray is often the examination which provides the most important clue to the diagnosis since hilar adenopathy is common. A gallium scan may display increased uptake in lung fields, parotid and lacrimal glands and thus can be conclusive. The gold standard remains a biopsy of a lymph node revealing noncaseating granulomas.

Case 24 A 62-year-old man is admitted to the Intensive Care Unit after a heart transplant. He had been suffering from a viral cardiomyopathy and congestive heart failure.

His past medical history is significant for hypertension and chronic renal insufficiency with a BUN of 50 mg/dl and a creatinine of 1.8 mg/dl.

Shortly after admission to the Intensive Care Unit he developed urosepsis and required treatment for gram negative septicemia. One week later he developed ventricular tachycardia and became hypotensive on one occasion. Renal function subsequently declined as the BUN and creatinine rose to 80 and 3.1 mg/dl, respectively.

After transfer back to a floor unit he complained of weakness and was unable to walk without support.

Neurologic Examination The patient is disoriented to year and place. He makes errors with short-term recall. There is 4/5 strength of deltoids, triceps, sternomastoids, and iliopsoas musculature. Anterior tibialis is 4−/5 bilaterally. Brachioradialis,

knee, and ankle reflexes are absent. Vibration perception is absent at the toes, ankles, and knees. Position sense errors are made at the toes. There is distal sensory loss to pin and temperature in all extremities.

Questions

1. Can a lesion in one anatomic site explain the neurologic abnormalities?
2. What is the differential diagnosis? What is the diagnosis?
3. What underlying illnesses predispose the patient to this disorder?
4. What is the prognosis?

Case 24 Analysis

1. No. The patient has significant proximal weakness indicating the likelihood of a myopathy. The distal weakness and sensory loss point to neuropathy. Moreover, his impaired cognition indicates bilateral cerebral dysfunction, evidently due to hypotension and an ischemic encephalopathy. Renal failure is a sign that he suffered a major hypotensive episode that could be a contributing factor to his abnormal mental status. Renal failure alone is less likely to be the sole cause of his abnormal mental status.
2. The main differential diagnoses to consider in a patient who is critically ill includes critical illness polyneuropathy, critical illness myopathy, and a neuromuscular junction disorder due to the use of nondepolarizing neuromuscular blocking agents (e.g., gentamycin). An acute cervical myelopathy can cause a quadriparesis and temporarily reduced reflexes. Metabolic abnormalities such as hypokalemia, hypophosphatemia, and hypermagnesemia should be ruled out. The sensory findings in this case, however, are most compatible with neuropathy. Proximal muscle weakness indicates a myopathy.

Diagnoses

1. Critical illness neuropathy and myopathy [2].
2. Ischemic encephalopathy.

Comment Urosepsis, hypotension, and multiorgan failure are the underlying associated illnesses. The prognosis is fair to good provided the medical illnesses are rapidly reversible.

Case 25 A 28-year-old man complains of numb, weak feet. This has been a steadily progressive problem over 10 years. He has been unable to run for 7 years. He reports that his foot and hand muscles are "shrinking." After completing his stationary bicycle exercises he notes twitching in his calf muscles and he has severe cramps in his calves.

Past medical history is remarkable for insulin-dependent diabetes mellitus beginning at age 12. It is under good control. His parents and three siblings have no neuromuscular disorders.

Neurologic Examination Blood pressure is 120/75; pulse is 84 and regular.

Strength of interossei, abductor pollicis brevis, opponens pollicis, extensor pollicis longus, anterior tibialis, gastrocnemius, peroneus longus and brevis muscles are all 4/5. The patient has high arches. There is wasting of the small muscles of the feet and hands, wrists, and ankles. An enlarged, hardened ulnar nerve is palpated just above the left elbow adjacent to the medial epicondyle. He has a steppage gait due to bilateral footdrop. Ankle, knee, brachioradialis and biceps reflexes are absent. Vibration sense is impaired at the toes.

Questions

1. Could these findings be consistent with a diabetic neuropathy?
2. What findings suggest a hereditary neuropathy?
3. Does the negative family history determine the diagnosis?
4. What are the most common types of hereditary sensory and motor neuropathies?
5. What is the diagnosis?

Case 25 Analysis

1. Not likely. The relentlessly progressive neuropathy despite good diabetic control would be an exceptional manifestation of diabetes. High arches and hypertrophic nerves do not develop.
2. Wasting of distal musculature, high arches (pes cavus), an enlarged hardened nerve are all characteristic abnormalities of Charcot–Marie–Tooth disease (CMT).
3. No. Although 50–70% of CMT cases are autosomal dominant, there are autosomal recessive and rarely X-linked forms.
4. Hereditary motor and sensory neuropathy (Charcot-Marie-Tooth disease).
   (a) HMSN 1 (CMT 1) demyelinating.
   (b) HMSN 2 (CMT 2) axonal.
   (c) HMSN 3 (CMT 3) severe hypertrophic demyelinating neuropathy beginning in infancy. This is known as Déjérine–Sottas disease.
5. *Diagnosis*: Hereditary motor and sensory neuropathy (HMSN 1)

Comment Electromyography and nerve conduction tests revealed a severe demyelinating neuropathy, a common diagnostic finding. HMSN 2 usually has a more benign course than HMSN 1 but they are commonly indistinguishable. A recent study proposed impaired sphingolipid metabolism as the etiology [1].

Case 26 A 56-year-old man complains of numbness and tingling of the feet associated with unsteadiness. This began 6 months ago and is progressively worsening. For the past month he has had lancinating pains in the soles of both feet which are nearly disabling.

The past medical history is negative and he takes no medicines.

Neurologic Examination Blood pressure is 140/90; pulse is 72 and regular.

He has normal strength and reflexes are 1+ and symmetrical. Vibration perception is impaired at toes and ankles and position sense is impaired at the toes. Light touch errors are made at the tips of the toes. He has a positive Romberg and inability to perform tandem gait.

Questions

1. What nerve fibers are involved in this neuropathy?
2. Is this neuropathy likely to be demyelinating or axonal?

   A workup is initiated. A cbc is normal except for thrombocytosis (platelet count 620,000). A complete metabolic panel is normal but the serum protein electrophoresis shows a large M-spike.

   The patient returns 2 months later having missed an earlier appointment. He complains of fatigue, mild weakness in both feet, and thickening of his skin. The neurologic examination now discloses 4/5 strength of anterior tibialis, bilaterally. Reflexes remain obtainable except for a markedly slow relaxing phase of brachioradialis and ankle reflexes.
3. What part of the general medical examination should be repeated more carefully?
4. What specific tests should be ordered?
5. What is the name of this syndrome? What are its constituents?
6. How does this compare with monoclonal gammopathy of undetermined significance (MGUS)?

Case 26 Analysis

1. This is a large fiber neuropathy since vibration sense, proprioception, and light touch perceptions are impaired.
2. Demyelinating. This is confirmed by an EMG-NCV study.
3. The abdominal exam is repeated and discloses hepatosplenomegaly.
4. The history of fatigue and, especially, the slow relaxing phase of the brachioradialis and ankle reflexes suggest hypothyroidism. A TSH is 70 μU/L. A metastatic bone survey reveals a sclerotic lesion in a thoracic rib. VEGF (vascular endothelial growth factor) is elevated and levels are a good predictor of disease activity.
5. *Diagnosis*: POEMS syndrome [9, 11].

Comment This is a combination of polyneuropathy, organomegaly, endocrinopathy, M-spike, and skin changes. This is an osteosclerotic myeloma, a rare variant of multiple myeloma, ordinarily without hypercalcemia, renal failure, anemia and bone pain. Biopsy of the sclerotic thoracic rib lesion reveals monoclonal plasma cells.

6. MGUS (monoclonal gammopathy of undetermined significance) refers to a paraproteinemia not necessarily associated with malignancy and with or without an associated neuropathy. IgM is more frequently associated with neuropathy. Twenty percent of patients with MGUS will eventually acquire a malignant plasma cell disorder.

Case 27 An 85-year-old woman is admitted to the medical service of the hospital because of hypertension, edema, and hematuria. On admission, the patient adds a history of "sticking pains" in both feet for the last 2 months. Over the past month she has noticed weakness of the left arm and leg.

Past medical history is remarkable for carcinoma of the breast treated by mastectomy and radiotherapy 8 years ago and mild hypertension. Current medicines are ramipril and hydrochlorothiazide.

General physical examination reveals a blood pressure of 160/100; pulse 104; temperature 100.4 °F. There is a grade 2/6 aortic systolic murmur, rales at the bases of both lungs and 2+ pitting edema of both legs.

Neurologic Examination She has decreased rapid alternating movements and finger tapping of the left upper extremity and decreased left foot tap. There is 4/5 strength of left interossei and adductor pollicis. Wasting of the first dorsal interosseus muscle is noted. There is 4+/5 strength of left arm supination and flexion at the elbow. The left anterior tibialis, peroneus longus and brevis strength is 4/5. Strength of right anterior tibialis is 4/5. Reflexes are 1+ and symmetrical in the legs, 2+ in the right arm and 1+ in the left arm. The sensory examination discloses decreased perception of pin and temperature distally in all extremities. There is absent vibratory perception at toes and ankles with barely perceived vibration at the knees.

Laboratory data. CBC shows a white count of 12,000/cu mm with 90% polys. The hematocrit is 32%. Urinalysis is significant for 100 red cells per high-powered field. Liver function studies are normal but BUN is 45 mg/dL and creatinine 2.0 mg/dL.

Questions

1. Are the findings compatible with a single neuroanatomic diagnosis?
2. What symptoms suggest a specific anatomic locus? How could you describe the pattern of weakness?
3. Name every test which should be performed.
4. What is the differential diagnosis?

Case 27 Analysis

1. Yes. Neuropathy. Impaired rapid alternating movements, finger and foot tap will occur as a result of weakness and thus only indicate motor system dysfunction. The left-sided weakness is accompanied by decreased reflexes in the left arm and wasting of the first dorsal interosseus muscle. These findings indicate peripheral (root or nerve) involvement, but not neuromuscular junction or muscle. AHC involvement is possible but can neither explain the "sticking pains" in both feet nor the sensory signs of impaired vibration, pin, and temperature sensibility.
2. The "sticking pains" in both feet strongly suggest neuropathy. Muscular involvement of the left leg includes the peroneus muscles (everters) innervated by the superficial peroneal nerve and the anterior tibialis innervated by the deep peroneal nerve. Hence the left common peroneal nerve is affected. The right deep

peroneal nerve is involved because of a weak right anterior tibialis muscle. The left arm reveals ulnar nerve involvement (interossei, adductor pollicis) and the musculocutaneous nerve (biceps). Thus this patient has mononeuritis multiplex.

3. Vasculitis is the most likely etiology since the patient has mononeuritis multiplex, hypertension, and renal disease.

Vasculitic diseases that cause mononeuritis multiplex include:

(a) Churg–Strauss disease. This is associated with pulmonary disease, especially asthma, allergic angiitis, and eosinophilia.
(b) Polyarteritis nodosa. This is associated with renal, gastrointestinal, central nervous system, joint, and muscular disease.
(c) Rheumatoid arthritis. This is associated with joint, skin, pulmonary, and cardiac disease.
(d) Sjögren's syndrome. This is associated with a sicca syndrome, pulmonary, musculoskeletal, and central nervous system involvement.
(e) Systemic lupus erythematosus (SLE). This disease involves joint, muscle, skin, pulmonary, cardiac, renal, central nervous system, and hematologic disorders.
(f) Wegener's granulomatosis. This disease affects upper airway, lower airway and musculoskeletal systems and it causes renal disease.

Laboratory Workup CBC, metabolic profile, TSH, ANA, anti-double-stranded DNA, SSA, SSB, ANCA-c (Wegener's), ANCA-p (polyarteritis and Churg–Strauss), RA factor, ESR, serum protein electrophoresis, serum immunofixation, blood and urine cultures, 2D echocardiogram, chest X-ray. The studies were all normal except for ANCA-p, creatinine and BUN. Subsequent renal angiograms disclosed multiple aneurysms typical of polyarteritis nodosa. An alternative diagnostic test would be a nerve and muscle biopsy which would likely reveal a necrotizing vasculitis.

4. *Diagnosis*: Mononeuritis multiplex secondary to polyarteritis nodosa [12].

Comment A good background knowledge of internal medicine is advantageous since the key to a precise diagnosis is uncovering the associated medical illnesses.

Case 28 A 46-year-old woman complains of a 1-week history of leg weakness and droopy eyelids. Four days ago she could no longer climb stairs and began to drag both feet. For 2 days she has been short of breath and has had difficulty swallowing liquids. Since yesterday she has required a walker and voiding is impaired.

Past medical history includes a 20-year history of insulin-dependent diabetes mellitus. She has had paresthesias of the toes for several years and this has been attributed to a diabetic neuropathy.

Neurologic Examination Blood pressure is 150/110; pulse is 120 and regular.

The patient has right ptosis and is mildly dyspneic, but her oxygen saturation is normal. She has moderate bilateral facial weakness. Head flexion is 4/5. There is generalized proximal and distal weakness in the range of 4 to 4+/5. Reflexes are 1+

other than absent brachioradialis and ankle reflexes. Plantars are flexor. Vibration perception is absent at the toes and diminished at the ankles. Proprioception is normal. There is distal sensory loss to pin and temperature in a stocking-glove pattern.

Questions

1. Where is the lesion or where are the lesions?
2. From the history alone what symptom is a major clue to the diagnosis?
3. What are the diseases associated with this disorder?
4. What diagnostic tests are indicated?
5. What is the diagnosis and current treatment approach?

Case 28 Analysis

1. This patient has a rapidly progressive illness which affects the right levator palpebrae superioris innervated by the right 3rd nerve, 7th nerve innervated muscles, 11th nerve innervated muscles (head flexion) and generalized weakness. This weakness is most compatible with an acute neuropathy or a disorder of the neuromuscular junction (myasthenia gravis). There are no signs of cerebral disease such as dementia, aphasia, seizure, or homonymous hemianopsia nor are there "crossed" findings or eye signs typical of brainstem pathology. Myelopathy is ruled out because of involvement of eyelids and face. The distal sensory loss and absent reflexes indicate a neuropathy, acute or chronic.

   At this point the primary diagnostic considerations include myasthenia gravis superimposed on a diabetic neuropathy and an acute neuropathy such as Guillain–Barré syndrome (acute inflammatory demyelinating polyneuropathy (AIDP)) superimposed on a diabetic neuropathy.
2. The patient has bladder dysfunction which does not occur with myasthenia gravis. Additionally, autonomic dysfunction such as hypertension and tachycardia often occurs with AIDP.
3. Associated illnesses include Epstein–Barr virus, Hodgkin's disease, cytomegalic virus, mycoplasma pneumonia and about 20% of patients have had campylobacter jejuni infection. These organisms contain lipopolysaccharides which induce anti-GM1 and anti-GQ1b antibodies to gangliosides located in peripheral nerves. Diseases which may mimic AIDP include porphyria, HIV, hypokalemic periodic paralysis, tic paralysis, and toxins such as lead, arsenic, hexacarbons, nitrofurantoin, and organophosphates.
4. An EMG reveals a severe demyelinating polyneuropathy. Cerebrospinal fluid shows a protein of 146 mg/dl and 4 wbc/cu mm (so-called "albuminocytologic dissociation"). This is actually a common nonspecific finding and seldom of diagnostic import.
5. *Diagnosis*: AIDP or Guillain–Barré syndrome.

Comment This illness requires a firm knowledge of clinical neuroanatomic localization. Relying on an EMG diagnosis is fraught with error since in the first several days after the illness onset this test may not be diagnostic. Treatment is plasma

exchange and/or intravenous immunoglobulin. Prognosis for improvement is good over several weeks to months.

Case 29 A 24-year-old man complains of tingling over the sole of the right foot with the exception of just under the heel. For 2 months he has had pain in the ankle which occasionally radiates up the leg posteriorly to the buttocks. For 2 weeks he has noted weakness when attempting to flex his toes. Past medical history is negative.

Neurologic Examination Blood pressure is 150/118; pulse is 80 and regular.

Strength of toe flexion is 3/5. There is numbness of the sole of the foot to pinprick stimulation except under the heel. Paresthesias are provoked in the valgus position (deviated away from the midline) and they are alleviated in the varus position (toward the midline). There is a positive Tinel's sign when tapping over the lancinate ligament located just below the medial malleolus. Eversion at the ankle causes paresthesias on the sole of the foot.

Questions

1. What element of the examination is most important?
2. Where is the lesion? Explain the anatomy.
3. What is the significance of pain radiation upwards?
4. What is the significance of the distribution of sensory symptoms and signs?
5. What are the two diagnoses?
6. What are your recommendations?

Case 29 Analysis

1. Hypertension. Vital signs are the first part of any neurologic examination. The well-known complications of untreated hypertension mandate immediate recognition and treatment.
2. The patient has an entrapment neuropathy at the tarsal tunnel affecting the posterior tibial nerve. The sciatic nerve divides in the distal thigh to the posterior tibial and peroneal nerves. The posterior tibial nerve runs down the posterior calf then passes under the lancinate ligament after which it divides into medial plantar, lateral plantar, and calcaneal branches. The calcaneal branches may separate before the nerve passes under the ligament (about 40% of the time), and therefore is often spared.
3. Retrograde pain radiation suggests that the origin of the pain is distal.
4. Sensory symptoms and signs indicate involvement of both medial and lateral plantar nerves. The calcaneus nerve must branch off above the tarsal tunnel. Valgus positioning (eversion of the ankle) will tighten the ligament over the posterior tibial nerve and may provoke paresthesias. The varus position (inversion) should relieve the pressure.
5. *Diagnoses*

   (a) Hypertension.
   (b) Tarsal tunnel syndrome [4].

6. Prompt referral to an internist or a family practitioner is required for evaluation and treatment of hypertension and, afterwards, an EMG-NCV. Surgery will be considered if the diagnosis is confirmed and the blood pressure is well-controlled.

Case 30 A 58-year-old man complains of excruciating left upper abdominal burning pain awakening him at 2:00 a.m. On arrival in the Emergency Room the pain intensity has subsided slightly from a 9/10 to an 8/10. The Emergency Room evaluation included an ECG, cardiac enzymes, cardiology, and surgical consultations. All evaluations were normal but he was admitted to the hospital for observation. The day after admission he noted an electrical sensation in the same region intermittently.

Past medical history is negative other than asthma. He takes no medicine. Over the past year he has lost about 30 lb., at least partly due to a new exercise program, but he has a good appetite and eats well.

A neurology consultation is requested on the second hospital day after thoracic spine films and an MRI (thoracic) were performed and were normal.

Neurologic Examination The neurologist obtained additional history on the morning of the second hospital day. The abnormal sensation had extended upwards and was in a dermatomal pattern encompassing T6–T8 levels. Examination was remarkable for bulging of the left upper abdominal muscles. Touching the involved area produced a disagreeable feeling which the patient could not explain other than stating it was not painful. Ankle reflexes were absent and vibratory sense was lost at the toes and ankles. Light touch was not perceived on the toes.

Questions

1. Is there a relationship between the absent ankle reflexes and impaired vibration sense with his pain syndrome?
2. Where is the lesion that causes the pain?
3. What is the name of his perception of touch in the involved area?
4. What history is commonly associated with his illness? What is the most likely underlying diagnosis?
5. Why is there bulging of left upper abdominal muscles?
6. What is the diagnosis?

Case 30 Analysis

1. Yes. It is often associated with a peripheral neuropathy.
2. The thoracic root or nerve.
3. Dysesthesia.
4. Type II diabetes. The hemoglobin A1C is 7.3%. The fasting blood sugar is 132 mg/dl.
5. Localized weakness due to damage of motor fibers to these muscles.
6. *Diagnosis*: Thoracoabdominal neuropathy secondary to diabetes [17].

Comment The intensity of the pain can be severe and may mimic gallbladder or coronary artery disease as well as other abdominal pathology which may prompt

excessive unrevealing studies. If the pain has a burning quality which is quite common or bulging abdominal muscles only a neurologic evaluation should be required.

Case 31 A 91-year-old woman complains of stiffness of the legs, loss of balance, and prickly sensations in the feet. The prickly feelings become painful at night and keep her awake. Infrequently, these symptoms affect the fingers of both hands. There has been progressive development of this symptom complex over 1 year.

Past medical history is remarkable for recurrent gastrointestinal bleeding due to angiodysplasia in the small intestine with resulting chronic iron deficiency anemia.

Laboratory data includes normal liver functions and metabolic panel. The cbc shows a hematocrit of 29% and normal blood indices.

Neurologic Examination Blood pressure is 110/70; pulse is 68 and regular.

There is a mild paraparesis with distal strength 4/5 and proximal 4+/5. The patient exhibits mild spasticity. She has a positive Romberg. Vibration sense is absent at toes, ankles, and knees. Position sense is absent at the toes. Ankle and knee reflexes are absent. There is a left Babinski sign.

Questions

1. What signs are compatible with neuropathy?
2. What signs suggest additional anatomic involvement?
3. Could there be a single etiology?
4. Could degenerative disease be a factor?
5. If there is a single diagnosis, what is the most likely one?
6. What normal laboratory data obscures the diagnosis?

Case 31 Analysis

1. Distal weakness, vibration and proprioception loss, absent reflexes in the legs, and a positive Romberg.
2. Spasticity and left Babinski sign. Myelopathy does not explain the absent reflexes in the legs although all the other findings are compatible with it.
3. Yes.
4. Yes. The patient could have cervical myelopathy due to spinal stenosis and/or spondylosis with spinal cord compression superimposed on a neuropathy. This could explain spasticity and the Babinski sign, but involvement of the dorsal column would be exceedingly rare. Spondylotic myelopathy usually affects only the anterior and lateral columns of the spinal cord. Absent reflexes in the legs do not result from a myelopathy unless the anterior horn cells are affected. Concomitant lumbar spinal stenosis with nerve root compression could explain the absent leg reflexes.
5. *Diagnosis*: Subacute combined degeneration (myelopathy) and neuropathy secondary to vitamin B_{12} deficiency.
6. Normal blood indices are not expected with vitamin B_{12} deficiency, but the superimposed, chronic, iron deficiency anemia which usually causes a microcytosis prevents the expression of an increased MCV.

Comment Since intrinsic factor is synthesized in the stomach and both hydrochloric acid and pepsin are required to release cobalamin to enter the duodenum, any gastric illness or surgery has the potential to produce vitamin B_{12} deficiency. Similarly, the distal ileum is the site for vitamin B_{12} absorption and any illness or surgery in that location may diminish vitamin B_{12} levels. The elderly population frequently develops achlorhydria or has a diet deficient in animal products and is therefore susceptible to B_{12} deficiency. Vegans may also be affected. Thus the protean manifestations of this disorder, dementia, depression, irritability, somnolence, paranoia, optic neuropathy with cecocentral scotomas, myelopathy and neuropathy should prompt laboratory studies. These include vitamin B_{12}, methylmalonic acid and homocysteine levels. The latter two are typically elevated. Vitamin B_{12} levels lower than 400 pg/mL may result in neurologic symptoms. Methylmalonic acid levels are increased with vitamin B_{12} but not folate deficiency, an important distinction should there be diagnostic uncertainty.

Case 32 A 55-year-old man complains of rapidly progressive left leg weakness over the last 6 months. There is no associated pain, numbness or paresthesias. Past medical history is remarkable for type II diabetes controlled with metformin.

Neurologic Examination Blood pressure is 110/70; pulse is 48 and regular.

Strength of all left leg musculature is 4/5 except iliopsoas, 3/5. Tone is normal. There is decreased bulk of left thigh musculature. Fasciculations are numerous in the left calf and thigh muscles. Sensory examination is normal. Reflexes are 2+ except for 3+ in the left leg and plantars are flexor bilaterally.

Questions

1. What single finding has the greatest localizing value?
2. What part of the examination should be evaluated in greatest depth?
3. What abnormal findings in combination strongly suggest the underlying diagnosis?
4. What investigation will confirm the diagnosis?
5. What is the diagnosis?

Case 32 Analysis

1. Fasciculations. This is the prototypical sign of anterior horn cell (AHC) disease also called motor neuron disease. Fasciculations may occasionally develop in radiculopathies but they are confined to the involved nerve root.
2. The observation of fasciculations anywhere mandates a careful search for additional fasciculations on a disrobed patient. Fasciculations noted elsewhere, such as in the pectoralis major and back musculature, will clinch a diagnosis of amyotrophic lateral sclerosis (ALS). Particular attention should be paid to the tongue where fasciculations can be prominent in the absence of symptoms. Localized fasciculations occur with radiculopathy, but this is ordinarily accompanied by pain and decreased reflexes in the same location.

3. The increased reflexes in the weak leg support a diagnosis of ALS.
4. Electromyography.
5. *Diagnosis*: Amyotrophic lateral sclerosis.

Comment Examination of the tongue is a critical part of the clinical assessment in any patient with a myelopathy absent sensory abnormalities. The tongue must be observed in the resting position in the mouth because, when protruded, fasciculation-like quivering can be seen and misdiagnosed as fasciculations.

Case 33 A 38-year-old man complains of chest, back and upper arm pain associated with muscular swelling of 4 days duration. This began with a prolonged workout which included heavy weightlifting for 2 h. Although he felt muscular pain during the workout, it increased in severity 1 h afterwards and it has persisted without abatement. His prior exercise programs never lasted more than 15 min. Beginning about the age of 15 he noted severe muscle cramps after exercise. Consequently, he independently limited his physical activity. After this particular exercise he noted that his urine turned brown. Now he has pain with any movement as well as nausea and malaise.

Neurologic Examination Blood pressure is 110/70; pulse is 70 and regular.

Strength of pectoralis major is 4/5. Deltoid, supraspinatus and infraspinatus are 4+/5. The weakness is bilateral and symmetrical. His calf muscles appear hypertrophied. Reflexes are 1+, symmetrical and the sensory examination is normal.

Questions

1. What causes the brown urine? How does it occur?
2. What is the function of this substance?
3. What medical complication may occur?
4. What blood tests are commonly abnormal?
5. What is a cramp? Why do muscles swell?
6. What is the suspected diagnosis? What is its etiology?
7. What test confirms the diagnosis?

Case 33 Analysis

1. Myoglobin. Lysis of striated muscle (rhabdomyolysis) causes myoglobinuria.
2. Myoglobin transports oxygen from hemoglobin to mitochondria.
3. When severe, myoglobinuria may lead to acute renal failure.
4. CK, BUN, creatinine. In this case the CK is 50,000 U/L and the BUN and creatinine are markedly elevated. Hemodialysis is required.
5. A cramp is a spontaneous shortening of muscle not caused by an act of contraction. Muscles swell due to shift of extracellular water into necrotic muscle.
6. *Diagnosis*: McArdle's disease (metabolic myopathy) [7].

Comment This is due to a myophosphorylase deficiency with resultant inability to metabolize glycogen. Although autosomal recessive it is most often found in males and typically becomes symptomatic in the teen years. Proximal weakness, which this patient exhibits, is usually a late development.

7. Ischemic forearm exercise test. This test measures the rise in lactic acid with ischemic exercise. Failure to increase indicates defective metabolism of glycogen. Deficiency of myophosphorylase is only one of several metabolic disorders that prevent glycogenolysis. This patient had no rise in his lactic acid.

Case 34 A 72-year-old man complains of excruciating right eye pain of 2 days duration. On the morning of this evaluation his right lid drooped and he noted double vision in all directions of gaze but questionably present when looking to the right. His past medical history is remarkable for well-controlled hypertension. His only medicine is atenolol.

Neurologic Examination Blood pressure is 135/80. Pulse is 84.

He has a mild right ptosis. The right eye is abducted and slightly below the horizontal meridian in a fixed position. On attempted downgaze there is intorsion O.D. Eye movements are entirely normal O.S. The pupils are 4 mm equal and with a 3+/4 reaction to light bilaterally. The entire neurologic examination is normal otherwise.

Questions

1. Why does the right eye intort on attempted downgaze?
2. What nerve is involved?
3. Why is the pupil spared? Does sparing of the pupil lead to the diagnosis?
4. If the right eye did not intort would the diagnosis change? Where would the lesion be?
5. Does the presence of excruciating pain suggest the underlying etiology?
6. What is the diagnosis and prognosis?

Case 34 Analysis

1. The right eye intorts because the fourth nerve is intact. Its function when the eye is abducted is intorsion but, when adducted, the eye moves directly downward.
2. Third nerve.
3. The lesion is in the center of the nerve whereas the pupillary fibers are peripherally located at the dorsal surface. This implies ischemia secondary to small vessel disease. A compressive lesion from a mass, such as an aneurysm, would primarily involve the pupil in most cases.
4. Yes. Involvement of the third and fourth nerves implies a lesion within the cavernous sinus where the two nerves are adjacent to each other. A likely etiology would then be a carotid aneurysm or neoplasm.
5. Yes. Pain is especially severe with an ischemic third nerve lesion; this is usually much more prominent than with the aneurysmal compression of the third nerve. The latter is often painless.
6. *Diagnosis*: Diabetic third nerve palsy.

Comment There are infrequent reports of aneurysms causing a pupillary-sparing third nerve palsy. These are located in the cavernous sinus. Consequently, an MRA

(intracranial) and an MRI (brain) with and without contrast should be performed. The prognosis of a diabetic third nerve palsy is excellent as there is usually a complete recovery within 2–3 months.

Case 35 A 33-year-old computer scientist is referred by his ophthalmologist because of bilateral ptosis. The patient reports that he became aware of his lid droop 2 years ago when an associate accused him of being arrogant. He then realized that he was extending his head backward to compensate for poor vision above the horizontal plane. Soon thereafter he had to use his forehead muscles to lift his eyelids. Over the past 2–3 months he has noted difficulty looking up or to the side. He denies double vision. He has occasional episodes of lightheadedness.

Past medical history is unremarkable and he takes no medications.

Neurologic Examination Neurologic examination reveals normal vital signs. Abnormal findings include severe bilateral ptosis requiring him to manually lift his lids in order to see. He has upgaze and horizontal gaze paresis and minimal medial rectus function O.U. Downgaze is spared. He has mild bilateral weakness of orbicularis oculi and oris musculature. Deltoid strength is 4/5 bilaterally. Reflex, gait and sensory examinations are normal.

Questions

1. Are the findings consistent with central nervous system pathology? Explain.
2. What is the main differential diagnosis?
3. How can the diagnosis be made at the bedside?
4. What is the diagnosis?
5. What are other features of this disease? How can the diagnosis be confirmed?

Case 35 Analysis

1. No. A focal brainstem lesion cannot produce this constellation of ophthalmoparesis and bilateral facial weakness. Furthermore, deltoid weakness would not be expected.
2. Chronic progressive external ophthalmoplegia (CPEO) vs. myasthenia gravis (MG).
3. Edrophonium (tensilon) test. The presence of heart block or bradycardia which may occur in CPEO, however, would be a contraindication. A consultation with cardiology first would be advisable, especially in view of the patient's history of periodic lightheadedness.
4. *Diagnosis*: Chronic Progressive External Ophthalmoplegia (CPEO) [7].
5. Deafness, retinal pigmentary changes, cardiac conduction defects, seizures, strokes and neuropathy. An EMG can show mild myopathic changes and the CK may be mildly increased. Muscle biopsy shows ragged red fibers, a hallmark of mitochondrial disease.

Comment CPEO is primarily a slowly progressive ocular myopathy that must be distinguished from myasthenia gravis. Oculopharyngeal dystrophy and thyroid eye

disease may occasionally exhibit similar signs. About one-half of cases are maternally inherited through deletion of a large mitochondrial gene. Other cases are autosomal dominant or recessive.

Kearns-Sayre's syndrome is CPEO in childhood and teen years. The classical presentation is the triad of external ophthalmoplegia, retinitis pigmentosa, and cardiac conduction abnormalities. Additional features are short stature, sensorineural hearing loss, endocrinopathies, cerebellar ataxia and a depressed respiratory drive. The majority of cases are due to a large, single, mitochondrial DNA mutation.

The main features of four ocular myopathies are listed in Table 9.1.

A positive sign (+) means it is likely to occur.

Case 36 A 25-year-old anxious man, an Army sergeant and drill instructor, requests an evaluation because of weak legs. He first noted weakness 6 months ago while leading recruits on a long forced march. One month ago he was unable to lead from the front and had leg cramps, a very distressing development. Last week he became short of breath after a vigorous workout in the gym.

Past medical history and family history are unremarkable. His parents and one sister are well. He takes no medication.

General Medical Examination He has a blood pressure of 95/60 and a regular pulse of 88. He is 6′2″, weighs 240 lbs. and is very muscular. He has rales at both bases.

Neurologic Examination Neurologic examination reveals a heavily muscled man with large biceps, triceps and especially large calf muscles. Strength is normal other than 4+/5 supraspinatus, infraspinatus and quadriceps, bilaterally. He uses both

Table 9.1 Differential diagnosis of ocular myopathies

	CPEO	MG	Graves	OPD (Fig. 9.3)
Ophthalmoplegia	+	+	+	+
Ptosis	+	+	+	+
Fluctuation of deficit	–	+	–	–
Diplopia	Infrequent	Common	Common	Infrequent
Facial weakness	+	+	–	+
Limb weakness	Mild	Variable	None or mild	Mild
Dry eyes	+	+	+	+
Congested conjunctiva	–	–	+	–
Lid retraction	–	Infrequent	+	–
Proptosis	–	–	+	–
Dysphagia	Mild	+	–	+
Forced duction	–	–	+	–

CPEO chronic progressive external ophthalmoplegia
MG myasthenia gravis
Graves thyroid eye disease
OPD oculopharyngeal dystrophy
Forced duction – After local anesthesia is given an eye muscle is grasped by a forceps and pulled. If the eye cannot be moved there is a mechanical restriction and the response is called positive

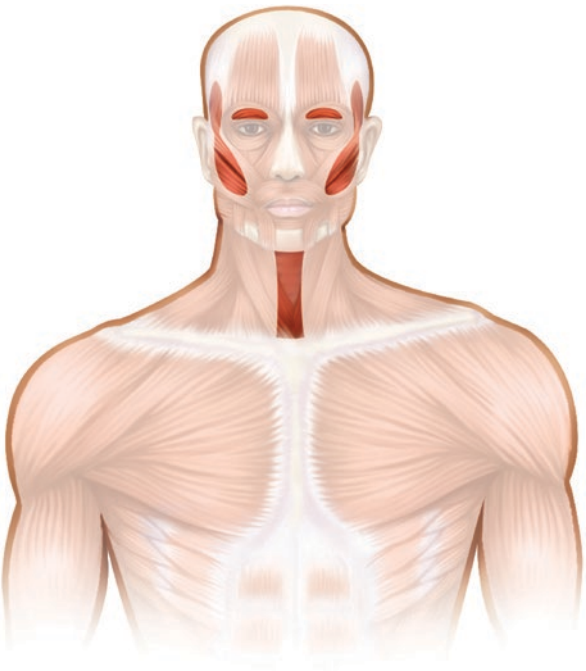

Fig. 9.3 Oculopharyngeal dystrophy

hands to push himself out of his chair to stand. Gait is normal. Reflexes are 1+ and symmetrical except for bilateral absence of biceps and triceps reflexes. Sensory examination is normal.

Questions

1. What are the two most likely anatomic diagnoses?
2. What sign eliminates one of them?
3. What finding on examination can be ignored? Which abnormal finding is the best clue for the diagnosis?
4. What blood test confirms the anatomic localization?
5. What is the differential diagnosis?
6. What test is diagnostic?

Case 36 Analysis

1. Myopathy and neuromuscular junction disorder.
2. Rales at both lung bases. This may occur with a cardiomyopathy associated with a myopathy but not with myasthenia gravis.
3. Absent biceps and triceps reflexes are not unusual in heavily muscled men. The markedly enlarged calf muscles are typical of both Duchenne's muscular dystrophy and Becker's muscular dystrophy (Fig. 9.5). The enlargement of calf muscles is actually a pseudohypertrophy since the muscle is infiltrated with fat and connective tissue.

4. The CK is 3050 u/L.
5. Inclusion body myositis (Fig. 9.1), limb-girdle muscular dystrophy (Fig. 9.4), spinal muscular atrophy and Becker's muscular dystrophy (Fig. 9.5).
6. Genetic testing confirms the diagnosis. Additional studies may include an MRI which demonstrates fatty replacement of calf muscles. Muscle biopsy discloses a decreased amount of dystrophin whereas in Duchenne's muscular dystrophy dystrophin is absent.

Diagnosis Becker's muscular dystrophy. (Fig. 9.5) [7].

Comment

Becker's muscular dystrophy is due to a defect of the dystrophin gene on the X chromosome. Dystrophin is a cytoskeletal protein located in the sarcolemmal membrane and plays an essential role in maintaining muscle fiber integrity. Whether deficient or absent the sarcolemma becomes unstable when contracting or relaxing with resulting damage producing increased calcium influx which leads to muscle

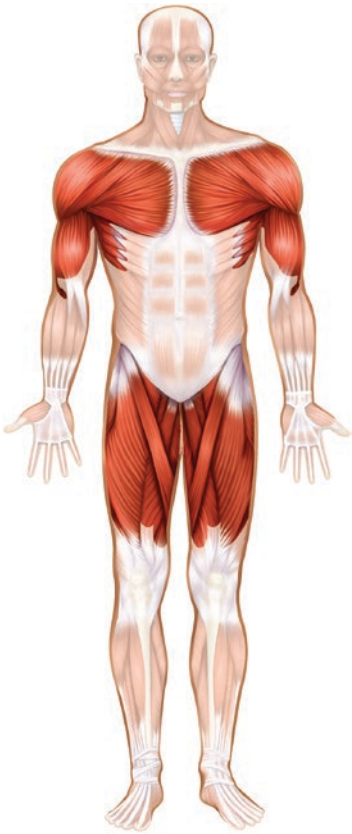

Fig. 9.4 Limb-girdle muscular dystrophy

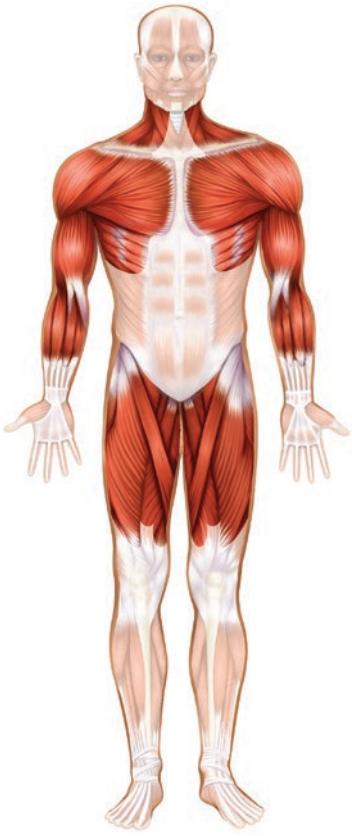

Fig. 9.5 Becker's muscular dystrophy (same as Duchenne's muscular dystrophy)

cell necrosis. About 10% of cases are due to a spontaneous mutation. This is an X-linked recessive gene. Dystrophin is completely absent in Duchenne's muscular dystrophy and, therefore, it begins in childhood. Partial loss as in Becker's muscular dystrophy results in later onset, usually after age 15, but reports indicate the onset ranges between ages 5 and 45.

Case 37 A 30-year-old woman complains of double vision present for 1 week. Four days ago her speech became slurred and swallowing was difficult. Yesterday she noted impaired balance. She reports that her double vision is reduced by head turn to the right.

Two weeks ago the patient had severe diarrhea and generalized weakness. A brief neurologic examination at that time disclosed no abnormalities.

Neurologic Examination Blood pressure is 116/70, pulse 80 and regular. Abnormal findings are hypertropia O.S. (left eye higher than right), diplopia on downgaze (especially down to the right); head tilt to the left increases the diplopia. The patient is dysarthric and has sluggish palate movements. Tandem gait is poor and deep tendon reflexes are absent.

Questions

1. What symptom suggests a single cranial nerve lesion?
2. What additional question would be useful?
3. What cranial nerve lesion is present?
4. What organism is most likely to have caused the diarrhea?
5. What finding on examination is not consistent with multiple sclerosis?
6. Why does this patient not have myasthenia gravis?
7. What test is commonly abnormal in this disease?
8. What is the diagnosis?

Case 37 Analysis

1. Double vision. Alleviation with head turn to the right suggests a right sixth nerve lesion.
2. Did she turn or tilt her head to the right? A tilt of her head towards her right shoulder may reduce diplopia from a left fourth nerve lesion. A head turn to the right often occurs with a right sixth nerve lesion. Diplopia present primarily at distance may indicate a sixth nerve lesion. Diplopia on downgaze connotes an inferior rectus or superior oblique muscle weakness. The patient reports that she tilted her head towards her right shoulder to lessen the double vision. This is consistent with a left 4th nerve lesion.
3. Trochlear nerve (fourth nerve). Hypertropia O.S. is also a good sign of an ipsilateral fourth nerve lesion.
4. Campylobacter jejuni, a Gram-negative rod.
5. Absent reflexes. Since multiple sclerosis affects only the central nervous system, abnormal reflexes, if present, are increased and ordinarily asymmetrical.
6. She has absent reflexes and poor tandem gait in the presence of normal strength; neither occur with myasthenia gravis.
7. Antibodies to GQ1b. The antigen is expressed in cranial nerves 3, 4, 6 and muscle spindles. Ataxia is most likely related to involvement of the superior cerebellar vermis which has been found to be abnormal on magnetic resonance spectroscopy. If caused by campylobacter jejuni, antibodies to this organism are present.
8. *Diagnosis*: Miller Fisher or Fisher syndrome.

Comment The distinctive features of Fisher syndrome are the ophthalmopareses, which are the initial manifestations in most cases, ataxia and absent reflexes. Treatment is the same as for Guillain-Barré syndrome, intravenous immunoglobulin (IVIg) or plasmapheresis. Recovery begins in 2–4 weeks and is nearly complete in 6 months.

Case 38 An 18-year-old male complains of right shoulder pain of 3 months duration. He has noted mild right arm weakness in the gym when sitting and pushing weights away from his chest.

Past medical history is negative. He takes no medicines and he is adopted. He does not use alcohol or drugs and is a nonsmoker.

Neurologic Examination Neurologic examination reveals normal vital signs. He has mild bilateral weakness of orbicularis oris, winging of the right scapula and 4+/5 strength of left arm supination. He cannot walk on his heels for more than 3 s.

Questions

1. What muscles are affected in the arms? in the legs?
2. What is their nerve supply? What tests confirm the neuroanatomic diagnosis?
3. What is the suspected diagnosis?

Case 38 Analysis

1. Right serratus anterior and left biceps muscles. The strongest muscle for supination is the biceps. Poor heel walk indicates anterior tibialis weakness.
2. Nerve to the serratus anterior (long thoracic nerve of Bell), musculocutaneous nerve which innervates the biceps muscle, and deep peroneal nerve which supplies the anterior tibialis muscle. There is a mild increase in CK and electromyography confirms the diagnosis of myopathy.
3. *Diagnosis*: Facioscapulohumeral dystrophy. (Fig. 9.6) [7].

Comment Although not expected, asymmetric muscle involvement is not unusual at the onset of the disease. Fascioscapulohumeral dystrophy is usually autosomal-dominant but 30% of cases are caused by a de novo mutation. Diagnosis is confirmed by mutation analysis on muscle tissue.

Case 39 A 55-year-old woman complains of chest, shoulder and low back pain of 2 years duration. Over the past year she has complained of palpitations, fatigue, muscular "stiffness," hip and knee pain and is troubled by "brain fog." Her internist referred her for cardiology and orthopedic consultations neither of which uncovered any pathology.

Past medical history is remarkable for diabetes, irritable bowel syndrome and depression. Current medicines are escitalopram 10 mg. q.d., metformin 500 mg. b.i.d. and dicyclomine 20 mg. t.i.d.

Social history: The patient does not smoke or drink. She is a technician in a chemical plant and works on a computer. She does no physical activity.

Neurologic Examination Neurologic examination reveals a blood pressure of 140/95 with a regular pulse of 102. Her affect is flat. Strength of quadriceps, iliopsoas and anterior tibialis is 4−/5, bilaterally. She walks with a normal base and stride. Reflexes are 2+ and symmetrical. There are no pathological reflexes. Sensory examination is normal.

Questions

1. What important function should she be questioned about? What can it mean?
2. What specific parts of the gait and station evaluation must be carefully examined? What additional exam might be useful?
3. What does the commonly used term "brain fog" usually imply?

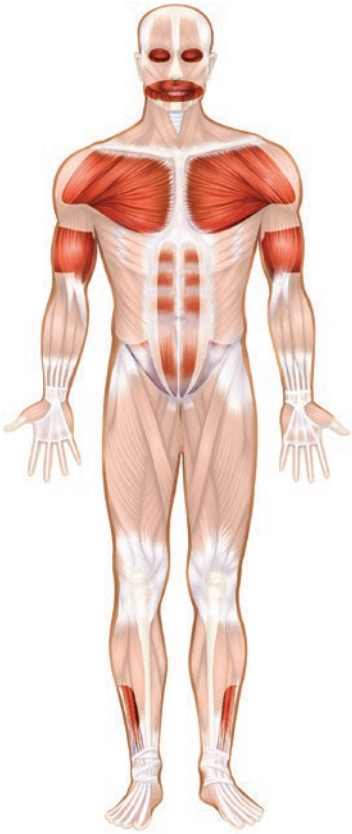

Fig. 9.6 Fascioscapulohumeral dystrophy

4. Where is the pathology and what diagnosis is suspected?
5. What is the differential diagnosis?
6. What triad of symptoms suggest the diagnosis?

Case 39 Analysis

1. Sleep. Does she have early morning awakening? She does. This history plus her flat affect points to depression.
2. Can the patient get out of a chair or walk on her heels? If she performs well on these tasks, then the demonstrable weakness is likely due to pain, a psychogenic disorder or malingering. This patient is able to get out of a chair independently and walk on her heels.

   Examining the patient for tender spots might add diagnostic information.

3. Depression. This patient is evidently undertreated.
4. Cerebral. Fibromyalgia is suspected. Augmented responses to pain have been demonstrated by functional magnetic resonance imaging (fMRI) studies and sleep EEG patterns may include periodic alpha wave intrusions.

5. The differential diagnosis includes polymyalgia rheumatica and polymyositis. Additional considerations include hypothyroidism, rheumatoid arthritis, systemic lupus erythematosus, Sjögren's syndrome, and exposure to a toxic chemical.
6. Muscle and joint pain, sleep disorder and depression (typically described as brain fog).

Diagnosis Fibromyalgia. (Fig. 9.7).

Comment This diagnosis has been a contentious one for many years probably because depression is a prominent feature. Nevertheless, depression has a well-documented cerebral underpinning which has been confirmed by abnormal PET scans (positron emission tomogram). Patients exhibit an associated, well-defined syndrome which is supported by abnormalities of fMRI studies and sleep electroencephalograms which may include alpha wave intrusions. These studies are not required for the diagnosis which is primarily made on the basis of the history. Treatment can significantly ameliorate and occasionally eliminate the symptoms.

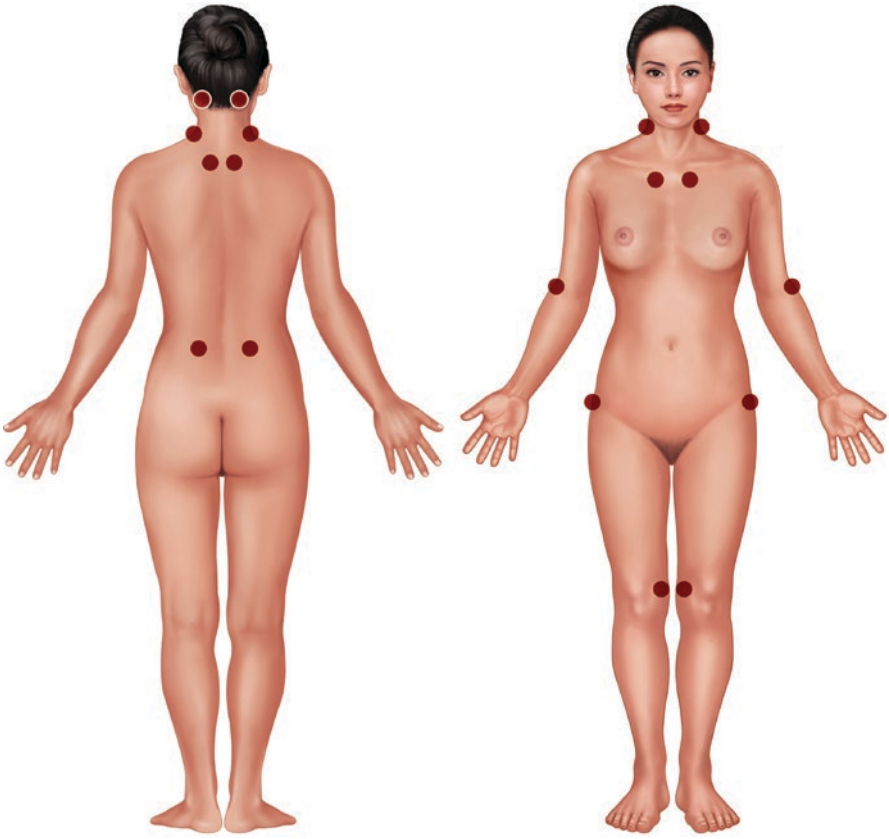

Fig. 9.7 Fibromyalgia with location of tender points

Case 40 A 45-year-old obese male is referred because of left facial weakness which developed the previous night. He denies any other new symptoms. He has a 1-year history of intermittent burning and tingling sensations on the left thigh.

Past medical history is remarkable for hypertension and his only medication is lisinopril.

Neurologic Examination A brief screening neurologic examination reveals normal vital signs and moderate weakness of left orbicularis oris. There is slight weakness of orbicularis oculi.

Questions (A)

1. Are these findings compatible with only central disease, only peripheral disease or both?
2. Why does he have left thigh burning and tingling?
3. What additional questions are essential?
4. What part of the neurologic examination absolutely differentiates central from peripheral origin of facial weakness?
5. What are the diagnoses?

The following day the patient has brief episodes of severe throat pain along with occasional stabbing pain in the left ear. While eating dinner he notes a loud high-pitched noise in the left ear as well as decreased hearing. He also has brief episodes of pallor, shortness of breath, diaphoresis, neck pain and dizziness.

Questions (B)

1. Why does he have episodes of stabbing left ear pain?
2. What is causing his auditory symptoms?
3. Is there a single cause of pallor, diaphoresis, dizziness, shortness of breath, and neck pain?
4. What additional examination is diagnostic?

Case 40 Analysis (A)

1. Both. Weakness of orbicularis oculi is common in central nervous system disease most often noted as a wider palpebral fissure when compared to the normal side.
2. Meralgia paresthetica. Many patients have more than one neurologic problem often irrelevant to the primary complaints. It is important to both recognize and discard immaterial symptoms.
3. Is there any change in your hearing or taste and has there been any pain behind your ear? The patient reports minimal pain behind the left ear and loud sounds are unbearably augmented (hyperacusis). He states that his sense of taste is diminished. These three symptoms are common with Bell's palsy.
4. Loss of taste on the left side of the anterior portion of the tongue, most reliably checked with a supersaturated sweet solution swiped by a Q-tip on the dorsal surface of the protruded tongue. The suspected abnormal side is always tested first.

5. *Diagnoses*

   (a) Bell's palsy, left.
   (b) Meralgia paresthetica, left.

Case 40 Analysis (B)

1. This is typical of glossopharyngeal neuralgia as a branch of the 9th cranial nerve, Jacobson's nerve, supplies the tympanic membrane.
2. 8th nerve dysfunction.
3. Yes. He has hypotensive episodes as part of glossopharyngeal neuralgia probably due to ephaptic transmission, nonsynaptic transmission between the motor and sensory fibers of the glossopharyngeal nerve. This augments the afferent discharges originating from the carotid sinus. This increased input continues in the medulla via the tractus solitarius, is received by vagal nuclei and interpreted as hypertension. Thus it provokes an increased efferent volley in the vagus nerve to cause bradycardia and hypotension. Symptoms of hypotension include shortness of breath due to lack of blood supply to the apices of the lungs and neck pain due to ischemia of neck musculature.
4. Examination of the external auditory canal which reveals a vesicular eruption. This actually occurs in only about 15% of patients.

Diagnosis Ramsay-Hunt syndrome involving 7th, 8th, 9th and 10th cranial nerves.

Comment The etiology is varicella-zoster virus which, although it most commonly affects only the facial nerve, may extend to adjacent cranial nerves. The 8th nerve is the second most commonly affected nerve in this syndrome.

Appendix A

Screening evaluation for an idiopathic neuropathy
CBC
BUN, creatinine
Liver functions
Calcium, phosphorus
Free T-4, TSH
ANA
B12 level
ESR
Rheumatoid factor
Serum protein electrophoresis and immunofixation
Review of occupational exposure to toxic agents and social history, primarily nutrition and alcohol consumption
Review of family history

Neuropathy with prominent dysautonomia
Diabetes
Amyloidosis
Hereditary sensory and autonomic neuropathy
Paraneoplastic sensory and autonomic neuropathy
Polyganglionopathy
Acute pandysautonomia
Guillain–Barré syndrome
Porphyria
HIV
Toxic drugs. Especially amiodarone, vincristine, and cisplatin
Toxic substances. N-hexane, arsenic, mercury, and thallium
Demyelinating neuropathies
Guillain–Barré syndrome (AIDP)
CIDP
Osteosclerotic myeloma
MGUS (monoclonal gammopathy of undetermined significance)
Hereditary susceptibility to pressure palsies
Hereditary sensorimotor neuropathy, types 1 and 3
Type 1 CMT 1 Charcot–Marie–tooth
Type 3 CMT 3 Déjérine–Sottas disease
Multifocal motor neuropathy
POEMS syndrome
Diabetes
HIV
Anti-MAG syndrome
Anti-Sulfatide syndrome
Leprosy
GALOP syndrome
Amiodarone
Chloroquine
Perihexaline
Refsums disease
Most common toxic neuropathies
Amiodarone
Phenytoin
Cisplatin
Vincristine
Isoniazid
Chloroquine
Thalidomide
Nitrofurantoin
Vitamin B6
Metronidazole
Taxols

Colchicine
Multiple mononeuropathies
Sarcoidosis
Vasculitis
Leprosy
Lyme disease
HIV
Cryoglobulinemia
Multifocal motor conduction block neuropathy
Diabetes
Neurofibromatosis
Hereditary susceptibility to pressure palsies
Case discussions related to anatomic site of pathology
Anterior horn cell. Cases 13, 32
Fibromyalgia. Case 39
Myopathy. Cases 6, 10, 16, 21, 23, 24, 33, 35, 36, 38
Neuromuscular junction. Cases 12, 16, 21
Neuropathy. Cases 3, 4, 5, 7, 8, 9, 14, 15, 17, 20, 22, 23, 24, 25, 26, 27, 28, 29, 30, 34, 37, 40
Myelopathy. 31
Plexopathy. Cases 2, 18, 19
Radiculopathy. 1, 7
Tendonitis. Case 11

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Suggested Reading

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Chapter 10
Myelopathies

This chapter, contrary to others in this text, commences with an established neuroanatomic diagnosis. Within the rubric of spinal cord pathology a more precise anatomic diagnosis can be made. Is the lesion extradural (epidural), extramedullary intradural, or intramedullary? For example, a typical epidural mass might be a metastasis, abscess or herniated disk. The most common extramedullary intradural lesion is a benign neoplasm such as a meningioma or schwannoma and it is also the location of leptomeningeal disease. The differential diagnosis of an intramedullary lesion is manifold and especially challenging. Multiple sclerosis, astrocytoma, ependymoma, vascular disease, subacute combined degeneration and syringomyelia are a few examples.

Fortunately, magnetic resonance imaging (MRI) solves many but certainly not all of these questions. In numerous instances cerebrospinal fluid studies and occasionally somatosensory-evoked potentials can be more useful. Moreover, an MRI may be contraindicated in patients who have a pacemaker or metallic implant.

There are a wide variety of unusual or rare etiologies that must be recognized to enable efficacious treatment, removal of a toxic substance or to initiate further investigations to unmask the underlying etiology. This will require familiarity with specific deficits involving sensory, motor, and autonomic systems, vascular anatomy and associated or causative medical illnesses.

Through case discussions I hope to convey some of this critical information plus expose the reader to the diagnostic challenges presented by many patients. An extensive review is clearly not intended but a fastidious analysis of symptoms and signs is essential. Answers to the questions raised on each case will be provided at the end of this chapter.

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Case Reports

Case 1 A 57-year-old chemical engineer requests an evaluation because of fatigue after prolonged work on his computer. His entire body is weak, especially later in the day, and he is now unable to do extra computer work after 6 p.m. This symptomatology began 3 months ago and he believes it is minimally progressive. His past medical history includes hypothyroidism and he is on replacement therapy.

Neurologic Examination Blood pressure supine is 96/60, sitting 90/60, standing at 1 min 88/58 and standing at 3 min 94/56. Heart rates are 64, 68, 72, and 76, respectively. He is asymptomatic during this time.

Neurologic abnormalities are head flexion 5−/5, head extension 4/5, iliopsoas 4+/5 bilaterally. Reflexes are 3+, symmetrical, with a left Hoffmann's and suspected right Babinski sign. At the end of the examination his head begins to drop.

MRI (head and cervical spine) is normal. An electromyogram and nerve conduction study is normal and this includes repetitive stimulation. CK is 325 U/L (NL 38-174 U/L).

Questions

1. What diseases commonly affect head extensor muscles?
2. How should his re-examination be conducted?
3. What part of the examination should be emphasized and why?
4. Is the modest increase of the CK supportive of the suspected diagnosis?
5. What is the diagnosis?

Case 2 An 86-year-old man has been referred because of poor balance, burning sensations in his feet and tremor present in all extremities. He has fallen frequently. These symptoms began 6 months ago and are increasing in severity.

Ten years ago he was referred for a neurologic consultation because of involuntary movements of his mouth and lips. Three months before the onset of these movements he had been prescribed chlorpromazine which he took for 2 weeks to treat intractable hiccups. This medicine is a D2 blocker and prolonged use for at least 3 months can result in tardive dyskinesias. His short exposure excludes this possible connection. Numerous medical treatments were ineffective until he saw his dentist 1 year later and was found to have severe periodontal disease in addition to having previously lost several teeth. Treatment included being fitted with dentures. The involuntary movements ceased and a final diagnosis of edentulous dyskinesia was made. Otherwise his past history includes hypertension, irritable bowel syndrome, left carotid stenosis treated by stent at age 77 and coronary bypass surgery at age 79. Current medicines are clopidogrel, aspirin and ramipril.

Neurologic Examination A first year medical resident conducts a neurologic examination and reports the following: Blood pressure is 140/92 and he has a regular pulse of 66. Strength is normal except anterior tibialis is 4/5 bilaterally. He has a positive Romberg test, wide-based ataxic gait with bilateral footdrop, mild finger-

to-nose ataxia and moderate heel-to-shin ataxia. Reflexes are 3+ except for 2+ knee jerks. He has 6 beats of clonus at the right ankle and 2 beats at the left ankle. Plantars are neutral bilaterally.

An EMG ordered by the resident confirms his initial impression of a mild sensory neuropathy, suspected because of his complaint of burning sensations in his feet, and a normal MRI (cervical and thoracic). A complete blood count reveals a white cell (wbc) count of 2500 with a normal differential; a hematocrit is 30% and there are macrocytic blood indices. The medical resident's diagnosis: Spinocerebellar degeneration associated with a neuropathy. Consider paraneoplastic disease.

Questions

1. What pertinent part of the neurologic examination was omitted from his report?
2. Could an abnormal finding explain the ataxia without implicating the cerebellar system? Are the ankle reflexes abnormal?
3. Could his edentulous dyskinesia be an indirect clue to his symptoms?
4. Is there a relatively common surgical procedure which can cause the same problem?
5. What tests confirm the anatomic location of the pathology and the etiology? Does the cbc support the diagnosis?
6. Are there other diseases associated with abnormal copper metabolism?
7. What is the diagnosis?

Case 3 A 60-year-old construction worker is referred because of a 2-week history of severe low back pain. Infrequently, it radiates posteriorly to both calves, left more than right. The pain is aggravated by movement. He has obstipation, urinary frequency, a slow urinary stream and occasional incontinence. His medical history includes smoking one pack of cigarettes per day for 35 years, chronic obstructive pulmonary disease and type II diabetes. Medicines are an albuterol inhaler and metformin.

Neurologic Examination Neurologic examination reveals a blood pressure of 138/90 and a regular pulse of 72. He has bilateral carotid bruits. The left pupil is 2 mm and the right 3 mm, both with 3+/4 reactions to light. In dark, after 10 s have elapsed, the left pupil is 3 mm and the right 4.5 mm. Palpebral fissures are asymmetric, right greater than left. He has 4+/5 bilateral plantar flexion strength and absent ankle reflexes.

An MRI (lumbar) with and without contrast is normal.

Questions

1. What part of the general physical examination is especially important?
2. What specific part of the sensory examination is critical?
3. What explains the bladder dysfunction? What test of bladder function would be useful?
4. What examination should provide diagnostic information?

5. Where is the lesion?
6. How can one guess the etiology?
7. How often does an MRI scan not disclose pathology in the cauda equina?

Case 4 A 25-year-old woman was brought to the Emergency Room after a motor-vehicle accident. Her car was struck from behind on the highway by a car traveling at 90 mph while she drove at 55 mph. She suffered a severe extension-flexion injury and complains of excruciating neck pain.

Neurologic examination was normal and spine films showed straightening of the cervical spine. Five days later she complained of severe right arm pain radiating from the neck down to the forearm. She was placed in a soft cervical collar and naproxen was prescribed. Seven days after the motor-vehicle accident she had the acute onset of moderate weakness of all extremities and within 2 h became quadriplegic. Her past medical history is negative and her only medicines are cyclobenzaprine and naproxen.

Neurologic Examination Neurologic examination discloses a blood pressure of 115/70 with a regular pulse of 88. Pertinent abnormalities are flaccid quadriplegia with absent reflexes (spinal shock) and a sensory level to pain and temperature at C5.

Questions

1. What could be the cause of this myelopathy?
2. What part of the spinal cord is involved?
3. Is this an intramedullary, extramedullary intradural, or extradural (epidural) lesion?
4. The MRI reveals a herniated nucleus pulposus at C4-5 with compression of the C5 nerve root on the right side. What is the anatomic basis of this patient's neurologic problem?
5. What is the etiology?

Case 5 A 55-year-old male dentist requests an evaluation because of a 4-month history of aching pain and stiffness in both legs especially involving the knees. As a result his walking is unsteady. He has seen a rheumatologist because of gout and his concern about having rheumatoid arthritis. Radiographic studies reveal osteoarthritis affecting knees, hips and distal interphalangeal joints. His past medical history includes gastroesophageal reflux disease (GERD) and several attacks of gout affecting both big toes. Current medicines are allopurinol and ranitidine.

Neurologic Examination Neurologic examination reveals a blood pressure of 150/90 and a regular pulse of 78 with occasional extra beats. Pertinent findings include normal strength, moderately severe spasticity of both legs, an abnormal gait manifested by circumduction of both legs and inability to perform tandem gait. Reflexes are 3+ and symmetrical except for a left Hoffmann's sign, sustained left ankle clonus and unsustained right ankle clonus of 5 beats. A vibration stimulus is not perceived from the hips down and he makes a few position sense errors at the toes. These findings are bilateral and symmetrical. There is no sensory loss to pain and temperature but he does have a deficit to light touch on the toes.

A cbc, metabolic panel and MRI of cervical and thoracic spinal cord are normal.

Questions

1. Does impaired tandem gait always indicate cerebellar dysfunction?
2. What general level of the spinal cord is involved? Why?
3. Is it usual to have severe impairment of vibration perception with minimal or no position sense loss?
4. What long tracts are involved?
5. Why is the MRI performed on both cervical and thoracic spine?
6. What is the name of this disorder?
7. What etiologies should be suspected?

Case 6 A 16-year-old boy enters the Emergency Room in a wheelchair at 1 a.m. Three months ago he was discharged from a hospital detoxification unit for drug abuse which included cocaine and heroin. He asserts that he has remained drug-free since then. He has been unable to void for 12 h and has minimal movement of both legs, the weakness beginning 36 h ago. Past medical history is otherwise negative and he takes no medicine.

Neurologic Examination Neurologic examination reveals normal vital signs. Pertinent abnormalities include 2/5 strength of all leg musculature. Reflexes are barely obtainable (trace) and he has bilateral Babinski signs. Catheterization of the bladder releases 600 cc of brown urine.

An MRI (cervical and thoracic) is normal.

Questions

1. What additional history would be useful and how should it be obtained?
2. What additional test should be performed?
3. What could it show?
4. What three findings support the anatomic diagnosis of myelopathy? Which one is most diagnostic?
5. What causes the brown urine?

Case 7 A 56-year-old woman is referred because of sharp, severe, right-sided abdominal pain of 18 h duration. Two hours after the onset of this pain she has difficulty urinating. General medical and surgical consultations find no pathology other than a neurogenic bladder. Her medical history includes type II diabetes, arthritis and glaucoma. Current medicines are metformin, cyclosporine ophthalmic eye drops (Restasis) and latanoprost eye drops (Xalatan).

Neurologic Examination Neurologic examination reveals a blood pressure of 135/85 and a pulse of 74, regular. Pertinent abnormalities: Hypesthesia to pin, right T7-T8 dermatomes, absent reflexes in the legs, a left Babinski sign and absent vibration perception at toes and ankles.

Questions

1. What specific questions should the patient be asked?
2. After listening to the answers what part of the examination should be re-evaluated?
3. If her only symptom was abdominal pain and the only sign was hypesthesia as described what would be a likely diagnosis?
4. Given her current examination plus her eye findings on re-examination what neuroanatomic diagnoses can be made?
5. What are the suspected primary diagnoses?

Follow-up Neurologic Examination the Next Morning The patient is now paraparetic with leg strength 2/5 throughout all musculature. She has 3+ symmetrical reflexes and bilateral Babinski signs. She is noted to have bilateral parotid gland swelling.

Questions

6. Does this change the differential diagnosis and what tests are indicated?
7. What is the diagnosis?

Case 8 A 38-year-old female nurse requests an evaluation because of numbness across both shoulders of 4 months duration. She adds that she is beginning to notice a little weakness of both arms over the last week. Her past medical history is negative. She uses birth control pills. She is a nonsmoker, acknowledges heavy alcohol consumption but eats well and is physically active as she surfs and plays golf.

Neurologic Examination Neurologic examination reveals a blood pressure of 110/56 and pulse 60 and regular.

Pertinent neurologic findings: A few fasciculations are seen over both shoulders. She has weakness of deltoids, supraspinatus and infraspinatus muscles with strength of 4+/5 bilaterally. Reflexes and gait are normal. She has sensory loss to pin over C4-C5 bilaterally.

An MRI (cervical) is scheduled in 3 weeks since the patient has other commitments. She returns in 1 week because she is alarmed about progressive weakness of the involved muscles which now have only 3+/5 strength.

Questions

1. What is the anatomic basis of the deficits.
2. Why does this determine the differential diagnosis?
3. Consequently, what syndrome is developing?
4. What type of lesions are suspected?
5. What is the differential and final diagnosis?

Case 9 A 74-year-old woman complains of back pain provoked by any movement and leg weakness, left greater than right, developing over 3 days. Additionally, she notes numbness beginning over the right lower abdomen. Her past medical history

includes type II diabetes, hypertension, and breast cancer 12 years ago treated by mastectomy and chemotherapy. Medications are metformin and lisinopril.

Neurologic Examination Neurologic examination reveals a blood pressure of 140/90, pulse 72 and regular.

Pertinent neurologic abnormalities: Paraparesis with distal strength 4/5 (ankle dorsiflexion) and proximal strength 5−/5 (iliopsoas). Reflexes in the legs are 3+ with bilateral 3-beat unsustained ankle clonus. Plantar responses are withdrawal but she has a left Chaddock's sign. She has a sensory level at T11 on the right side. Head flexion induces upward movement of the umbilicus.

Questions

1. What additional physical finding might help uncover the etiology?
2. What is the meaning of the response to head flexion?
3. What etiology is suspected and is the lesion most probably intramedullary, extramedullary intradural, or extradural?
4. Does the location provide the likely specific etiology?

The patient was treated by surgery followed by radiotherapy to cervical and thoracic spine with complete recovery. Two years later she complained of a 2-month history of electricity-like sensations radiating down her spine when putting on her shoes. One month ago she developed severe constipation and urinary frequency. Two weeks ago she began to lose her balance which alarmed her sufficiently to seek medical attention.

Neurologic Examination Neurologic examination reveals normal vital signs. She has 5−/5 strength in all leg muscles except bilateral toe extension which is 4/5. Vibration perception is absent from the knees down and position sense errors are found at the toes. Light touch deficits are present on the toes and dorsum of both feet. These sensory abnormalities are bilateral and symmetrical. Deep tendon reflexes are 3+ with bilateral unsustained ankle clonus plus left Hoffmann's and Chaddock's signs. The lower quadrant abdominal reflexes are absent and plantar reflexes are neutral. She cannot perform tandem gait and has mild bilateral heel-to-shin ataxia.

Questions

5. What parts of the spinal cord are affected? Why?
6. Does the ataxia indicate cerebellar pathology?
7. Are the deep tendon reflex findings useful for precise localization purposes?
8. Why is there loss of light touch perception?
9. What is the diagnosis?

Case 10 A 46-year-old man is referred by his primary physician because of right leg weakness progressive over 3 months. He has a 2-year history of chronic middle-to-low back pain. An MRI (thoracic and lumbar) performed 2 years ago revealed moderate spinal stenosis at L3-4. A neurosurgeon felt that this finding could not

explain the weakness and conservative management was recommended. He was sent to physical therapy, showed minimal improvement overall and was fitted with a brace for a right footdrop. Over the last year he has become impotent, severely constipated and has occasional urinary incontinence. Two months ago he had the onset of intermittent tingling of the fingers of both hands. Three days ago the weakness of his right leg became markedly worse. The weakness was aggravated by exercise.

Past medical history includes a 5-year history of hypertension which was initially difficult to treat, but has been controlled with amlodipine, lisinopril and hydrochlorothiazide.

Neurologic Examination Neurologic examination reveals a blood pressure of 185/98, pulse 60 and regular. Pertinent findings are spasticity of the right leg associated with diffuse 4/5 weakness, right ankle clonus and a right Babinski sign. As of 2 days ago he has required a walker.

Questions

1. What additional history about the fingers should be obtained which would aid in establishing an anatomic diagnosis?
2. Is the lesion localizable?

An MRI (brain) reveals several punctate T2/FLAIR subcortical hyperintensities and a single 1 cm nonspecific right parietal subcortical T2/FLAIR hyperintensity.

Questions

3. Should the MRI (brain) have been performed? Could the use of contrast be of diagnostic value?
4. Explain the significance of the MRI (brain) abnormalities.
5. Should any treatment be initiated promptly?

A lumbar puncture discloses a normal opening pressure with clear spinal fluid containing 43 rbc/mm^3, 5 mononuclear wbc/mm^3, protein of 102 mg%, glucose 83 mg%, normal IgG index and the presence of oligoclonal bands. The same bands are present in the blood.

Questions

6. Are the cerebrospinal fluid (CSF) findings compatible with a diagnosis of multiple sclerosis?
7. What diagnostic test is now performed?

Case 11 A 52-year-old woman is referred by her family physician because of clumsy hands. This first became apparent 7 years ago but has been disabling for the last 6 months. Because of occasional paresthesias, often nocturnal, carpal tunnel syndromes were suspected and nerve conduction tests revealed mild abnormalities supporting the diagnosis. She had surgery on the left hand 5 months ago followed 1 month

later on the right hand. The patient thought there might be slight improvement. Currently, however, she cannot sew and she drops pots and pans in the kitchen. She cannot distinguish coins or find her small key which opens the back door of her house.

Past medical history is remarkable for a pacemaker implanted for sick sinus syndrome, type II diabetes and gastroesophageal reflux. Her medicines are omeprazole and glipizide.

Neurologic Examination Blood pressure 115/70 and pulse 84, regular.

Pertinent findings: Motor, gait and reflex examinations are normal. She makes position sense errors at the fingers of both hands. Vibration stimuli are perceived but only for 2 s at the fingertips (decreased to adaptation). Light touch is not detected over the dorsal surface of the fingers of both hands. Tinel's signs are present.

Questions

1. What additional sensory testing would likely be abnormal?
2. Where is the lesion and what is the importance of the electromyogram and nerve conduction study?

A CT (cervical) reveals spondylosis at C5-C7 but no stenosis. A lumbar puncture follows and reveals a protein of 1320 mg%, xanthochromic (yellow) spinal fluid, 1 wbc (lymphocyte)/mm^3, 10 rbc/mm^3 and the fluid coagulates.

Questions

3. What syndrome does this describe and what causes it?
4. What examination is diagnostic?

Case 12 A 44-year-old male lawyer is referred by his family doctor because of weak, stiff legs progressing in severity over the last 3 months. Initially, he was only dragging his feet but now he has difficulty climbing steps. Additionally, he has poor balance especially in the dark and he complains of burning feet. His wife adds that his ability to concentrate has dropped and she is worried about his efficiency at work since he spends an extra 1–2 h working on his computer after dinner. The patient reports that his workload has increased and he dismisses her observations. His past medical history is negative and he takes no medicines. He smokes one-half pack of cigarettes per day and drinks only on social occasions.

Neurologic Examination Neurologic examination reveals normal vital signs.

Pertinent abnormalities include making errors on reversing 5-letter words although he corrects himself on a third try. He recalls 1 of 3 words after 2 min have elapsed. His legs are spastic with iliopsoas strength of 4/5, anterior tibialis strength of 4+/5 and he has 3+ reflexes with bilateral unsustained clonus, 5 beats at each ankle. He has a probable left Babinski sign but a definite left Oppenheim's sign. Vibration perception is absent at toes and ankles and proprioception is absent at toes. There is distal impairment of pinprick sensibility on hands and feet.

Laboratory data includes a CK of 310 IU (nl, 38-174). His cbc shows a white count of 3000 with a normal differential, hematocrit 33%, platelet count 95,000 and he has normal blood indices.

Questions

1. What leg reflexes are abnormal?
2. What is the anatomic source of each sensory abnormality?
3. Does the muscle weakness influence what laboratory tests will be ordered?

An MRI (cervical and thoracic) was done. It reveals a hyperintense T2 lesion involving the posterior column of the thoracic cord extending from T3 to T6. A lumbar puncture is then performed and reveals clear, colorless fluid but when the bottom of the test tube is snapped and held in direct sunlight there is a snowy appearance caused by the Tyndall effect. This is due to suspended cells causing light to scatter. Ordinarily at least 400 cells are necessary to perceive this turbidity. The fluid contains 196 wbc's all of which are lymphocytes; the protein is 77 mg% and glucose 88 mg%.

Questions

4. How does one explain the Tyndall effect given the established reference range?
5. Why was an MRI (cervical) performed?
6. What are the neuroanatomic sites of the pathology? Does this affect the differential diagnosis?
7. Are there other examinations that should be done?
8. What is the differential diagnosis and final diagnosis?

Case 13 A 66-year-old man complains of burning feet, stiffness and weakness of both legs. He has had hot sensations in his feet for about 10 years and these became burning and painful over the past year. Over the last 5 months his legs have become stiff and progressively weaker. He is now able to walk only 2 blocks without rest.

Past medical history includes renal stones on 2 occasions treated by lithotripsy 22 years ago. Peptic ulcer disease complicated by a major gastrointestinal hemorrhage requiring transfusions and hospitalization occurred 30 years ago. He has diabetes type II and the diagnosis was made 2 years ago. He had major depression 8 months ago which responded to treatment. Current medications are metformin and sertraline.

Neurologic Examination Blood pressure is 130/72 and pulse 102 and regular.

Pertinent neurologic findings include 4/5 strength of iliopsoas and anterior tibialis, 5−/5 strength of quadriceps, all bilateral. Reflexes are absent in the legs and he has a right Babinski sign. Spasticity of mild degree is noted in both legs. He cannot perceive vibration from the knees down and he has no proprioception at the toes. He makes light touch errors over the dorsum of both feet.

Laboratory Data ALT (alanine aminotransferase) 80 IU, hemoglobin A1C 6.8%, FBS 110 mg%, creatinine 2.0 and BUN 60.

Questions

1. What symptoms have localizing value?
2. What findings have contradictory localizing value?
3. What abnormalities on examination take precedence for the initial investigation? What was done?
4. What is the most important laboratory abnormality? Why?
5. What major clue for the etiology is obtained from the past medical history?
6. How is the diagnosis made?

Case 14 A 54-year-old woman is admitted to the hospital with the acute onset of fever, stiff neck, muscular jerks and blurred vision. Her past medical history is remarkable only for diabetes type II treated with metformin.

Neurologic Examination Neurologic examination reveals an irritable patient who is disoriented to place and recalls just 1 of 3 words after 1 min has elapsed. She has chaotic rapid saccadic eye movements in all planes, periodic generalized multifocal muscular jerks, moderate finger-to-nose and heel-to-shin ataxia and mild nuchal rigidity.

A lumbar puncture yields clear, colorless fluid with an opening pressure of 20 cm H_2O (normal is $\leq$20 cm/H_2O), protein 122 mg%, glucose 81 mg%, 72 wbc/mm^3 with 91% neutrophils and 9% lymphocytes. Gram stain, acid fast and fungal smears, cryptococcal antigen and VDRL are negative.

Questions

1. What syndrome is described? Where is the pathology?
2. Is the cerebrospinal fluid cell count unusual?
3. What is the diagnosis and most common etiology?

A CT (brain) without contrast performed after the lumbar puncture followed several hours later by an MRI (brain) with and without contrast are performed.

Questions

4. Is this the correct sequence of testing?

The MRI (brain) reveals a few T2/FLAIR hyperintensities in the cerebral cortex. The patient steadily improves, returns to normal by the 8th hospital day and is discharged. Two days later she complains of fatigue, severe low back and left leg pain and has an erythematous, macular, diffuse rash. The following day she has mild proximal weakness of the right leg followed within 24 h by a flaccid paraplegia accompanied by absent reflexes and normal sensation. Plantar responses are absent (mute or neutral).

Questions

5. Where is the lesion? What part of that structure is involved? To confirm the location what other abnormalities could be present?

A thoracic MRI with and without contrast shows a T2/FLAIR hyperintensity in the lumbar cord. There is no contrast enhancement. A repeat lumbar puncture reveals clear, colorless fluid with an opening pressure of 17 cm H_2O showing a protein of 101 mg%, glucose 96 mg% and 52 wbc/mm^3 with 98% lymphocytes and 2% neutrophils.

Questions

6. What is the significance of the changes in the CSF white blood cell profile?
7. What is the etiology?

Case 15 A 46-year-old male petroleum engineer has just returned from a 6-month job in Nigeria. For the last 2 weeks he has had severe midback pain and progressive right leg weakness. He now requires a cane. His past history is negative.

Neurologic examination Pulse 66, regular, blood pressure 150/90. Abnormal findings include 4/5 proximal and distal weakness of right leg musculature. He walks with a cane and circumducts the right leg. He has no abdominal or cremasteric reflexes on the right side. There is unsustained right ankle clonus. Vibration perception is absent at the right toes, ankle, knee, and left toes. Position sense errors are made at the right toes. He has a T12 sensory level on the left side. He is tender to percussion over the midthoracic spine.

Questions

1. How does one explain the reflex abnormalities.
2. Does this patient have abnormal muscular tone?
3. What syndrome does the patient have and what is the localizing value of the abnormal findings?
4. An MRI scan of the cervical and thoracic spine is performed. Why would both cervical and thoracic regions be imaged if there is a sensory level at T12? The absent abdominal reflexes on the right side support this level of involvement.
5. What is the differential diagnosis of a rapidly progressive lesion affecting the thoracic spinal cord?
6. The MRI scan shows a T6 epidural mass. What is the next step? What studies should be performed?

Case 16 A 40-year-old Hispanic woman is referred for a neurologic consultation because of poor balance and stiff legs. An abnormal electromyogram (EMG) showed a few myopathic features which prompted the referral. The patient first noted mild stiffness in the right leg 8 years ago. Simultaneously, she developed urinary frequency and occasional incontinence which has persisted. Additionally, she has muscular aches and a dry mouth.

Past medical history includes arthritis of unknown type and a history of uveitis. She takes no medications other than cyclosporine ophthalmic eye drops (Restasis).

Neurologic Examination Neurologic examination reveals a blood pressure of 122/80 and regular pulse of 82. Pertinent neurologic abnormalities include a posi-

tive Romberg test, symmetrical 4+/5 strength of deltoid and iliopsoas musculature. Knee reflexes are 3+. There are 6 beats of ankle clonus on the right and 2 beats on the left. Plantar responses are flexor bilaterally. Vibration perception is absent at toes, ankles and barely perceived at the knees.

Questions

1. What other neurologic findings, not mentioned, would be expected?
2. What neurologic signs appear unrelated to the primary diagnosis?
3. Are the ankle reflexes abnormal?
4. Where is/are the lesion(s)?
5. Are there any other questions which could provide clues to the diagnosis?
6. The MRI (cervical and thoracic) reveals increased signal in the lateral columns of the thoracic cord associated with cord atrophy. If the MRI (cervical and thoracic) is not diagnostic what test should be performed?
7. Are any additional laboratory tests indicated?
8. What are the diagnoses?

Case 17 A 48-year-old man is referred to a neurology clinic because of left foot weakness progressive over 6 months. He now complains of a footdrop and fatigue.

Past medical history is negative and he takes no medicines.

Neurologic Examination Neurologic examination reveals a blood pressure of 145/100 and a pulse of 110. His BMI is 32. Abnormal neurologic findings include a decreased left foot tap, 4/5 strength of left anterior tibialis, asymmetric ankle reflexes which are 2+ on the left and 1+ on the right.

An MRI (lumbar) ordered by his internist reveals a herniated disk on the left side at L4-5. Conservative treatment with physical therapy is initiated and he is placed on a strict diet and exercise program.

One year later the patient returns and reports that he received little benefit from physical therapy. Over the last 2 months his weakness has ascended to the left knee and his right foot is weak. His fatigue is severe.

Neurologic examination now reveals left leg strength of 4+/5 except for the anterior tibialis which is 4/5. The right anterior tibialis is 4+/5. Plantar responses are extensor on the left and equivocal on the right.

Questions

1. What critical part of the most recent examination was not commented on?
2. What findings on the first neurologic examination should have prompted neuroimaging of the spinal cord?
3. Why is the patient's fatigue increasing?
4. An MRI is indicated. Of what structure or structures should it be ordered?
5. What other examination should be considered? What might it show to support the suspected diagnosis?
6. What is the most likely diagnosis?

Answers

Case 1

1. Myasthenia gravis especially the muscle-specific tyrosine kinase (MuSK) variant, chronic inflammatory demyelinating polyneuropathy, amyotrophic lateral sclerosis (ALS), polymyositis, dermatomyositis facioscapulohumeral dystrophy and acid maltase disease. The sternomastoid muscles, the main head flexors, might be mildly weak but a slight give in this muscle is common in the normal population. Clinical judgment is required to determine significance.
2. He must be disrobed except for underwear.
3. There must be careful inspection for fasciculations on the chest, back, extremities and especially the tongue. Fasciculations at more than one location are nearly diagnostic of ALS. Fasciculations were observed over chest and back.
4. Yes. CK is mildly increased in many ALS patients.
5. *Diagnosis*: Amyotrophic lateral sclerosis.

Comment Repeated examinations frequently provide the diagnostic clues. Never assume that the first neurologic examination is sufficient particularly when imaging and laboratory studies do not confirm a diagnosis.

Case 2

1. Sensory examination.
2. Yes. Severe position sense loss can be associated with ataxia. Asymmetric unsustained ankle clonus is abnormal. Symmetrical unsustained clonus is normal.
3. Yes. Briefly, denture adhesives often contain zinc. When zinc levels rise copper absorption is impaired. The copper-dependent enzyme, methionine synthase, is deficient thus interfering with methylation. This results in impaired myelination of the spinal cord.
4. Yes. Gastric bypass.
5. Somatosensory-evoked potentials (SSEP) and serum copper levels. The SSEP was abnormal indicating spinal cord disease. Copper levels were low and this may cause neutropenia and macrocytic or microcytic anemia.
6. Menkes disease, Wilson's disease and nephrotic syndrome.
7. *Diagnosis*: Myeloneuropathy due to copper deficiency [6].

Comment The findings mimic those of subacute combined degeneration due to vitamin B12 deficiency. Furthermore, patients with copper deficiency may also present with optic neuropathy and peripheral neuropathy. Thus the illness can simulate both multiple sclerosis and neuromyelitis optica. A careful history should uncover the pathology and lead to prompt improvement with treatment.

Case 3

1. Rectal examination. This patient has a patulous anal sphincter.
2. Check for perianal (saddle) anesthesia. The patient has hypesthesia in this region (S3-S5).

3. Urinary retention with poor detrusor function because the disease impairs parasympathetic function (S2-S4 roots). The patient's post-void residual is measured at 250 cc. The normal is less than 50 cc.
4. Lumbar puncture with detailed cerebrospinal fluid analysis on a 10 cc fluid sample is essential. The protein is 82 mg%, glucose 30 mg%, red blood cells (rbc's) are 12/mm^3 and wbc's are 80/mm^3 with 90% lymphocytes and 10% neutrophils. Low spinal fluid sugar is common with leptomeningeal metastases. Cytology is positive for malignant cells. Flow cytometry is often more sensitive but this is most diagnostic for hematologic malignancies. A total of three lumbar punctures with 10 cc samples of spinal fluid may be required to establish a diagnosis. Typically, 50% of patients have a positive first lumbar puncture, 80% by the second and 90% by the third.
5. These neurologic findings are characteristic of cauda equina pathology.
6. The patient has a left Horner's syndrome, a characteristic finding when carcinoma of the lung invades the cervical sympathetic chain. The key finding is slower pupillary dilation O.S. than O.D. when the patient is first examined in the dark. This patient initially shows a 1 mm asymmetry in light (>0.5 mm asymmetry is abnormal) but a 1.5 mm asymmetry in the dark after 10 s have elapsed. This increased asymmetry in dark indicates sympathetic system impairment on the left, a typical diagnostic finding of Horner's syndrome. Additionally, there is a slight left lid droop (weakness of Müller's muscle).
7. Estimates vary from 30% to 70%.
8. *Diagnosis*: Cauda equina syndrome due to leptomeningeal (extramedullary intradural) metastases from carcinoma of the lung involving the left apex [15].

Comment The most common location of epidural metastasis is the cauda equina. Other etiologies include herniated lumbar disk, trauma, abscess and cytomegalovirus. The latter occurs especially in HIV-AIDS patients. Schistosomiasis is a consideration in countries where it is endemic.

The cauda equina syndrome is comprised of severe low back and leg pain, urinary and fecal incontinence or retention, loss of anal sphincter tone, sexual dysfunction and saddle hypesthesia.

The conus medullaris syndrome can be difficult to distinguish from the cauda equina syndrome. The level of pathology is usually at T12 or L1, and the symptoms are nearly identical to those of the cauda equina lesion. Differences can be milder pain and commonly a spastic paraparesis, absent ankle jerks, preserved knee jerks, and dissociated sensory loss. The latter usually means loss of pain and temperature sensation with preserved light touch, vibration and proprioception. The reverse which is less common is still termed sensory dissociation. Etiologies are identical with the cauda equina location.

Case 4

1. Spinal cord compression due to a herniated disk, vertebral subluxation, and a spinal cord infarction are the major diagnostic considerations.
2. The anterior cord which encompasses the lateral corticospinal tract (flaccid quadriplegia) and the lateral spinothalamic tract (sensory level to pin and temperature) is the likely anatomic basis.

3. Intramedullary if of vascular origin and extradural (epidural) if caused by mechanical compression.
4. The herniated disk caused an acute radiculopathy with severe right arm pain but this alone does not explain the devastating myelopathy. Consequently, there is an intramedullary lesion affecting the anterior portion of the spinal cord which produced a flaccid quadriplegia.
5. There was a fibrocartilaginous embolism from nucleus pulposus fragments into a cervical radicular artery which then migrated to the anterior spinal artery thus causing a spinal cord infarction. Figures 10.1 and 10.2 outline the vascular supply to the spinal cord.

Diagnosis Anterior spinal artery syndrome with infarction of the anterior spinal cord due to fibrocartilaginous embolism to the anterior spinal artery arising from a herniated nucleus pulposus [11].

Comment In a retrospective review from the Mayo Clinic of 154 patients with spinal cord infarctions, 5.5% had a diagnosis of suspected fibrocartilaginous embolism [11]. The most common cause of spinal cord infarction, however, is a complication of thoracic or abdominal aorta surgery or endovascular repair.

Case 5

1. No. It is also commonly impaired with vestibular, sensory and other motor system (corticospinal tract and extrapyramidal) disorders.
2. The cervical level is affected because of the unilateral Hoffmann's sign. Bilateral symmetrical Hoffmann's signs are often found in normal individuals.
3. Yes. It is common. Therefore, a standard 128 cps tuning fork is required for a sensory examination. Checking only proprioception is unsatisfactory.
4. Posterior column and lateral corticospinal tract.
5. Both cervical and thoracic MRIs are ordered since the spinal cord is located in those areas, not in the lumbar region. Follow-up examinations, when indicated, can focus on the primary area of involvement.
6. Subacute combined degeneration.
7. Vitamin B12 deficiency and nitrous oxide toxicity. Nitrous oxide has a mood elevating property and medical personnel, especially dentists, have been known to abuse it.

Diagnosis: Cervical myelopathy, subacute combined degeneration secondary to nitrous oxide abuse [10].

Comment Nitrous oxide irreversibly oxidizes the cobalt center of methylcobalamin, the active form of vitamin B12. Its toxicity therefore causes subacute combined degeneration.

Case 6

1. Question the patient again to see if he took at least 1 additional dose of heroin indicating that a complete understanding of his history is essential for good medical care. He did take a single dose.

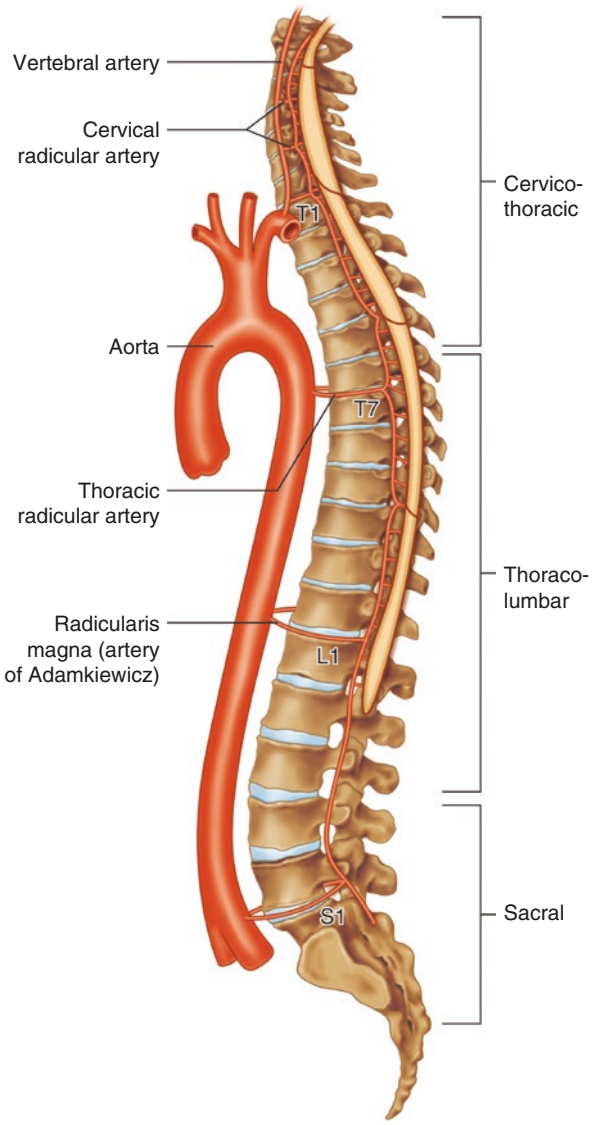

Fig. 10.1 Arterial supply of the spinal cord, lateral view

2. Lumbar puncture.
3. High protein, low glucose, with or without pleocytosis or normal spinal fluid. Central nervous system infection should be excluded.
4. Paraparesis, Babinski signs and neurogenic bladder. These three findings make another neuroanatomic diagnosis nearly impossible. The Babinski signs are diagnostic. A paraparesis and neurogenic bladder might conceivably be due to a severe bilateral lumbosacral radiculopathy or plexopathy were it not for the Babinski signs. The decreased reflexes in this case relate to the acuteness of the illness.

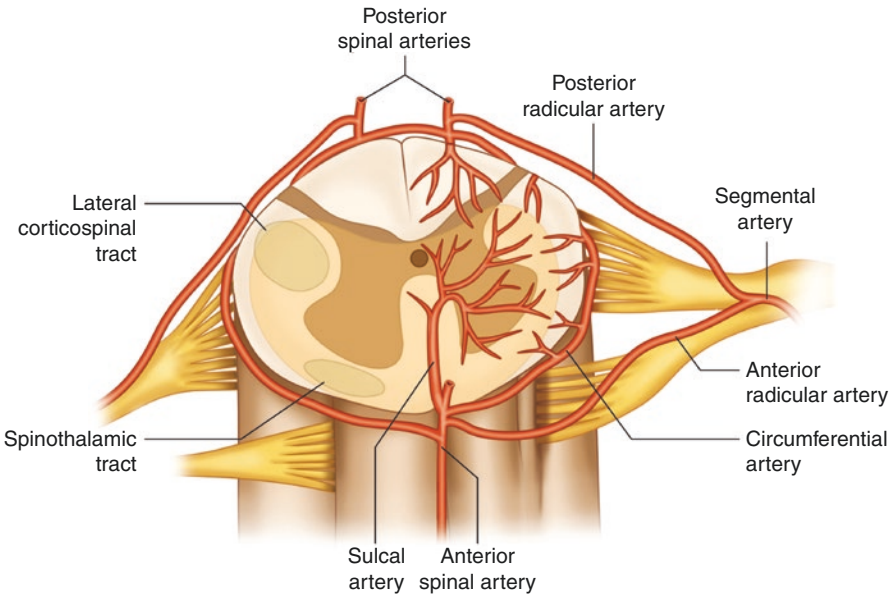

Fig. 10.2 Arterial supply of the cervical spinal cord, axial view

5. Myoglobin. Rhabdomyolysis, acute renal failure and liver failure are known complications of heroin use.

   Diagnosis: Myelopathy due to heroin use [6].

Comment A single experience with heroin in a patient with a history of prior heroin abuse after a significant abstinent period can cause a severe myelopathy. This might be due to an immune-mediated hypersensitivity reaction.

Case 7

1. A complete review of medical and neurologic symptoms should be obtained and would uncover the essential clues. Specifically, however, the patient complains of arthritis and eye pathology and that should be the focus of additional history. What symptoms of arthritis do you have and was a diagnosis made? Which eye drops did you start first? Have you ever had temporary loss of vision?

   The patient responds: "I have a 20-year history of intermittent knee, shoulder and hand pain but no joint swelling. I began Restasis (cyclosporine) eye drops about 10 years ago and Xalatan eye drops about 2 years ago." Therefore, she had dry eyes before using Xalatan which can also cause dry eyes. "Eight years ago I had loss of vision in my right eye for two weeks and recovered completely."
2. Since she has a history of transient visual impairment O.D., additional examination of the eyes is indicated. She has impaired color perception (color desaturation O.D.) with 20/20 vision and a RAPD O.D. A normal visual acuity does not

rule out an optic neuropathy. Funduscopic examination is normal. The RAPD confirms a prior optic nerve lesion.
3. Thoraco-abdominal neuropathy secondary to diabetes.
4. Myelopathy and optic neuropathy O.D. and possible neuropathy.
5. Sjögren's disease, neurosarcoidosis and systemic lupus erythematosus (SLE) are associated with the sicca syndrome, joint pain, transverse myelitis, optic neuropathy and peripheral newropathy. Other considerations not associated with arthritis or the sicca syndrome include neuromyelitis optica, multiple sclerosis, antiphospholipid antibody syndrome, copper and vitamin B12 deficiencies. Neurosarcoidosis and SLE are often present without arthritis or the sicca syndrome.
6. No. The differential diagnosis is the same. A lumbar puncture is normal except for the presence of oligoclonal bands. Protein and glucose are normal. There are 18 lymphocytes mm^3. The ANA is positive 1:1280, SSA is 2.0 U and SSB is 2.2 U. Rheumatoid factor is negative.
7. *Diagnosis*: Transverse myelitis and optic neuropathy O.D. secondary to Sjögren's disease [17].

Comment Initially, the neurologic examination pointed to a diabetic neuropathy and thoraco-abdominal neuropathy. The one finding that indicated central nervous system involvement was the Babinski sign. Parotid swelling raised the question of Sjögren's disease, SLE and neurosarcoidosis. The sicca syndrome and optic neuropathy may also occur with these illnesses. The laboratory data and the prominent sicca syndrome associated with arthritis strongly support the diagnosis, Sjögren's disease. Of note, oligoclonal bands may be present in many diseases besides multiple sclerosis some of which include Sjögren's disease, SLE, syphilis, Lyme disease, Guillain-Barré syndrome, neuromyelitis optica, meningeal carcinomatosis and primary central nervous system lymphoma.

Case 8

1. The suspected lesion is likely to be in the center of the spinal cord as it may interfere with crossing fibers at the anterior commissure at the C4-C5 level. These fibers mediate pain and temperature sense and merge with the lateral spinothalamic tract. The injured crossing fibers at that level result in impaired pain perception in dermatomes C4 and C5. Fasciculations are seen in the deltoid muscle supplied partly by the C5 root probably because of damage to anterior horn cells. Reflexes are spared since the lateral corticospinal tract is not involved. Bilateral C4-C5 radiculopathy cannot technically be ruled out.
2. The lesion is intramedullary and affects anterior horn cells! The latter does not occur with demyelinating disease such as multiple sclerosis. ALS does not cause sensory abnormalities.
3. Man-in-a-barrel syndrome is emerging, bilateral arm paresis with preserved motor function of the legs.
4. Mass lesions such as neoplasm and syringomyelia. The latter is unlikely since progression is ordinarily quite slow.

5. The differential diagnosis of cervical myelopathy due to an intramedullary mass lesion is astrocytoma, ependymoma or metastasis. Metastasis best explains the rapid progression of weakness.

Diagnosis Cervical myelopathy secondary to an intramedullary neoplasm [7].

Comment The MRI (cervical) reveals findings most compatible with intramedullary metastatic disease. This is rare as nearly all metastases are located in the extradural space. This patient has a melanoma which comprises 8% of spinal cord metastases. The melanoma was located on her left shoulder presumably related to sun exposure.

Case 9

1. If percussion of the spine elicits pain, neoplasm, especially metastatic, would be suspected.
2. Head flexion elicits Beevor's sign, an upward movement of the umbilicus that occurs because of intact upper and weak lower abdominal muscles, i.e. sparing of T9 and above thus localizing the lesion to about T10.
3. Metastatic breast cancer is often a very late development after successful initial treatment. Metastases are usually extradural (epidural).
4. Yes. The MRI discloses a T10 extradural lesion with spinal cord compression, by far the most likely location of metastatic disease. A tiny asymptomatic extradural lesion is also noted at C4.
5. Posterior column and lateral corticospinal tract. Lhermitte's sign, electricity-like sensations as described, when flexing her head to put on her shoes, is likely due to demyelination in the posterior columns. The left Hoffmann's and Chaddock's signs are evidence for left lateral corticospinal tract involvement.
6. It may, but severe position sense loss commonly causes heel-to-shin ataxia and is move likely.
7. No. The brisk (3+) symmetrical reflexes and symmetrical unsustained ankle clonus can be seen in the normal individual. However, a left Hoffmann's and Chaddock's signs indicate left cervical and possibly left thoracic cord pathology. The superficial reflexes, in this instance, are precisely localizing, specifically the absent lower abdominal reflexes which indicate a lesion around T10.
8. The majority of fibers mediating light touch travel in the posterior columns.
9. *Diagnosis*: Radiation myelopathy [2].

Comment Transient radiation myelopathy usually occurs between 6 weeks and 6 months post-treatment and resolves over a few months. Delayed radiation myelopathy begins between 6 months and 2 years but even longer delays have been observed. The pathology is vascular and/or demyelinating. Spontaneous resolution does not occur.

Case 10

1. When is the tingling most bothersome? The patient responds that it often awakens him at night. This is a nearly universal symptom of carpal tunnel syndrome. This history makes cervical myelopathy unlikely. An EMG-NCV confirms the diagnosis of bilateral carpal tunnel syndromes.

2. No. Isolated right leg weakness with spasticity and increased reflexes may occur with cerebral or spinal cord disease, rarely brainstem.
3. Yes. Multiple sclerosis is a diagnostic consideration and asymptomatic cerebral pathology is common. Contrast enhancement could reveal an acute multiple sclerosis lesion or a neoplasm might become visible.
4. These MRI abnormalities are often present in patients with a history of hypertension.
5. Yes. An increase or change in antihypertensive medicine is indicated should elevated blood pressures be confirmed on additional monitoring. Never overlook reversible medical conditions despite their irrelevance to the primary problem.
6. No. High CSF protein levels virtually excludes multiple sclerosis. Oligoclonal bands are not required for a diagnosis of multiple sclerosis and they may occur in other diseases such as neurosarcoidosis and SLE. Here they are not abnormal since the same bands are present in blood. Since the tap was not traumatic the 43 rbc's suggest vascular pathology or neoplasm.
7. A repeat thoracic MRI reveals tortuous massively enlarged veins on the dorsal surface of the spinal cord. The etiology may be higher pressure within the dura transmitted to the spinal venous plexus which produces venous stasis and spinal cord infarction. An arteriovenous fistula is likely to be the etiology. The key principle here is to always repeat the investigations, MRI in this case, when new serious symptoms and signs develop unexpectedly.

   Diagnosis: Foix-Alajouanine syndrome [8, 12].

Comment The clinical manifestations are usually a progressive spastic paraplegia over 1–5 years with prominent bowel, bladder and sexual dysfunction. This syndrome often mimics multiple sclerosis. "Exertional claudication" with exercise due to transient spinal cord ischemia may be a diagnostic clue. Initial MRI scans may be normal and must be repeated even after a short interval if there is an exacerbation of a neurologic deficit. CSF findings can spur a more extensive diagnostic assessment. Surgery has been reportedly helpful in a few patients.

Case 11

1. Stereognosis, graphesthesia and 2-point discrimination. The history already includes a description of astereognosis which is confirmed. Not only can she not distinguish a key from a coin but she cannot discriminate a rubber band from a wooden match. Thus the perception of both form and texture are impaired. Two-point discrimination at the fingertips is 10 mm (between 2 and 4 mm is normal). She cannot identify numbers written on the palms of her hands. Thus she also has impaired graphesthesia. These abnormal sensory signs, commonly identified as cortical, are often found in high cervical cord lesions.
2. Cervical spinal cord. The EMG-NCV findings take second place, in this instance, to the clinical findings. Cervical myelopathy is suspected because both hands are affected with findings atypical for median neuropathies.

3. This patient has Froin's syndrome, the triad of xanthochromic (yellow) cerebrospinal fluid which coagulates and contains an extremely high protein level. Xanthochromia may be visible with protein levels exceeding 150 mg%. It is otherwise due to bilirubin associated with hemorrhage.
4. CT myelography is performed since an MRI is contraindicated because of her pacemaker. It shows a large extramedullary intradural mass located over the dorsal portion of the cervical spinal cord at C2-C3 causing a complete block. The lesion location is typical of a benign tumor. A noncontrast CT scan cannot be relied upon to expose many significant pathologies.

Diagnosis: Cervical myelopathy due to a meningioma, C2-C3.

Comment Several lessons can be learned from this patient. So-called cortical sensory signs may also be observed in high cervical cord lesions affecting the posterior columns. Complete reliance on EMG-NCV is hazardous since mild abnormalities may be present in asymptomatic patients and not be relevant in symptomatic patients. Clinical findings, obvious in this case, take precedence over neurophysiologic or initial imaging studies. Bilateral arm involvement points strongly to cervical cord pathology. Froin's syndrome is a triad of CSF abnormalities which include extremely high protein, xanthochromia and coagulation of spinal fluid. This occurs with mass lesions which cause a complete block of spinal fluid movement.

Case 12

1. The left Oppenheim's and suspected left Babinski signs are abnormal. Symmetrical unsustained clonus can be normal. Asymmetric clonus is abnormal. Sustained clonus is always abnormal.
2. Vibration and position sense loss in both legs is due to either neuropathy or myelopathy (posterior column). Distal impairment of pinprick of hands and feet is due to neuropathy.
3. Yes. Proximal weakness (iliopsoas 4/5) may occur with spinal cord disease but also raises a question about a myopathy. Hence a CK was ordered. Distal weakness in this setting is compatible with either neuropathy or myelopathy.
4. Published standards need not be considered sacrosanct.
5. When a myelopathy is suspected both cervical and thoracic MRI scans should be performed. For example, thoracic sensory levels may be present with cervical cord lesions and a cervical lesion may be asymptomatic.
6. The differential diagnosis depends on the neuroanatomic diagnosis. Myelopathy is suspected because of spasticity affecting both legs and the abnormal plantar responses. The abnormal thoracic MRI confirms the anatomic diagnosis. Neuropathy is likely to be present because of distal sensory loss to pinprick. A diagnosis of myopathy is supported by the presence of proximal weakness and a high CK level. Bilateral cerebral dysfunction is documented by the presence of poor short-term recall and difficulty reversing the spelling of five-letter words. The differential diagnosis must explain involvement of cerebrum, spinal cord, nerves and muscle.

7. Yes. The presence of short-term memory loss requires investigation. An MRI (brain) shows several subcortical but nondiagnostic T2/FLAIR hyperintensities. HIV (human immunodeficiency virus) serology and an RPR should be obtained because of multiple areas of neurologic pathology. Cerebrospinal fluid examination should be done to evaluate for infection. This was normal and included acid-fast smear, fungal smear, cryptococcal antigen, VDRL and appropriate cultures. An EMG-NCV reveals both neuropathic and myopathic features.
8. Diagnostic considerations include HIV-AIDS (acquired immunodeficiency syndrome), cytomegalovirus (CMV) disease, vitamin B12 deficiency, neurosyphilis and fungal disease. Both HIV-AIDS and CMV, which can also be a complication of HIV-AIDS, may affect muscle, nerves, spinal cord and cerebral hemispheres. Neurosyphilis may attack cerebral hemisphere, spinal cord and dorsal root ganglia but not peripheral nerves. Fungal disease, if fulminant, may affect all sites but, rarely the peripheral nerves and vitamin B12 deficiency does not cause myopathy.

Diagnosis: Vacuolar myelopathy, neuropathy, myopathy and mild cognitive impairment due to HIV-AIDS [3, 4].

Comment Marriage does not exclude risky behavior with prostitutes or gay sex. The focal pathology affecting posterior and lateral portions of the spinal cord is the same pattern as subacute combined degeneration of vitamin B12 deficiency. Vacuolar myelopathy has a predilection for involvement of the thoracic cord. If the MRI was normal then somatosensory-evoked potentials might localize the pathology and support the diagnosis. There is impaired ability to utilize vitamin B12 which may be a factor in the selective involvement of these tracts.

Case 13

1. Burning feet are common symptoms of neuropathy. Stiff legs suggest spasticity which implies involvement of the lateral corticospinal tract in the lateral column of the spinal cord. Spinal cord pathology is suspected because symptoms are bilateral.
2. Reflexes. Absence of reflexes at knees and ankles is common in neuropathy. Asymmetric hyperreflexia is expected in myelopathy. Proximal weakness is not common in neuropathy whereas it is not unusual in myelopathy.
3. The Babinski sign and spasticity in both legs take precedence. MRI of cervical and thoracic spine was normal.
4. ALT. Diabetes and renal disease do not cause myelopathy. Hepatic disease may rarely cause myelopathy.
5. The patient had a major gastrointestinal hemorrhage requiring transfusions and hospitalization in the 1980s prior to optimum screening evaluations for hepatitis C. These were established in 1999 although less precise testing was initiated in 1990, still later than when he likely had a transfusion.
6. Hepatitis serology confirms the diagnosis.

Diagnosis: Hepatic myelopathy and neuropathy secondary to hepatitis C [1].

Comment The most common laboratory abnormality in hepatitis C is the ALT. Demyelination in the lateral column of the thoracic cord is most common. Transverse myelitis is a well-established but rare complication. Diabetes type II is often associated with hepatitis C. The described sensory abnormalities are consistent with both myelopathy and neuropathy. The neuropathy may be due to either hepatitis C or diabetes.

Case 14

1. Opsoclonus, myoclonus, cerebellar syndrome. Pathology is in the cerebellum and/or pons. The two most common etiologies are viral encephalitis and a paraneoplastic syndrome.
2. No. An acute viral illness often shows an initial neutrophil predominant pleocytosis.
3. Meningoencephalitis. "Meningo" refers to the stiff neck. If nuchal rigidity is absent then a more appropriate term for the disorder would be "encephalitis" which is nearly always due to a viral infection.
4. Yes. Nuchal rigidity and fever mandate an immediate lumbar puncture. The clinical picture is not consistent with a mass lesion which would require neuroimaging first.
5. Back pain and flaccid paraplegia with areflexia of acute origin point towards a myelopathy with spinal cord shock. Technically, an acute polyradiculoneuropathy (Guillain-Barré syndrome) is a diagnostic consideration but opsoclonus, myoclonus and cerebellar ataxia are not presenting manifestations. The anterior horn cells may also be involved because of the absent reflexes. Fasciculations would confirm that localization. The thoracic MRI findings support the presence of a myelopathy.
6. The initial neutrophil predominance followed promptly by a lymphocytic predominance in the CSF is not unusual for a viral infection.
7. *Diagnosis*: Thoracic myelitis and meningoencephalitis due to West Nile Virus [14].

Comment West Nile Virus IgM antibodies were positive 5 days after meningoencephalitis was diagnosed. Ordinarily, they become positive between the 3rd and the 8th day and remain positive for 1 to 3 months. IgG becomes positive a few days after the IgM becomes positive but can persist for years and therefore is not diagnostic.

The opsoclonus-myoclonus-cerebellar syndrome is exceptionally rare and is usually due to a viral encephalitis or paraneoplastic disorder. The physiologic basis is hypothesized to be increased excitatory output from the cerebellar fastigial nuclei due to interruption of inhibitory pathways from Purkinje cells or excessive activity of burst neurons located in the nucleus raphe interpositus in the pons, also a release

from inhibitory input. Meningoencephalitis often precedes the signs of a myelitis which commonly begins with proximal weakness of one limb followed by spread to other limbs. This typically results in an areflexic paraplegia or quadriplegia due to involvement of anterior horn cells, a mimic of poliomyelitis and characteristic of West Nile viral infections. Eighty percent of West Nile Virus infections are asymptomatic and, of the rest, just 1% have neurologic complications. Prognosis for recovery from a myelitis is poor.

Case 15

1. The loss of superficial reflexes, abdominal and cremasteric, and the unsustained right ankle clonus are caused by a lesion of the corticospinal tract on the right side of the spinal cord at T7 or above. The upper abdominal reflexes are mediated by T7-T10 roots and lower abdominal reflexes by T10-T12 roots. Absence of a Babinski sign does not affect the anatomic diagnosis. A neuroanatomic diagnosis depends on the observed findings but not the absence of an expected abnormality.
2. Yes. Circumduction of the right leg occurs with spasticity.
3. The patient has a partial Brown-Séquard syndrome as there is involvement of the corticospinal tract on the right side causing right leg weakness with spasticity, right ankle clonus, and loss of the superficial reflexes on the right side. The posterior columns are affected in view of position and vibration sense loss primarily on the right side. The sensory level at T12 on the left side indicates lateral spinothalamic tract involvement on the right as these fibers immediately cross the midline in the anterior commissure. Consequently, this patient most likely has a thoracic myelopathy. The level should be at T7 or higher on the right side in view of loss of the abdominal reflexes on that side. A sensory level commonly varies from one to two segments below the lesion, but to a much lower level on frequent occasions.
4. An MRI of cervical and thoracic spine is ordered with and without contrast as the diagnosis is myelopathy, most likely thoracic, but a cervical lesion cannot be entirely excluded. The lesion is at T7 or above since abdominal reflexes on the right side are absent. Generally, myelopathies require both cervical and thoracic visualization if the diagnosis has not yet been made. As previously noted, a cervical lesion may cause a thoracic sensory level.
5. The differential diagnosis includes transverse myelitis, transverse myelitis as a manifestation of multiple sclerosis, herniated thoracic disk, neoplasm, infection, and vascular disease. Transverse myelitis usually develops more rapidly than 2 weeks. Multiple sclerosis is most definitely a consideration since the patient is age 46 (usual age range is 15–50). Herniated thoracic disks are rare. Neoplasm, especially a malignancy such as lymphoma, is a definite consideration. A benign lesion such as a meningioma or schwannoma would be most unlikely to develop in this rapid fashion. Infection such as osteomyelitis with abscess formation is a major possibility.

   The neuroanatomic diagnosis, as expected, will still determine the differential diagnosis. There are three anatomic sites of lesions which affect the spinal cord,

intramedullary, extramedullary intradural, and extradural (epidural). Transverse myelitis with or without associated multiple sclerosis and gliomas are intramedullary (within the spinal cord). Meningiomas and schwannomas are usually extramedullary intradural (outside the spinal cord but within the dura). Herniated disks and spinal stenosis are extradural (outside the dura). Mass lesions such as metastatic neoplasm or abscess are most often extradural. Consequently, the lesion in this case is most likely metastatic neoplasm or abscess.

6. A lumbar puncture is performed and the fluid is sent for cell count, protein, glucose, gram stain, acid-fast smear, fungal smears, cryptococcal antigen, VDRL, cytology and appropriate cultures.

   The spinal fluid glucose is 20 mg/dl, protein 120 mg/dl, and there are 58 white cells/cu mm all of which are mononuclears. The acid-fast smear shows gram-negative rods.

   Diagnosis: Thoracic myelopathy, T6, secondary to an epidural tuberculous abscess associated with osteomyelitis [9].

Comment Tuberculosis must be considered when patients have lived in Africa, Asia or South America where it is not unusual. The cerebrospinal fluid findings are characteristic of this disease. The acid-fast smear is diagnostic.

Case 16

1. Impaired proprioception is suspected because of the history of poor balance, a positive Romberg and loss of vibration perception. Spasticity is likely since the patient complains of stiffness and has asymmetric unsustained clonus, consistent with spinal cord pathology.
2. Proximal weakness might occur but would not be expected.
3. Yes. Asymmetric unsustained clonus is abnormal.
4. Spinal cord and muscle, the latter because of proximal weakness.
5. Where were you born? Response: Dominican Republic.

   Do you have dry eyes? This question is prompted by the patient's use of cyclosporine eye drops. Response: Yes.

   A follow-up question is: Do you have a dry mouth? Again the patient responds: Yes, extremely dry.
6. Lumbar puncture.
7. HTLV-1 antibodies in blood and cerebrospinal fluid. The lymphocytes may have multilobed nuclei. Useful blood tests would include an ANA, SSA and SSB. These are abnormal.
8. Diagnoses:

   1. Thoracic myelopathy secondary to HTLV-1 virus (tropical spastic paraparesis) [5].
   2. Sjögren's syndrome associated with myopathy and the sicca syndrome.

Comment Endemic areas for HTLV-1 virus are the Caribbean, Central and South America, Japan and Africa. Associated symptoms or illnesses include Sjögren's syndrome, uveitis, arthritis, Raynaud's syndrome, pulmonary lymphocytic alveolitis, myopathy and neuropathy. The MRI (thoracic) can be abnormal and may demonstrate lateral and posterior column involvement as well as spinal cord atrophy as in this patient. There is a predilection for thoracic cord pathology. This virus is also responsible for adult T-cell leukemia-lymphoma (ATLL).

Case 17

1. Vital signs. The nurse now reports a blood pressure of 155/102 and a pulse of 110 by machine. Two days later the neurologist finds the heart rate is periodically irregularly irregular and an EKG confirms atrial fibrillation. Oral anticoagulation is initiated.
2. Weakness of left anterior tibialis with asymmetric ankle reflexes greater on the left side. Lumbar root compression would have decreased the left ankle reflex.
3. Fatigue is probably due to hyperthyroidism with its complication of atrial fibrillation although multiple sclerosis, if confirmed, is likely a contributing factor for fatigue. The free T4 is 3.8 ng/dL (nl. 0.8–2.4 ng/dL) and the TSH is 1 μ/mL (nl. 2–10) confirming the presence of hyperthyroidism.
4. Brain, cervical and thoracic cord. Since multiple sclerosis is a diagnostic consideration, even though the primary lesion is in the cervical or thoracic cord, asymptomatic cerebral pathology may be visible.
5. If there is no lesion or just one T2/FLAIR hyperintense lesion in the brain typical of multiple sclerosis, then a lumbar puncture (LP) is indicated. The MRI (brain) disclosed a single T2/FLAIR hyperintense lesion perpendicular to the left lateral ventricle characteristic of multiple sclerosis. The LP was performed prior to beginning oral anticoagulation and CSF examination revealed oligoclonal bands.
6. Diagnoses:

    1. Primary progressive multiple sclerosis. (*See* Tables 10.1 and 10.2) [16].
    2. Atrial fibrillation.
    3. Hyperthyroidism.

Comment Machine-recorded blood pressure and pulse does not assess rhythm which must always be checked by the attending physician.

The diagnosis of multiple sclerosis is often challenging and, consequently, much thought has been given to establish guidelines. Tables 10.1 and 10.2 summarize the diagnostic criteria for multiple sclerosis, the primary progressive form. Other diagnostic criteria for the clinically isolated, radiologically isolated and secondary progressive syndromes are outlined thoroughly elsewhere [13, 16].

Table 10.1 Diagnosis of multiple sclerosis

Clinical attacks	# Lesions with objective clinical evidence	Additional data needed for diagnosis in patients with an attack at onset
≥2	2	None
≥2	1 as well as clear-cut historical evidence of a previous attack involving a lesion in a distinct anatomic location	None
≥2	1	Dissemination in space demonstrated by an additional clinical attack implicating a different CNS site or by MRI
1	≥2	Dissemination in time demonstrated by an additional clinical attack or by MRI or demonstration of CSF-specific oligoclonal bands
1	1	Dissemination in space demonstrated by an additional clinical attack implicating a different CNS site or by MRI AND Dissemination in time demonstrated by an additional clinical attack or by MRI OR Demonstration of CSF-specific oligoclonal bands

Table 10.2 Primary progressive multiple sclerosis

2017 McDonald criteria for diagnosis of multiple sclerosis in patients with a disease course characterised by progression from onset (primary progressive multiple sclerosis)
Primary progressive multiple sclerosis can be diagnosed in patients with:
1 year of disability progression (retrospectively or prospectively determined) independent of clinical relapse
Plus two of the following criteria:
One or more T2-hyperintense lesions* * characteristic of multiple sclerosis in one or more of the following brain regions: periventricular, cortical or juxtacortical, or infratentorial
Unlike the 2010 McDonald criteria, no distinction between symptomatic and asymptomatic MRI lesions is required
Two or more T2-hyperintense lesions* * in the spinal cord
Presence of CSF-specific oligoclonal bands

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Chapter 11
Common Symptoms in the Neurology Clinic

The majority of patients referred to neurologists and a large proportion of patients seen by primary care providers complain of headaches, dizziness or vertigo, episodes of loss of consciousness, sleep disorders and other transient symptoms such as confusion, amnesia, weakness, blurred vision, numbness or tingling sensations and muscle cramps or pain in the extremities. Since most residency programs focus on in-patient experience, the graduating resident is often unprepared for the deluge of patients with such complaints. He or she must be able to sift through the history to extract the critical information and, most important, to ask the pertinent questions which elicit diagnostic information. Lurking within this patient load are undoubtedly a significant number with serious illnesses which must be detected and treated promptly. Many of these patients either do not have abnormal laboratory values that easily facilitate making a diagnosis or they provide misleading neuroimaging data that, if totally relied upon, result in misdiagnosis.

This chapter aims to provide an incentive to obtain a meticulous history which is the essential ingredient for making an accurate diagnosis. Additionally, there will be a focus on the interpretation of the patient's responses. Short discussions of pertinent neurophysiology and neuroanatomy will be included. The symptoms and disorders to be examined include headaches and facial pain, dizziness and vertigo, syncope and seizure, sleep disorders and other transient neurologic symptomatology.

Headache

Although tension-type headache (TTH) is the most common form of headache, the incidence is probably markedly lower in those people who seek medical attention. Certainly, in most neurology practices the majority of patients have other types of headache or facial pain, especially migraine. Passively obtaining a history without probing questions is usually inadequate. Here is a typical example.

J. N. Alpert, *The Neurologic Diagnosis*,
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Case 1 A 28-year-old woman requests an evaluation for recurrent "sinus headaches," pressure-like sensations in her forehead. They began about 6 months ago, occur two or three times per week and last several hours. She has occasional nasal drainage and "acetaminophen-sinus" relieves the pressure after 4 or 5 h. She specifically denies nausea, light and sound intolerance. When home she keeps busy around the house even when the headache is severe. She is worried about keeping her job since she loses 2–3 days per month due to these headaches.

Additional history is obtained.

Questions:

1. If you are home alone when you have a sinus headache what would you do? "I would get all of my housework done."
2. If you are home alone and all of your housework was already completed, what would you do? "My housework is never finished."
3. Let us assume the nearly impossible situation that your husband arranged for an excellent service to clean your house and then took your two children camping. What would you then prefer to do if you had a severe "sinus headache"? "I would take a nap."
4. Would you prefer the lights on or off? "Off." Would you listen to music? No, I prefer quiet.
5. Would you have a snack before your nap? "No, I'm usually queasy and have no appetite." (This patient uses the word "queasy" in place of nausea; nausea to her means vomiting).

Diagnosis: Migraine without aura (previous diagnosis – common migraine).

This patient has migraine without aura since she loses her appetite and prefers to lie down in a dark, quiet environment. Thus, the five key questions: Is there nausea, sensitivity to movement, light, sound, and smell? Nasal congestion is not unusual in migraine patients and response to "acetaminophen-sinus" is doubtful since she improves only after 4–5 h. The presence of severe intensity, a throbbing quality, and unilaterality are not required for the diagnosis of migraine. Headaches due to sinus diseases are relatively uncommon. Symptoms that support a diagnosis of a sinus headache include a profuse nasal discharge which is often purulent, severe congestion, fever, and altered sense of smell. Severe recurrent pain in maxillary or supraorbital locations unaccompanied by major nasal symptomatology is usually due to migraine.

Migraine Without Aura[1] (previous diagnosis – common migraine)
Diagnostic Criteria:

A. At least five attacks fulfilling criteria B-D.
B. Duration: 4–72 h (untreated or unsuccessfully treated).

[1] Adapted from International Headache Society. The International Classification of Headache Disorders (ICHD-3) [13].

C. The headache has at least two of the following four characteristics:

   1. Unilateral location.
   2. Pulsating quality.
   3. Moderate or severe pain intensity.
   4. Aggravation by or causing avoidance of routine physical activity.

D. During headache at least one of the following:

   1. Nausea and/or vomiting.
   2. Photophobia and/or phonophobia.

E. Not better accounted for by another ICHD-3 diagnosis.

Notes:

1. When sleep eliminates the headache the migraine duration is from the time of onset until the time of awakening.
2. In children and adolescents (less than 18 years of age) headaches are often bilateral, frontotemporal, facial and can be associated with cutaneous allodynia.
3. Migraine without aura is often related to menstruation.
4. Photophobia and phonophobia are direct complaints or inferred by the patient's behavior.
5. Pain is often evoked by a nonpainful stimulus such as touch (cutaneous allodynia).

Migraine With Aura[2] (previous diagnosis – classical migraine)
Diagnostic Criteria:

A. At least two attacks fulfilling criteria B and C.
B. One or more of the following fully-reversible aura symptoms:

   1. Visual.
   2. Sensory.
   3. Speech and/or language.
   4. Motor.
   5. Brainstem.
   6. Retinal.

C. At least two of the following four characteristics:

   1. At least one aura symptom spreads gradually over ≥5 min and/or two or more symptoms occur in succession.
   2. Each individual aura symptom lasts 5–60 min.
   3. At least one aura symptom is unilateral.
   4. The aura is accompanied or followed within 60 min by headache.

D. Not better accounted for by another ICHD-3 diagnosis, and transient ischemic attack has been excluded.

[2] Adapted from International Headache Society. The International Classification of Headache Disorders (ICHD-3) [13]. Cephalgia 2013;33:629–88

Notes:

1. When three symptoms occur during an aura the acceptable maximum duration is 3 × 60 min. Motor symptoms can last up to 72 h.
2. Visual symptoms comprise approximately 90% of the aura symptoms in patients who have migraine with aura. Typical symptoms are fortification figures (teichopsia) which are zig-zag lines similar to a medieval fort, begin near the fixation point, are typically bright, and spread to the right or left leaving an absolute or relative central scotoma. There is typically a scintillating edge on the lines.
3. Sensory. These are second in frequency to the visual aura and are manifested by migrating paresthesias which are typically unilateral, especially involving the face, tongue and arm.
4. Speech disorder. Aphasia which is considered unilateral and dysarthria which is nonlocalizing may occur.
5. Motor. When hemiparesis occurs it should be considered hemiplegic migraine.
6. The aura usually precedes but may overlap into the headache or occur during the headache.
7. Prodromes may last from 24 to 48 h during which there are variable symptoms which include inability to concentrate, fatigue, changes in mood and poor comprehension.
8. Before or with the aura rCBF (regional cerebral blood flow) is decreased in the cortex corresponding to the clinically affected area. The reduction in blood flow is a consequence of depression of brain electrical activity (cortical spreading depression (CSD) of Leão). The reduction in blood flow begins posteriorly and spreads anteriorly.
9. Rarely, mimics of the symptoms of aura are focal seizures with awareness (simple partial seizures), carotid dissection and arteriovenous malformations.

Typical Aura Without Headache[3]

Description:

Migraine with typical aura in which aura is neither accompanied nor followed by headache of any sort.

Diagnostic Criteria:

A. Attacks fulfilling migraine with typical aura including criterion B.
B. No headache accompanies or follows the aura within 60 min.

Comment: In some patients there may be an indistinct headache. This condition may mimic serious disease such as a transient ischemic attack. When aura occurs for the first time after age 40 and symptoms are exclusively negative (e.g. hemianopsia) and when the aura is prolonged or very short, other causes, particularly transient ischemic attack (TIA) should be excluded.

[3] Adapted from International Headache Society. The International Classification of Headache Disorders (ICHD-3) [13].

Migraine With Brainstem Aura* (previous diagnosis – basilar migraine)
Diagnostic Criteria:

A. At least two attacks fulfilling criteria B-D.
B. Aura consisting of visual, sensory and/or speech/language symptoms, each fully reversible, but no motor or retinal symptoms.
C. At least two of the following brainstem symptoms:

    1. Dysarthria.
    2. Vertigo.
    3. Tinnitus.
    4. Hypacusis.
    5. Diplopia.
    6. Ataxia.
    7. Decreased level of consciousness.
    8. No motor or retinal symptoms.

D. At least two of the following four characteristics:

    1. One aura symptom spreads gradually over ≥5 min and/or two or more symptoms occur in succession.
    2. Each aura symptom lasts 5–60 min.
    3. At least one aura symptom is unilateral.
    4. Aura is accompanied or followed within 60 min by headache.

E. Not better accounted for by another ICHD-3 diagnosis, and transient ischemic attacks have been excluded.

Notes:

1. Dysarthria must be distinguished from aphasia.
2. Vertigo does not embrace and should be distinguished from dizziness.
3. Diplopia does not embrace or exclude blurred vision.
4. Hypacusis is not fulfilled by ear fullness.

Hemiplegic Migraine*
Diagnostic Criteria:

A. Attacks fulfilling criteria for migraine with aura and criterion B below:
B. Aura consisting of both of the following:

    1. Fully reversible motor weakness.
    2. Fully reversible visual, sensory and/or speech/language symptoms.

C. At least two of the following four characteristics:

    1. At least one aura symptom spreads gradually over ≥5 min and/or two or more symptoms occur in succession.
    2. Each individual nonmotor aura motor symptom lasts 5–60 min, and motor symptoms last less than 72 h.
    3. One aura symptom is unilateral.
    4. The aura is accompanied or followed within 60 min by headache.

D. Not better accounted for by another ICHD-3 diagnosis and transient ischemic attack or stroke have been excluded.

Notes:

1. Plegic usually means paralysis, but most attacks are characterized by motor weakness.
2. Motor symptoms usually last for less than 72 h but may persist for weeks.

Familial Hemiplegic Migraine[4]

Diagnostic Criteria:

At least one first or second degree relative has had attacks fulfilling criteria for hemiplegic migraine.

Notes:

1. Familial hemiplegic migraine (FHM) often presents with brainstem symptoms.
2. FHM can be mistaken for epilepsy.
3. There are rare instances of loss of consciousness, confusion, fever and CSF pleocytosis.
4. FHM can be triggered by mild head trauma.

Retinal Migraine[5]

Diagnostic Criteria:

A. At least two attacks fulfilling criteria B and C.
B. Aura consisting of fully reversible monocular positive and/or negative visual phenomena (e.g. scintillations, scotomata or blindness) confirmed during an attack by either or both of the following:
    1. Clinical visual field examination.
    2. The patient's drawing (after clear instructions) of a monocular field defect.
C. At least two of the following three characteristics:
    1. The aura spreads gradually over ≥5 min.
    2. The aura symptom lasts 5–60 min.
    3. The aura is accompanied or followed within 60 min by headache.
D. Not better accounted for by another ICHD-3 diagnosis and other causes of amaurosis fugax have been excluded.

Notes: Many patients who complain of monocular visual disturbances actually have unrecognized hemianopsias so that true retinal migraine is extremely rare. Scintillating scotomata, for instance, are usually bilateral and are associated with an occipital lobe origin. Amaurosis fugax, a positive monocular event often described

[4] Adapted from International Headache Society. The International Classification of Headache Disorders (ICHD-3) [13].

[5] Adapted from International Headache Society. The International Classification of Headache Disorders (ICHD-3) [13].

as a descending black curtain, is a very rare migrainous phenomenon and requires documentation of the absence of vascular disease or cardioembolic event.

Chronic Migraine*
Diagnostic Criteria:

A. Headache (tension type-like and/or migraine-like) on ≥15 days per month for more than 3 months and fulfilling criteria B and C.
B. Occurring in a patient who has had at least five attacks fulfilling criteria B-D for Migraine Without Aura and/or criteria B and C for migraine with aura.
C. On ≥8 days per month for greater than 3 months, fulfilling any of the following:
    1. Criteria C and D for migraine without aura.
    2. Criteria B and C for migraine with aura.
    3. Believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative.
D. Not better accounted for by another ICHD-3 diagnosis.

Notes:

1. Chronic migraine is differentiated from episodic migraine because it is impossible to distinguish individual episodes in patients with frequent or continuous headaches.
2. New daily persistent headache may have features of chronic migraine but the time of onset is distinctly remembered.
3. Medication overuse headache may be diagnosed as chronic migraine. Around 50% of patients who are diagnosed with chronic migraine revert to episodic migraine after drug withdrawal.

Complications of Migraine[6]

Status Migrainosus*

Diagnostic Criteria:

A. Headache attack fulfilling criteria B and C.
B. Occurs in patient with either migraine with or without aura.
C. Both of the following characteristics:
    1. Unremitting for greater than 72 h.
    2. Pain and/or other symptoms are debilitating.
D. Not better accounted for by another ICHD-3 diagnosis.

[6]Adapted from International Headache Society. The International Classification of Headache Disorders (ICHD-3) [13].

Persistent Aura Without Infarction*
Description: Aura symptoms persisting for 1 week or more without evidence of infarction on neuroimaging.

Notes: There are instances when the aura lasts for months and even years.

Migrainous Infarction*
Diagnostic Criteria:

A. Migraine attack fulfilling criteria B and C.
B. Occurring in a patient who has migraine with aura and typical of previous attacks except that one or more aura symptoms persist for greater than 60 min.
C. Neuroimaging demonstrates ischemic infarction in a relevant area.
D. Not better accounted for by another ICHD-3 diagnosis.

Notes: Migrainous infarction usually occurs in the posterior circulation in young women.

Migraine Aura-Triggered Seizure*

Description: This is a seizure triggered by an attack of migraine with aura. It occurs during or within 1 h after the headache. This has been referred to as migralepsy. It has not been documented to occur in patients who have migraine without aura.

Episodic Syndromes Associated with Migraine*
1. **Recurrent Gastrointestinal Disturbance* (functional abdominal pain)**

Description: These are recurrent episodic attacks of abdominal pain, nausea and vomiting that may be associated with migraine.

2. **Cyclic Vomiting**[7]

Description: These are recurrent episodic attacks of intense nausea, vomiting and with predictable timing associated with pallor, lethargy and complete resolution between the attacks. They are self-limited and occur primarily in childhood.

3. **Abdominal Migraine***

Description: This occurs especially in children and is manifested by recurrent attacks of moderate-to-severe midline abdominal pain with vasomotor symptoms, nausea and vomiting lasting 2–72 h. There is no associated headache.

[7] Adapted from International Headache Society. The International Classification of Headache Disorders (ICHD-3) [13].

4. **Benign Paroxysmal Vertigo***

Description: These are brief attacks of vertigo resolving over minutes associated with usually at least one of the following, nystagmus, ataxia, vomiting, pallor and fear. The patient is normal between attacks.

5. **Benign Paroxysmal Torticollis***

Description: This occurs in infants and small children and is manifested by a head tilt with one of the following signs, pallor, irritability, malaise, vomiting and ataxia.

Tension-Type Headache* (previous diagnosis – muscle contraction headache, stress headache)

Description: Tension-type headache is bilateral, dull, tight, pressure-like or squeezing. The location is usually on the forehead, occipital or posterior cervical regions. The pain is mild to moderate, typically lasting 4–6 h but ranges from one-half hour to several days. Pericranial tenderness is the most significant abnormal finding on the examination.

There are episodic and chronic forms. There is no nausea in the episodic form but there may be either photophobia or phonophobia. In the chronic form these headaches occur at least 15 days per month for greater than 3 months. Neither the episodic nor the chronic form are aggravated by physical activity. In the chronic form there is no more than one of photophobia, phonophobia or mild nausea. Triggers include alcohol, anxiety, dehydration, depression, eye strain, fatigue, hunger, low iron levels, sleep deprivation and stress.

The suspected basis for pain is hyperexcitability of nociceptive neurons located in the trigeminal nucleus caudalis, thalamus and cerebral cortex. Generation of pain by activation of nitric oxide synthase may be the etiology.

Medication Overuse Headache[8]

Diagnostic Criteria:

A. Headache occurring on 15 or more days per month in a patient with a preexisting headache disorder.
B. Regular overuse for more than 3 months of one or more drugs that can be taken for acute and/or symptomatic treatment of headache:
   - Regular intake for ≥10 days per month for >3 months of ergotamines, triptans, opioids, or combination analgesics, or any combination of ergotamines, triptans or simple analgesics, or NSAIDS and/or opioids without overuse of any single drug or drug class alone or when the pattern of overuse cannot be reliably established.
   - Regular intake for ≥15 days per month for >3 months of simple analgesics (i.e., acetaminophen, aspirin, or NSAIDS).
C. Not better accounted for by another ICHD-3 diagnosis.

[8] Adapted from International Headache Society. The International Classification of Headache Disorders (ICHD-3) [13]. Cephalgia 2013;33:629–88

Case 2 A 48-year-old man complains of seeing multicolored zigzag lines in his left visual field. These gradually enlarge and encompass most of the left visual field. He then notes numbness and tingling of the left hand which gradually ascends up to the face (march of paresthesias) over 5 min. The total duration of symptoms is 30 min. He has had two similar attacks over the past year. The patient denies headache.

Diagnosis: Typical migrainous aura without headache.

Comment: Other visual phenomena described in this disorder include light flashes (phosphenes), an arc of lights typically in a C pattern, geometric designs and teichopsia. Teichopsia is a jagged shimmering visual image resembling fortifications of a walled medieval town. Visual illusions are much less frequent but most important to be cognizant of since they can also be manifestations of epileptiform events. Migraineurs may experience, for example, metamorphopsia, micropsia, macropsia, déjà vu, and jamais vu symptomatology. See Chap. 13 for definitions of these illusions.

A brief review of migraine physiology is now appropriate [2]. Positron emission tomography (PET) scans have repeatedly demonstrated increased activity in the brainstem at the onset of migraine [1]. (Fig. 11.1). Additionally, the premonitory phase has been examined by PET scans which expose simultaneous activation in the hypothalamus and thus conceivably explaining the mood changes, polyuria, and appetite alterations. Increased activity in the occipital lobe correlates with light sensitivity. Subsequent brainstem activation likely generates nausea. Additional findings are changes in thalamo-cortical circuits which are probably responsible for cutaneous hypersensitivity (allodynia). Associated cognitive dysfunction relate to changes in brain connectivity.

Approximately 30% of patients with migraine have an aura. It is associated with cortical spreading depression (CSD) of electrical activity. This activity begins in the occipital lobe and migrates anteriorly at about 2–3 mm/min., about the same velocity as the aura of fortification figures. Coincident with CSD is a reduction in

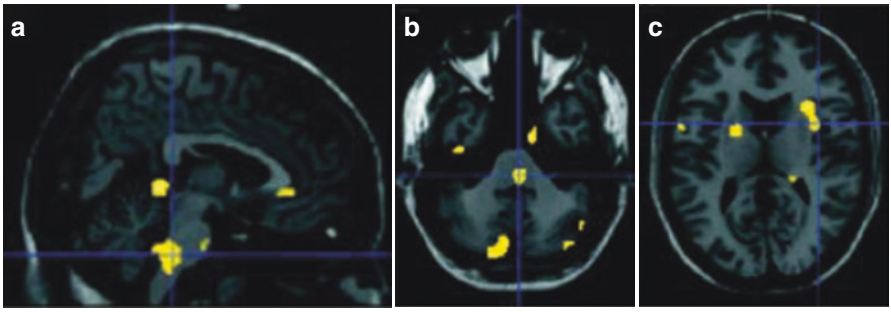

Fig. 11.1 PET (positron emission tomography) scan of migraine demonstrating brainstem activation by glyceryl trinitrate during migraine. Unilateral ipsilateral activation is identified primarily in the dorsolateral pons in this patient with migraine. A and B show activation in the dorsolateral pons with anterior cingulate activation present in A and insula activation in C. (Brain 2005, through the courtesy of Oxford University Press) [1]

blood flow which has been termed spreading oligemia. The oligemia, however, does not follow vascular territories but rather the pathway of decreasing electrical activity. Consequently, the primary underlying basis for migraine is neuronal, not vascular. CSD may play a role in central pain modulation by activating trigeminal axons and central projections in the trigeminal nucleus caudalis. Since CSD occurs without headache its role in pain generation remains moot.

A compilation of recent experimental data has added further understanding of the complex interplay of numerous factors in the generation of migraine. Perhaps the wide variability in manifestations reflect the origin of polygenetic loci (at least 38) in migraine patients. These same loci are also expressed in vascular and gastrointestinal tissue. Thus there is some basis for the initial theory of migraine as primarily a vascular disorder. Undoubtedly, this is an associated factor but not a primary initiator. Neurogenic inflammation [14] is the terminal element of the migraine diathesis. It is mediated by vasoactive polypeptides, primarily calcitonin gene related peptide (CGRP), which are stored within axons projecting from the trigeminal ganglia. CGRP is predominant and is elevated in external jugular vein blood during both migraine and cluster headache. Infusion of CGRP induces migraine in a susceptible individual. CGRP levels return to normal after treatment with a triptan. A confounding fact is the lack of proof for a significant amount of CGRP passing the blood-brain barrier. Nevertheless, suspected remaining targets outside the blood-brain barrier include the trigeminal ganglia, area postrema, pineal gland and median eminence in the floor of the 4th ventricle. Another neuropeptide has emerged from recent studies, pituitary adenylate cyclase-activating polypeptide (PACAP). Its intravenous infusion induces migraine in a susceptible person. Blood levels also increase in the headache phase of migraine.

Inflammation of the meninges probably results from CGRP release and afferent pathways for pain pass from the meninges through the trigeminal ganglia, synapse in second order neurons in the trigeminocervical complex. This complex extends from the trigeminal nucleus caudalis to the dorsal horn in the upper cervical cord. The C1 root, specifically, is a potential modulator of migraine pain. The associated neurons in these structures have axons which cross the midline and ascend to synapse with thalamic neurons. Additionally, there are neural connections with the superior salivatory nucleus which results in parasympathetic outflow and vasodilation.

Although there are numerous inputs, genetic, environmental, stress, diet, neuroendocrine function, hormones and drugs, impinging on the brain, the brainstem is the ultimate generator. This has been established by PET scans which measure regional blood flow [1]. (Fig. 11.1). This study used a glyceryl trinitrate model, an established, reliable method of migraine induction, to allow for a thorough evaluation of migraine from its earliest symptom to its resolution after therapeutic intervention. The primary activated region was the dorsolateral pons and the unilateral headaches disclosed ipsilateral activation in this region. Despite resolution of the headache this region remained active. Other secondary activated sites include prefrontal cortex, anterior cingulate, insula, cerebellum and putamen.

Serotonin (5-hydroxytryptamine) is intimately associated with migraine generation. The median raphe nuclei in the rostral pons and midbrain contain serotonin and

a much fewer number in the lateral reticular formation. This area is adjacent to, and may be partially incorporated by, the primary activated region during migraine in the dorsolateral pons. The main metabolite, 5-hydroxyindoleacetic acid, is increased in the urine in migraine patients. Platelet serotonin decreases at onset of migraine and intravenous serotonin aborts migraine. Therefore, serotonin agonists, dihydroergotamine (DHE) and sumatriptan, treat migraine whereas reserpine, a 5-HT depleter, provokes it. There are several 5-HT receptors and one of them, 5-HT1B/1D, is the major site of action of DHE and triptan medications.

Additional recent findings of clinical interest include the effect of triptans on the basilar artery, just an insignificant 2% constriction effect. Hence, there is no experimental support for the avoidance of triptans when treating migraine patients who have brainstem aura (usually vestibular migraine). Use of occipital muscle steroid and/or analgesic injections have long been proposed as a temporary amelioration of migraine pain but there are conflicting reports of its benefit. The C2-C3 roots supply the occipital nerves but only C1 is believed to be a potential modulator of migraine pain.

Case 3 A 42-year-old woman requests an evaluation because of severe headaches and a mood disorder. The headaches are unilateral, pulsating and associated with nausea, photophobia, phonophobia and last 12–24 h. Although she has just one or two headaches a month, the prodromal phase manifested by depression and irritability and residual symptoms in the postdrome of fatigue and stiff neck last 1–1/2 days and 1 day, respectively. One of the headaches invariably occurs the day before her menses. After the headache has subsided her scalp is extremely sensitive and it is too painful to comb her hair. This is known as cutaneous allodynia.

Diagnosis: Migraine without aura.

Comment: There are four phases of migraine, prodrome, aura, headache and postdrome. (Fig. 11.2) This patient exhibits a typical prodrome syndrome of migraine which can last 1–2 days. Some common symptoms are lassitude, hunger, depression, thirst, and irritability. Headache associated with menses most often occurs as the estrogen level falls. There is no proven association of migraine with ovulation, however, despite the falling estrogen levels at that time. Cutaneous allodynia manifested by this patient's extreme scalp sensitivity is quite common after migraine as well as either recurrence or persistence of the prodrome symptoms. Cutaneous allodynia is due to sensitization of nociceptive neurons in the trigeminal nucleus caudalis. Other symptoms of the migraine postdrome include fatigue, poor concentration and stiff neck.

Case 4 A 14-year-old girl complains of periodic pain in the left eye over the previous 4 months. The pain varies from sharp to throbbing and is usually associated with light sensitivity. It has been occurring a few times per week, each time persisting for 4–6 h. The pain is perceived as within the eye or just behind it. An ophthalmologist found no ocular pathology.

Examination discloses normal fundi, visual fields and visual acuities of 20/60 O.D. and 20/50 O.S. Acuity is normal with pinhole. There is no pain with eye move-

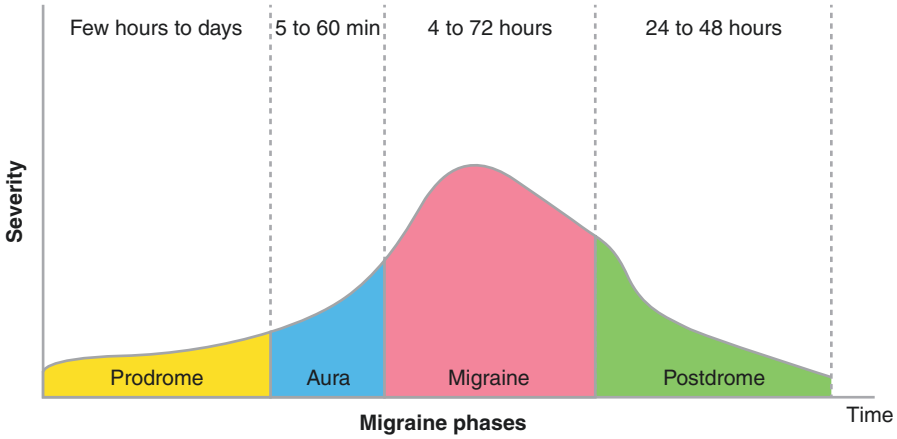

Fig. 11.2 Development and resolution of migraine

ment. Perception of light and color are normal. There is no scleral injection. The pupils are normal.

Questions:

1. Can this young girl's headache be due to impaired visual acuity associated with nearsightedness?
2. Is there any eye disease that might cause this patient's headache?

Answers:

1. No. Eye strain does not cause this type of headache. This patient has migraine because of the unilateral, throbbing and sharp eye pain associated with photophobia lasting over 4 h.
2. A generally accepted principle is that a "white" eye is not the source of headache. Conjunctival injection which occurs with iritis or conjunctivitis and a cloudy cornea associated with acute angle closure glaucoma are the visible signs of ocular diseases which may cause headache. The one possible exception is the intermittent headache of subacute angle closure glaucoma, a rare disorder. These headaches usually last less than 1 h, however.

Diagnosis: Migraine without aura.

Case 5 A 56-year-old woman complains of severe headaches subsequent to a motor-vehicle accident which occurred 10 months ago. Her car was struck on the passenger side as she was driving through an intersection and she bumped her head on the car window. She did not lose consciousness or suffer a visible injury. Two days afterwards she had the first of numerous headaches occurring without warning. They are bilateral, frontal, pulsating, last 6–7 h, and occur about three times per week. Associated symptoms are mild nausea, phonophobia, and aggravation with quick head movement. After the headache she feels dizzy, fatigued, and cannot concentrate. Because litigation

was initially involved, she was diagnosed as having headaches on a psychogenic basis, a compensation neurosis. The case was settled after 4 months but the headaches increased in intensity afterwards. Her neurologic examination is normal.

Diagnosis: Post-traumatic migraine [15].

Comment: This patient was initially diagnosed as having a compensation neurosis but the characteristics of her headaches are quite compatible with migraine. There is a pulsating quality with nausea and photophobia. The subsequent inability to concentrate associated with fatigue is called a migraine postdrome.

This is a remarkably underdiagnosed and treatable disorder. This patient needs both prophylactic treatment, since there is more than one headache per week, and abortive therapy. The physiologic basis for posttraumatic migraine is unknown. Possible contributing factors include genetic predisposition, stress, or even the minor rotational forces from the injury. Of practical importance is its recognition and application of treatment as with anyone who has migraine.

Case 6 A 58-year-old woman complains of an unrelenting, bilateral, occipital headache for 5 weeks. The headache has a boring-to-piercing quality, stronger on the left side. Two weeks ago she had a brief loss of vision O.S. lasting just 1 min. She describes it as blackening of vision crossing her visual field from left to right. Carotid angiography was promptly performed and was normal. A cardiology consultant found no cardiac source for embolism. The evaluation included a transesophageal echocardiogram.

Subsequent to this evaluation the patient had at least four more episodes of visual loss O.S. lasting from 30 s to 2 min. Neurologic examinations were normal.

What other questions might add diagnostic information? The patient was asked the following questions:

1. Have you had fever, joint or muscle pain?
2. Have you any pain on chewing? Response: The patient reports repeated episodes of low-grade fever without explanation in the past year. She has mild, migrating muscle pain involving all extremities and aching in her jaws when chewing.

Diagnosis: Temporal arteritis associated with amaurosis fugax, jaw claudication, and polymyalgia rheumatica.

Comment: Any patient over age 50 who has new onset headaches must be evaluated for temporal arteritis with a sedimentation rate and a C-reactive protein. The headache of temporal arteritis can be anywhere on the head, unilateral or bilateral. There is a predilection for involvement of arteries in the external carotid artery system. When the internal maxillary artery is involved, jaw claudication occurs. Most often the superficial temporal artery is affected causing the typical temporal pain with associated soreness. Involvement of the internal occipital artery may result in occipital pain and soreness.

The feared complication of temporal arteritis is loss of vision which is nearly always due to vasculitic involvement of the posterior ciliary arteries causing an anterior ischemic optic neuropathy. In this patient's case the central retinal artery is involved in view of amaurosis fugax, transient loss of vision in one eye. As this his-

tory demonstrates, the curtain-like effect is not the exclusive manifestation of amaurosis fugax and should not be relied upon for a diagnosis. Temporal arteritis is a rare etiology of amaurosis fugax but it must always be suspected especially in the absence of either ipsilateral internal carotid artery disease or a cardiac source of embolism. Polymyalgia rheumatica frequently precedes or follows temporal arteritis. Fever of unknown origin may also be the initial presentation of temporal arteritis.

Case 7 A 40-year-old man arrives in the Emergency Room because of the abrupt onset of a severe, throbbing, occipital headache occurring during orgasm. It is now 3 h since the onset of headache and it is beginning to subside. He complains of nausea and photophobia. The neurologic examination is normal and this includes the absence of nuchal rigidity although head movement increases the pain.

Diagnosis: Primary headache associated with sexual activity [5].

Comment: Headache with sexual activity can begin prior to or during orgasm [5]. A rare third type is postural, occurs after intercourse and resembles a post-lumbar puncture headache. The preorgasmic form is commonly milder, builds up in intensity gradually and has features of a TTH. It is often aborted by ceasing sexual activity. The more alarming throbbing, explosive orgasmic headache often prompts a search for immediate medical care. It is estimated that in 4–11% of all patients with subarachnoid hemorrhage the provoking factor is sexual activity. Thus, a thorough workup is necessary.

This patient had a CT scan followed by a lumbar puncture both of which were normal. The lumbar puncture was performed because CT scans diagnose just 90–95% of patients with subarachnoid hemorrhage.

Primary Headache Associated With Sexual Activity[9]

Description: Headache precipitated by sexual activity, usually starting as a dull bilateral ache as sexual excitement increases and suddenly becoming intense at orgasm in the absence of any intracranial disorder.

A. At least two episodes in head and/or neck fulfilling criteria B and C.
B. Brought on by and occurring only during sexual activity.
C. Either or both of the following:
    1. Increasing in intensity with increasing sexual excitement.
    2. Abrupt explosive intensity just before or with orgasm.
D. Lasting 1 min to 24 h with severe intensity or up to 72 h with mild intensity.
E. Not better accounted for by another ICHD-3 diagnosis.

Case 8 A 56-year-old woman complains of severe, frequent, left-sided headaches beginning 2 years ago. The average frequency is two per week and they occur without an aura but during the first hour of the headache she feels unsteady, has tinnitus and periodic episodes of incapacitating vertigo. Nausea and vomiting can be severe.

[9] Adapted from International Headache Society. The International Classification of Headache Disorders (ICHD-3) [13].

Occasionally, she notes numbness and tingling around the mouth. The headache itself lasts from 6 to 8 h.

Her neurologic examination is normal. MRI and MRA studies are normal.

Diagnosis: Migraine with brainstem aura (previous diagnosis –basilar migraine) [11].

Comment: Ordinarily, patients with this disorder have brainstem symptomatology such as dysarthria, vertigo, tinnitus, hypacusia (impaired hearing), diplopia, visual symptoms affecting both temporal and/or nasal fields of both eyes, ataxia, or decreased level of consciousness. Bilateral paresthesias, numbness, stinging or burning sensations typically involve face and hands (the cheiro-oral syndrome). Occasionally, auras occur during the headache.

For diagnostic criteria see full description in the preceding text.

Case 9 A 28-year-old man requests an evaluation for severe headaches provoked by playing tennis in the summer. They usually occur after playing for more than 1 h. They are bilateral, pounding, associated with nausea and photophobia, and last 1–2 h. This information prompts additional inquiries from the examining physician.

Questions:

1. Do you have headaches on other occasions? "Yes, rarely I have similar headaches preceded by seeing bright lights directly in front of me which persist for 15 min." The duration of the headaches is several hours.
2. Do you play indoors or outdoors? "Outdoors."

Diagnoses:

1. Primary exercise headache.
2. Migraine with aura.

Comment: This patient has migraine with aura predisposing him to primary exercise headache. Heat and high altitude are provoking factors.

Primary Exercise Headache[10]
Description:

A. This headache is precipitated by any form of exercise in the absence of any intracranial disorder. Two headache episodes fulfilling criteria B and C.
B. Brought on by and occurring only during or after strenuous physical exercise.
C. Lasting less than 48 h.
D. Not better accounted for by another ICHD-3 diagnosis.

[10] Adapted from International Headache Society. The International Classification of Headache Disorders (ICHD-3) [13].

Case 10 A 63-year-old woman is admitted to the hospital with a 2-day history of a severe, left frontal headache and horizontal double vision. The double vision is evident mainly at distance and looking to the left. She had a similar episode 8 years ago and does not recall the details but medical treatment cured her in 2–3 weeks.

Neurologic Examination: There is subjective impairment of color and light perception O.S. but visual acuity is 20/20 O.U., visual fields are normal and there is no central scotoma. Pupils are 4 mm and reactions to direct light stimulation are 4+/4 O.D. and 2+/4 O.S.; consensual reactions are 3+/4 O.D. and 2+/4 O.S. The left corneal response is sluggish and the right is normal. Corneal stimulation on the right elicits a strong blink on the left. On red glass testing the left lateral rectus muscle is weak. The red glass covers the right eye and the distal image on left lateral gaze is white.

Reminder: When double vision is present on looking left the image farthest to the left comes from the weak muscle, when looking right the image farthest to the right comes from the weak muscle, etc.

Questions:

1. What cranial nerves are involved?
2. Where is the lesion?
3. What does the MRI show?
4. What is the etiology?

Answers:

1. The left optic nerve is involved because of subjective impairment of color and light perception. The pupillary response to direct light O.D. is better than consensual response O.D.; thus afferent input O.S. is decreased indicating a left optic nerve lesion. A normal visual acuity is often present with optic nerve lesions. Never depend on it to make a diagnosis of an optic neuropathy.

   The left 3rd nerve is affected since even the consensual pupillary response O.S. remains decreased at 2+/4.

   The left ophthalmic division of the trigeminal nerve is involved because of the sluggish corneal response. The strong left eyelid blink with right corneal stimulation excludes left orbicularis oculi or 7th nerve pathology.

   The left 6th nerve is damaged as attested by left lateral rectus weakness. Diplopia due to 6th nerve palsies is most prominent at distance when the eyes have to diverge.

2. The lesion is primarily in the cavernous sinus since the left 3rd, 5th, and 6th nerves are affected.
3. The MRI shows an enlarged left cavernous sinus due to abnormal tissue which enhances with contrast and extends into the orbital apex also affecting the left optic nerve.
4. *Diagnosis*: Tolosa–Hunt syndrome.

Comment: This disorder is manifested by intense, unilateral orbital or periorbital pain associated with ocular pareses of one or more of the 3rd, 4th and 6th cranial nerves. The ocular paresis may coincide with the pain and, if so, would distinguish it from recurrent painful ophthalmoplegic neuropathy. MRI scans reveal abnormalities in the cavernous sinus with occasional extension into the superior orbital fissure and involvement of the optic nerve. The 6th nerve is most commonly affected. The ophthalmic division of the trigeminal nerve is frequently affected. The pathologic basis is an idiopathic granulomatous inflammatory disease which is visible about 50% of the time by MRI imaging. Patients respond promptly to corticosteroid treatment.

A disorder which often has strong similarities to Tolosa-Hunt syndrome is recurrent painful ophthalmoplegic neuropathy. The ICHD-3 classifications of both are outlined below in order to assist in differentiating them.

Tolosa-Hunt Syndrome[11]
Criteria:

A. Unilateral orbital or periorbital headache fulfilling criterion C.
B. Both of the following:
    1. Granulomatous inflammation of cavernous sinus, superior orbital fissure or orbit demonstrated by MRI or biopsy.
    2. Paresis of one or more ipsilateral 3rd, 4th or 6th cranial nerves.
C. Evidence of causation demonstrated by both of the following:
    1. Headache ipsilateral to the granulomatous inflammation.
    2. Headache has preceded ocular paresis by ≤2 weeks or developed with it.
D. Not better accounted for by another ICHD-3 diagnosis.

Notes:

1. Additional nerves that may be involved include the optic nerve, ophthalmic division of the trigeminal nerve, 7th and 8th cranial nerves.
2. Sympathetic system involvement is occasionally evident as manifested by the presence of a Horner's syndrome.

Recurrent Painful Ophthalmoplegic Neuropathy[12] **(previous diagnosis – ophthalmoplegic migraine)**

Description: Repeated attacks of paresis of one or more ocular cranial nerves, especially the 3rd nerve, with an ipsilateral headache.

Criteria:

A. Two attacks fulfilling criterion B.
B. Both of the following:

[11] Adapted from International Headache Society. The International Classification of Headache Disorders (ICHD-3) [13].

[12] Adapted from International Headache Society. The International Classification of Headache Disorders (ICHD-3) [13].

1. Unilateral headache.
2. Ipsilateral paresis of one, two or three ocular motor nerves.

C. No evidence of ocular, parasellar, or posterior fossa lesion by appropriate investigation.
D. Not accounted for by another ICHD-3 diagnosis.

Notes:

1. Headache can develop up to 14 days prior to an ocular paresis.
2. MRI scan may show nerve thickening.

Case 11 A 45-year-old man requests an evaluation for a severe, pounding, occipital headache lasting just 3 min. This has been occurring over the last 5 years typically while weightlifting. He works out on a regular basis and the headache is often provoked when he uses heavy weights. One month ago, during an upper respiratory infection, a cough would invariably produce an even more severe occipital headache.

Questions:

1. What other history should be obtained?
2. What part of the examination requires special attention?

Answers:

1. Occipital headaches provoked by coughing suggest pathology at the foramen magnum. Pertinent questions, therefore, include whether similar headaches occur with any other activity. Does he note any difficulty walking or change in leg strength and balance? Does he have dizziness or blurred vision? The patient reports that he has had mild headaches when laughing or straining to move his bowels for many years. Additionally, he finds that his legs feel tight when running.
2. Examination of eye movements and a search for signs of cerebellar system or corticospinal tract dysfunction.

Neurologic examination reveals downbeat nystagmus with oblique component to the left on left lateral gaze and to the right on right lateral gaze. He has mild spasticity in both legs, bilateral sustained ankle clonus, a left Babinski sign, and mild bilateral heel-to-shin ataxia. His gait has spastic features because of circumduction and stiffness.

With chronic symptoms, such as this patient reports, Chiari 1 malformation must be suspected. Presenting manifestations often occur in adolescence and less frequently in adults. Compression of structures in the vicinity of the foramen magnum include the cerebellar flocculus and nodulus which cause the downbeat nystagmus. Spinal cord compression produces the spasticity, spastic gait, ankle clonus and Babinski sign. Mass lesions or bony abnormalities such as atlantoaxial dislocation may cause some of these signs and are considerations in the differential diagnosis. Much more common in patients with headaches only with coughing and who have normal neurologic examinations and neuroimaging is primary cough headache. This is a diagnosis of exclusion, however.

Diagnosis: Chiari 1 malformation.

Comment: Chiari 1 malformation is manifested by herniation of the cerebellar tonsils below the foramen magnum. Abnormal descent is usually considered ≥5 mm and an associated syrinx is not unusual. The presumed headache mechanism is increased intrathoracic pressure from coughing or straining which causes impaired venous return increasing cerebral blood volume thus resulting in a transient increase in intracranial pressure. This is transmitted through a pressure wave displacing the cerebellar tonsils further into the foramen magnum. Complications include hydrocephalus, increased intracranial pressure, syringomyelia and disorders of the lower cranial nerves. Hydrocephalus with increased intracranial pressure may be due to obstruction of the foramina of Luschka and Magendie. The Chiari type 2 malformation is associated with a meningomyelocele and is usually symptomatic at birth with severe involvement of the lower cranial nerves.

Case 12 A 54-year-old woman complains of daily headaches for 2 years. They last 8–10 h. She describes them as a constricting band around the head sometimes associated with tightness in the lower occipital or upper cervical region. About twice per week she has a severe, throbbing, bi-occipital headache accompanied by nausea, photophobia, osmophobia, and it is aggravated by movement. Neurologic examination is normal.

Diagnosis: Chronic migraine [3, 4].

Comment: Chronic migraine can be diagnosed when the patient has headache on 15 or more days per month for more than 3 months and, on at least 8 days per month, has migraine features. For details of diagnostic criteria see the preceding text.

Cases 13A–13F

A. A 55-year-old man complains of a 3-year history of severe right-sided eye and facial pain. The pain is described as stabbing, mainly behind the eye and excruciating as it reaches an intensity of 9–10/10. This prompts an occasional Emergency Room visit. Infrequently, it extends down to the upper jaw and teeth. He has had tearing, nasal congestion and lid droop on a few occasions. The pain lasts 45–60 min and forces him to pace the room. The frequency is two to three times per day throughout the year. The patient smoked two packs of cigarettes per day until 4 years ago when he permanently ceased smoking. His neurologic examination reveals ptosis and miosis, O.D.
B. A 45-year-old woman complains of 20–30 headaches daily for 12 years. They are unilateral, left-sided, periorbital and temporal, with a stabbing character and lasting 5–20 min. She notes a red eye, nasal congestion, and tearing. Rarely, there is a lid droop. Her neurologic examination is normal.
C. A 48-year-old man complains of excruciating orbital and temporal, right-sided, paroxysmal headaches for 2 years. They last from 10 s to 2 min, occur about 20 times per day and are associated with tearing, a swollen eyelid, and reddening of

the eye. His forehead on the right side becomes moist. His heart rate declines from 60 to 42 beats per minute. There are no trigger points on examination.

D. A 72-year-old man complains of frequent nocturnal headaches invariably awakening him at 2:00 a.m. for the last 5 years. He describes the pain as generalized, dull, with an intensity of 5–6/10, lasting 45 min and occurring about 15 times per month. There are no associated migrainous or autonomic features. After sitting up and having a cup of coffee he obtains modest relief in about 20 min.
E. An 80-year-old woman complains of a 3-week history of severe, sharp, stabbing pains in her left cheek and forehead. They last for 30 s to 2 min, occur numerous times per day and are provoked by chewing, less often brushing her teeth. In between the paroxysms of pain there is a constant dull ache.
F. A 28-year-old woman arrives in the Emergency Room because of "throat spasms" and left ear pain of 12 days duration. The pain is excruciating and most frequent during meals preventing her from eating more than a few bites. The ear pain has been particularly acute. These symptoms have resulted in a weight loss of 5 lb. over 1 week. During meals she feels faint, turns pale, and becomes diaphoretic.

What are the diagnoses?

A. Cluster headache, chronic.
B. Paroxysmal hemicrania, chronic.
C. Short-lasting, unilateral neuralgiform headaches with conjunctival injection and tearing (SUNCT).
D. Hypnic headache.
E. Trigeminal neuralgia.
F. Glossopharyngeal neuralgia.

A. *Cluster headache.*

Four characteristics of cluster headache include unilateral, mainly periorbital-temporal pain rarely switching sides. Less often the pain manifests in other locations such as upper or lower teeth, jaw, cheek, nose, ear, and occipital area. The frequency is commonly two to six times per day. There are often autonomic features such as lacrimation, nasal congestion, conjunctival injection, eyelid swelling, ptosis, and Horner's syndrome. The etiology of the Horner's syndrome may be edema of the intracranial internal carotid artery wall with compression of sympathetic nerve fibers which travel within the carotid sheath. This mechanism is supported by the absence of anhidrosis in these patients (sudomotor fibers travel to the face with the external carotid artery). The headaches may be episodic, seasonal or chronic.

The most useful diagnostic features are the duration, 15 min to 2 h, and the patient's behavior of restlessness and pacing the room. Conversely, the migraine patient prefers to lie down quietly since movement aggravates pain. A smoking history is extremely common. These headaches have recently been provoked by IV CGRP [16].

B. *Paroxysmal hemicranias.*

These unilateral headaches have a strong similarity if not nearly identical to cluster headache. The pain is usually fronto-temporal, excruciating, lasts just 2–45 min and occurs 20–40 times per day. Ordinarily, they are associated with autonomic symptoms of conjunctival injection, rhinorrhea, lacrimation, ptosis, and eyelid edema. Attacks may be provoked by head movement. They may also be episodic or chronic but the episodic form can be diagnosed only when there are remissions of at least 1 month. Genetic factors are important.

C. *SUNCT.*

These are severe, unilateral, orbital-temporal, stabbing headaches, or "pains" as many patients describe them. They last 1–300 s with a frequency of 3–200 per day. At least one of the following autonomic symptoms always occurs: nasal congestion, rhinorrhea, eyelid edema, facial sweating and flushing, fullness in the ear, miosis and/or ptosis. Bradycardia is sometimes present due to activation of the parasympathetic system. SUNA (short-lasting, unilateral neuralgiform headache with cranial autonomic symptoms) is nearly identical. However, it may include only one or neither of conjunctival injection and lacrimation.

D. *Hypnic headache.*

Hypnic headaches usually occur in the older population, nearly always over age 50 years. They erupt during nocturnal sleep and rarely during daytime naps. They tend to strike at the same time at night, last 15 min to 3 h, are of moderate-to-severe intensity, and are generally described as throbbing or dull, bilateral, diffuse, or fronto-temporal. The majority of recorded cases have occurred during REM sleep. Because of the unexpected prevalence in the older individual who may not have a history of headaches, structural pathology must be excluded before the diagnosis is established.

E. *Trigeminal neuralgia.*

Trigeminal neuralgia is manifested by brief paroxysms (less than 2 min) of intense, sharp, lancinating, or electricity-like pain in one, two, or all three divisions of the nerve. Infrequently, patients complain of an itching sensation which is commonly an indication of a partially treated disorder. The second and third divisions are most often affected. The examining physician must be alert to the disorder since many patients say that the pain is constant and may use other descriptive adjectives for the pain such as hot, twisting, or boring. A simple query regarding the presence of exacerbations will clarify the history. Triggering factors are nearly always present and include talking, chewing, shaving, and brushing the teeth. The examination is normal except for the frequent presence of trigger points which, when touched or pressed, provoke pain. An abnormal neurologic sign compatible with a lesion in the cerebellopontine angle raises a high suspicion for neoplasm in that location. In patients under age 50, multiple sclerosis should be considered. Otherwise, compres-

sion of the nerve by an ectatic vascular loop, is the presumed etiology. The compression leads to demyelination, nerve irritability and possibly ephaptic transmission, which is nonsynaptic cross-talk between motor and sensory fibers.

F. *Glossopharyngeal neuralgia.*

Paroxysmal stabbing pains in the throat provoked by swallowing, talking, and coughing are the cardinal manifestations. Jacobson's nerve, a branch of the glossopharyngeal nerve, innervates the tympanic membrane, eustachian tube, and mastoid region. Thus, sharp ear pain is quite common and the disorder may present itself solely with unilateral deep ear pain. Nervus intermedius neuralgia would then be in the differential diagnosis. Although the neuralgia is unilateral, the patient's complaint will often refer to nonfocal throat pain which may obscure the diagnosis. Near-syncope, syncope, and convulsive syncope may occur since a large volley of efferent neuronal discharges may be incorporated in the ascending sensory fibers which innervate the carotid sinus. This augmented discharge, when reaching the medulla, can provoke a reflex vagal response causing bradycardia, rarely asystole, and result in hypotension. The etiology is presumed to be compression of the nerve by a vascular loop, especially the posterior inferior cerebellar artery. Ephaptic transmission, cross-talk (non-synaptic) between motor and sensory fibers may be the physiologic mechanism.

Trigeminal Autonomic Cephalgias

1. *Cluster headache, episodic or chronic.* (See Case 13A.)
2. *Paroxysmal hemicranias, episodic or chronic.* (See Case 13B.)
3. *Short-lasting unilateral neuralgiform headache attacks.*
   (a) *SUNCT.* Short-lasting unilateral neuralgiform attacks with conjunctival injection and tearing, episodic or chronic. (See Case 13C.)
   (b) *SUNA.* Short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms. This disorder is the same as SUNCT except there is only one or neither of conjunctival injection and lacrimation.
4. *Hemicrania continua.*

This is a persistent unilateral headache associated with ipsilateral conjunctival injection, lacrimation, nasal congestion, rhinorrhea, forehead and facial sweating, miosis/ptosis and/or restlessness or agitation. It is an indomethacin sensitive headache disorder.

Notes:

1. Positron emission tomography has shown activation of the posterior hypothalamus in all of them [12].
2. On rare occasions they may be symptomatic of underlying structural pathology.
3. There are instances of associated pituitary and paracavernous sinus lesions lending even more credence to a hypothalamic origin.
4. Internal carotid artery dissection has been discovered on a few occasions.

Primary Headache Disorders

1. *Primary cough headache.*

This is a benign disorder, has an abrupt onset, is bilateral and lasts less than 1 min. The diagnosis can be made only after neuroimaging has excluded a Chiari type 1 malformation, posterior fossa neoplasm and, rarely, a colloid cyst obstructing the foramen of Monro. The latter typically causes an acute frontal or frontotemporal headache due to a stooped posture which produces a ball valve obstruction of the third ventricle. (See discussion under Case 11.)

2. *Primary exercise headache.* (See Case 9.)

This headache is precipitated by any form of exercise in the absence of an intracranial disorder. It is brought on by and occurring only during or after strenuous physical exercise and lasts less than 48 h.

3. *Primary headache with sexual activity.*

This headache is precipitated by sexual activity, usually starting as a dull, bilateral ache as sexual excitement increases and suddenly becomes intense at orgasm in the absence of an intracranial disorder. It increases in intensity with increasing sexual excitement and has an abrupt explosive intensity just before or with orgasm. It lasts 1 min to 24 h with severe intensity or up to 72 h with mild intensity. (See Case 7.)

4. *Primary thunderclap headache.*

This headache is the worst the patient has ever experienced. It peaks in 60 s and lasts anywhere from 1 h to 10 days. It may occur anywhere in the head, neck and sometimes affects the low back. There can be concomitant brief loss of consciousness. Nausea and vomiting is uncommon but may occur. It is provoked by hard physical labor, use of illegal drugs and drinking hot liquids too quickly. Other associated but uncommon symptoms include a change in vision, confusion, weakness and numbness.

Etiologies can be a subarachnoid hemorrhage due to a ruptured cerebral aneurysm, reversible cerebral vasoconstriction syndrome (RCVS), venous sinus thrombosis, cerebrospinal fluid leak, hypertensive emergency, cerebral infection, internal carotid or vertebral artery dissections, intracerebral hematoma, 3rd ventricular tumor such as a colloid cyst and, particularly important, pituitary hemorrhage or infection which is called pituitary apoplexy.

5. *Cold stimulus headache.*

Headache brought on by cold stimulation applied externally to the head, ingested or inhaled. It resolves within 30 min after removal of the cold stimulus.

6. *Primary stabbing headache (previous terms include icepick pains).*

This is manifested by transient, localized stabs of pain in the head that occur spontaneously in the absence of organic disease of underlying structures or cranial nerves. The head pain occurs spontaneously as a single stab or series of stabs which last up to a few seconds and occur with an irregular frequency of one to many times per day.

7. *Nummular headache (previously termed coin-shaped headache).*

This is a pain of variable duration but often chronic, located in a small circumscribed area of the scalp in the absence of any underlying structural lesion. It is 1–6 cm in diameter, round or elliptical, sharply contoured and mildly-to-moderately painful. It usually persists for more than 3 months. The etiology is unknown.

8. *Hypnic headache.* (See Case 13D with subsequent discussion.)
9. *New daily persistent headache.*

This is a daily, unremitting headache with migraine or tension-type features. Of critical import is that its onset is clearly remembered by the patient who commonly has no prior headache history.

10. *External traction headache.*

This headache is a result of sustained compression of cranial soft tissues such as the use of a tight band around the head, hat or helmet, the use of a very tight ponytail or goggles worn during swimming or diving without evidence of scalp damage. The headache resolves within 1 h.

Painful Cranial Neuropathies and Other Facial Pains

1. *Trigeminal neuralgia.*

   (a) *Classical.* (See Case 13E with subsequent discussion.)

2. *Glossopharyngeal neuralgia.* (See Case 13F with subsequent discussion.)
3. *Nervus intermedius neuralgia (facial nerve).*

This is a rare neuralgia manifested by severe deep pain in the ear which can spread to the external auditory canal, outer ear, mastoid and eye. Many patients describe this as an icepick in the ear as well as dull, burning and shock-like. Triggers are ear stimulation, swallowing and talking. Differential diagnoses include carcinoma of the nasopharynx, temporomandibular joint disorder, herpes zoster and Eagle's syndrome (facial pain due to an elongated styloid process).

4. *Occipital neuralgia.*

This is a rare type of pain in the distribution of the greater, lesser or 3rd occipital nerve. The pain is episodic, brief, shock-like and radiates along the course of the nerve. Triggers include brushing the hair or resting the head on a pillow as well as moving the head. Tenderness of the nerve to palpation is common. Many patients are diagnosed with occipital neuralgia when in fact other etiologies have been overlooked such as migraine and tension-type headache. Exploration of the history in depth is required before this diagnosis can be accepted.

5. *Headache attributed to ischemic oculomotor nerve palsy* [8].

This is a severe, unilateral, frontal, and/or periorbital pain associated with ipsilateral 3rd, 4th or 6th nerve paresis of presumed ischemic origin. The headache is followed within 4 days by dysfunction of the involved nerve which is nearly always the 3rd

cranial nerve. Diabetes mellitus is always the suspected etiology but other pathology must be ruled out such as neoplasm or aneurysm. The ocular motor weakness may last days to months and on rare occasions remains persistent.

6. *Paratrigeminal oculosympathetic syndrome (Raeder's).*

Raeder's syndrome has been divided into two subtypes. Type 1 is manifested by unilateral periorbital or frontal pain which is in the distribution of the ophthalmic division of the 5th cranial nerve, a partial Horner's syndrome (no anhidrosis) and parasellar nerve involvement. Type 2 is identical except for the absence of parasellar nerve involvement. Lesions are infrequently found but if present are most often located in the middle cranial fossa. The differential diagnosis includes head trauma, vasculitis, migraine, neoplasm and internal carotid artery dissection or aneurysm.

7. *Burning mouth syndrome.*

This disorder causes daily intraoral burning or dysesthetic sensations for more than 2 hours per day and lasting for more than 3 months without any known underlying etiology. It is bilateral with fluctuating levels of pain and especially involves the tip of the tongue. Dryness and altered taste are common associated symptoms.

8. *Persistent idiopathic facial pain (atypical facial pain).*

Patients have daily facial and/or oral pain lasting at least 2 h and continuing for over 3 months. The pain does not follow a specific nerve distribution and is dull, aching and rarely sharp in character. There is a high level of psychological comorbidity.

9. *Central neuropathic pain.*

   (a) An example is multiple sclerosis and the etiology is a demyelinating lesion of ascending trigeminal nerve connections or involving the trigeminal rootlets in the brainstem. Commonly, the pain has a classical trigeminal neuralgia character.
   (b) Post-stroke pain. The pain develops within 6 months after the stroke which is documented by an abnormal MRI scan. It usually involves the ascending projections of the trigeminal nerve, commonly dorsolateral medulla and thalamus. Less often it occurs with parietal lobe lesions.

Miscellaneous Pain Syndromes

1. *Alcohol-induced headaches.*

This develops within 3 h of alcohol ingestion. It is bilateral, pulsating, aggravated by physical activity and resolves within 72 h.

2. *Caffeine withdrawal headaches.*

The headache develops within 24 h after cessation of regular caffeine consumption in excess of 200 mg. per day for more than 2 weeks. The headache resolves within 7 days if there is no further caffeine ingestion.

3. *High altitude headaches.*

This is a bilateral mild-to-moderately severe headache which is provoked by exertion and exceeding an altitude of 2500 meters. It resolves within 24 h after descent to below 2500 meters. Risk factors are migraine, low oxygen saturation, high exertion, fluid intake of less than 2 liters in 24 h and ingestion of alcohol.

4. *Acute mountain sickness.*

This is a combination of nausea with headache, anorexia, fatigue, photophobia, dizziness and sleep disturbances. It can be prevented with the use of acetazolamide and steroids which should be considered in susceptible individuals. Beginning treatment 2–3 days before a planned climb is advisable for prophylaxis.

Treatment Options for Headache Disorders

Treatment options for headache disorders are numerous. Drug selection often depends on comorbid conditions such as obesity which can be treated simultaneously. Avoidance of some medications is critical such as beta blockers in a patient with bradycardia or asthma. The aim of this brief and cursory introduction to treatment is merely to acquaint the student or resident with the wide range of available therapies, both medical and nonmedical. Dosing methods, adverse reactions, contraindications, and drug interactions will not be included because of space limitations. Obviously, this list contains my personal preferences (2018). Lastly, these treatments will very likely be of historical interest only since new medicines and therapeutic techniques are constantly being developed.

Migraine

A. Abortive

1. Triptans [9] – Pill, melt, nasal spray, subcutaneous.
2. Dihydroergotamine – Nasal spray, I.M. or I.V.
3. Ketorolac nasal spray, 60 mg I.M. or 30 mg I.V., a superb acute treatment.
4. Ergotamine.
5. Diclofenac powder.
6. Isometheptene/dichloralphenazone/acetaminophen (for mild migraine).
7. Naproxen, ibuprofen, aspirin with or without caffeine (for mild migraine).
8. Tramadol if options 1–7 are contraindicated or have failed.
9. Valproate – 500 mg I.V.
10. Compazine (prochlorperazine) – 10 mg p.o. or I.V. for headache or nausea.
11. Promethazine – suppository or I.M., for nausea. This is not for I.V. use due to the risk of severe tissue injury if there is perivascular extravasation.
12. Metoclopramide 10 mg. I.V. q. 1/2 h × 4 doses and diphenhydramine 25 mg. I.V. with first and third dose.
13. Magnesium sulfate 1 g I.V.
14. Butorphanol nasal spray (last resort to prevent an Emergency Room visit).
15. Timolol eye drops.

16. Vagal nerve stimulation (percutaneous).
17. Avoidance of narcotics such as meperidine, morphine, and hydromorphone which usually require repetitive dosing and are less effective than ketorolac as well as possibly leading to addiction.

B. Prophylaxis

1. Beta blockers

   (a) Propranolol
   (b) Nadolol
   (c) Timolol

2. Anticonvulsants

   (a) Topiramate
   (b) Valproate
   (c) Pregabalin
   (d) Gabapentin
   (e) Zonisamide
   (f) Levetiracetam

3. CGRP inhibitors

   (a) Erenumab a human monoclonal antibody which binds to CGRP receptors.
   (b) Monoclonal antibodies which block the ligand.

4. Tricyclics

   (a) Nortriptyline
   (b) Amitriptyline
   (c) Doxepin

5. Miscellaneous

   (a) Duloxetine
   (b) Venlafaxine
   (c) Verapamil
   (d) Lisinopril
   (e) Magnesium
   (f) Riboflavin
   (g) Melatonin

6. Botulinum toxin
7. Biofeedback
8. Cefaly. This is a device which provides external trigeminal nerve stimulation.

C. Treatment of comorbidity

Since depression is a frequent comorbid factor, the addition of an SSRI or SNRI is often essential but is generally not efficacious as sole therapy. An SNRI is preferable. Contrary to some opinions complications of a serotonin syndrome when used with a triptan is theoretical only. Most neurologists have no hesita-

tion in adding a triptan p.r.n. Dietary and hormone manipulations are seldom useful. When patients have hypertension or tachycardia, beta blockers are a good selection. When obesity is a major issue topiramate or zonisamide are ideal treatments.

D. *Hospital admission*
In-hospital treatment for 48–72 h should remain an option in cases of treatment failure. A protocol using DHE/Reglan combined with scheduled ketorolac I.V. is particularly useful. The addition of diphenhydramine can be efficacious.

Trigeminal Neuralgia

A. Medications (ticylaxis only).
    1. Carbamazepine, oxcarbazepine, gabapentin, baclofen, and lamotrigine.
B. Cyberknife, gamma knife radiotherapy, and radiofrequency lesions.
C. Craniotomy with microvascular decompression of the trigeminal nerve.
D. Selection of one of the above options depends on numerous factors including age, drug complications, contraindications, and patient preference.

Temporal Arteritis

Corticosteroids are required daily for a minimum of 6 months and often lifelong at low dosage. The initial dose ranges from 60 to 100 mg of prednisone with a gradual taper depending on headache and sedimentation rate plus occasionally C-reactive protein. There is no definitely proven successful alternative. Options are azathioprine, cyclosporine, methotrexate and tocilizumab (approved by FDA 5/17). In recent reports this new treatment reduced prednisone requirements to less than half.

Cluster Headache

A. Medications
    1. Abortive
        (a) Oxygen 7–10 L/min by mask for 10–15 min.
        (b) Sumatriptan subcutaneous and nasal spray or zolmitriptan nasal spray.
    2. Prophylaxis
        (a) Corticosteroids for 3–4 weeks followed by a tapering dose and discontinuation.
        (b) Verapamil.
        (c) Combined verapamil and corticosteroids at treatment initiation.
        (d) Indomethacin.

(e) Lithium (for chronic cluster).
(f) Melatonin.
(g) Possibly anti-CGRP drugs.

B. Surgical options (rare)

1. Radiofrequency lesion of trigeminal nerve.
2. Deep brain stimulation, still experimental.

Chronic Paroxysmal Hemicrania

A. Prophylaxis only.

1. Indomethacin.
2. Verapamil.
3. Other anti-inflammatory medicines: aspirin, diclofenac, naproxen and prednisone.

Hypnic Headache

A. Abortive – caffeine.
B. Prophylaxis – indomethacin, lithium, melatonin, gabapentin.

Short-Lasting, Unilateral Neuralgiform Headaches with Conjunctival Injection and Tearing (SUNCT)

A. Prophylaxis.

1. Lamotrigine.
2. Prednisone, gabapentin.
3. Microvascular decompression of the trigeminal nerve.

Glossopharyngeal Neuralgia

A. Prophylaxis only.

1. Carbamazepine.
2. Oxcarbazepine.
3. Gabapentin.

B. Intracranial section of the IX cranial nerve.
C. Microvascular decompression.

Case 14 A 33-year-old obese woman complains of an intractable headache for 3 months. A few weeks before the headache occurred she noted intermittent interscapular pain. Both the interscapular pain and the headache have persisted and occur only in the upright position. The severity has gradually increased and has forced her to remain in bed.

Neurologic examination is normal other than mild end nuchal rigidity.

A lumbar puncture yields clear fluid with 52 white cells/cu mm and a protein of 135 mg/dl.

Questions:

1. What additional information should be obtained from the lumbar puncture?
2. What neuroimaging test may be diagnostic?
3. What is the most common cause and how is it diagnosed?
4. Why is the CSF abnormal?
5. What is the diagnosis?

Answers:

1. What was the opening pressure? CSF pressure is low when it is less than 60 mm of H_2O. This patient's opening pressure was 40 mm H_2O.
2. MRI (head) with contrast discloses diffuse dural enhancement, present in about 90% of patients who have low intracranial pressure. The cerebellar tonsils are 6 mm below the foramen magnum which caused the nuchal rigidity. Greater than 5 mm is considered abnormal. Subdural fluid collections may occur and if large enough may prompt a surgical procedure, a serious error. A CT (head) would provide only an incomplete diagnosis. Lastly, there is often sufficient venous engorgement to cause pituitary hyperemia and occasional enlargement, another confusing discovery.
3. Rupture of a thoracic meningeal diverticula can often be demonstrated by CT/myelogram as contrast extravasates in the region of the CSF leak. Radionuclide cisternography is less precise.
4. The abnormal CSF findings are due to decreased CSF fluid volume.
5. *Diagnosis*: Spontaneous intracranial hypotension [7, 10] due to rupture of a thoracic meningeal diverticulum.

Comment: Other etiologies of this disorder include complications of spinal surgery, CSF rhinorrhea or otorrhea which can be a result of head trauma or a postoperative complication of cranial surgery. Additional considerations include a lumbar puncture, nerve sleeve tear after a fall on the buttocks and medical problems such as dehydration and possibly connective tissue disease. Examples of the latter are Marfan's syndrome, Ehler-Danlos Syndrome Type 2 and autosomal-dominant polycystic kidney disease.

Case 15 A 35-year-old obese woman complains of a 4-month history of moderately severe generalized headache. She has periodic exacerbations associated with nausea and vomiting, episodic tinnitus, and occasional diplopia primarily when driving. She notes overlapping images of an approaching car at distance but the image becomes single when the car is about one-half block away.

Past medical history: The patient had an unexplained fever 6 months ago for which she was hospitalized. Blood, urine, spinal fluid, and throat cultures were negative. A vasculitis evaluation was normal. She had a wbc count of 16,000/cu mm with 87% neutrophils. Treatment with ampicillin was curative in 5 days. She does not recall why it was given.

Neurologic examination: Blood pressure is 130/95. Funduscopic examination discloses bilateral blurred disk margins, absent venous pulsations, and a few small splinter hemorrhages at the disk margins. Red glass testing reveals diplopia on left lateral gaze. When the red glass covers the right eye the image to the left is white. CT scan (head) is normal.

Questions:

1. Why does the patient have diplopia at distance?
2. What does the red glass test demonstrate?
3. What diagnosis is suspected?
4. Is the past medical history relevant?
5. What test is next? What is its most important result?
6. What examination should follow?
7. Can pseudotumor cerebri occur with normal fundi?

Answers:

1. Diplopia is common with 6th nerve palsies since the eyes must diverge at distance.
2. Left lateral rectus paresis. The distal image comes from the weak muscle.
3. Pseudotumor cerebri [6].
4. Yes. This patient had an otitis media.
5. Lumbar puncture. The opening pressure is the critical finding. An opening pressure $\geq$ 250 mmH_2O is clearly abnormal and < 200 mmH_2O is clearly normal. 200–250 mmH_2O is borderline. Her opening pressure was 290 mmH_2O.
6. MRI (head) and MRV. The latter test reveals a transverse sinus thrombosis.
7. This has been described but it is controversial.

Diagnosis: Idiopathic intracranial hypertension (IIH) secondary to a transverse sinus thrombosis, a complication of an otitis media [6].
Comment: Other causes of IIH are numerous and include high doses of vitamin A or its derivatives such as isotretinoin (for acne), long-term tetracycline antibiotics, hormone contraceptives, obstructive sleep apnea, systemic lupus erythematosus, Behçet's disease, and chronic renal disease. The primary risk factor, however, remains severe or morbid obesity in a young woman.

Vertigo

Dizziness is one of the most frequent complaints in the general medical and neurologic clinic [20]. The plethora of etiologic possibilities is unsettling to many physicians, especially those under a mandated time constraint to unravel an often complex history. The symptom usually revolves about five disorders which include vertigo

(vestibular system pathology), visual impairments, imbalance or gait disorders, near-syncope (lightheadedness), and psychogenic factors (lightheadedness). This section will focus on vertigo. The other etiologies of dizziness will be covered under different categories.

Vertigo, an objective or subjective illusory sensation of movement, is the prototypical symptom of the patient with a disorder of the vestibular system [17]. Lesions which cause vertigo involve the peripheral vestibular apparatus, the semicircular canals and otolith organs, the 8th cranial nerve, the vestibular nuclei, or pathways within the brainstem passing to the cerebellum, especially its midline structures. Those pathways to the cerebellum travel primarily to the inferior portion, especially the nodulus and flocculus. There is vestibular representation in the cerebral cortex which is probably multifocal. The incidence of vertigo as a presenting symptom of cerebral hemisphere disease is negligible, nearly always as a focal aware seizure (simple partial seizure) with or without a secondary tonic-clonic seizure. The focus of the assessment of vertigo must be on the differentiation between the major central and peripheral vestibular connections and neurons.

The vestibular triad is composed of vertigo, nausea and/or vomiting, and diaphoresis (an autonomic component). These symptoms are the hallmark complex of vestibular system diseases. Fortunately, patients seldom camouflage its identification with verbal obfuscation. If the spontaneous complaints are vague a simple query such as "Do your surroundings seem to move or do you sense your body moving?" may suffice to evoke a diagnostic reply. Especially helpful additional questions include, "Do the symptoms occur as you lie down or turn over in bed?" or "Do they occur as you rise up from a supine to a sitting position or when moving from a sitting to a standing position?" "Does the environment seem to shift when you move your head?"

Neurologic signs which may accompany these symptoms are nystagmus and postural instability. Usually, one of these is present but with some peripheral vestibular disorders, both may be absent. A brief review of vestibular physiology may be helpful.

A visible and measurable expression of the vestibular system is the generation of slow eye movements. The visual system also produces slow eye movements through visual fixation and ocular pursuit. These are the two primary afferent pathways which produce eye movements involving slow system pathways.

The origin of the vestibular afferents resides in the otolith organs, utricle and saccule, and the three semicircular canals which are the anterior, posterior, and horizontal. The otolith organs mediate linear motion and orientation according to gravity. The utricle senses movement in the horizontal plane and the saccule in the sagittal plane. The semicircular canals contain an ampulla within which is the cupula sealing the canal. When the head moves, the cupula bends and activates the underlying hair cells innervated by a branch of the 8th nerve, a semicircular canal nerve. Thus, there is a transduction of rotational movement into neural activity.

The left 8th nerve generates slow eye movements to the right and vice versa. Therefore, symmetrical function results in no ocular deviation with eyes open or closed. If, for example, the left 8th nerve is damaged, the right 8th nerve is unopposed. This generates eye movements to the left. In the brainstem, the paramedian

pontine reticular formation (PPRF) produces a compensatory quick response back to a central point of fixation, i.e., contralateral nystagmus. This occurs when the eyes are closed but, if they are open, visual fixation may override eye deviation induced by vestibular dysfunction thus preventing the observation of the compensatory nystagmus. Therefore, the standard neurologic examination commonly uncovers no abnormal signs even though the patient complains of typical vertigo.

To summarize, an acute left 8th nerve lesion generates right-beating nystagmus with a slight rotatory counterclockwise element; this torsional component is the summation of vectors produced by the three semicircular canals. Central compensation develops slowly, gradually, and inevitably.

Special bedside examination techniques are required to assess these patients. The techniques are described in Chap. 4 (neurologic examination). These include observation of saccadic refixations, the head thrust (impulse) test, induction of oscillopsia by head shake, dynamic visual acuity test, stepping (Fukuda) test, Romberg and Dix–Hallpike tests. The examinations are quick and easy to accomplish. Other options are pastpointing, head shake nystagmus, caloric testing, and use of Frenzel glasses. Finally, an indeterminate examination mandates a referral for electronystagmography [19].

Five of the most common disorders which cause vertigo are described in the following case reports. Answers will be given after the fifth report.

Case 16 A 24-year-old longshoreman fell off a platform striking the back of his head. He was unconscious for approximately 10–15 s and thought to be dazed plus mildly confused for half an hour. One hour later, in the Emergency Room, his examination followed by a non-contrast CT scan (brain) were normal.

The following day the patient complains of vertigo. Specific questioning elicits a comment that he especially notes vertigo when he lies down or gets up from bed. A complete neurologic examination is normal. Past medical history is negative.

Questions:

1. What is the next step?
2. What is the diagnosis?
3. What treatment cures this disorder?

Case 17 A 57-year-old woman complains of episodic vertigo usually lasting 15–20 min associated on a few occasions with brief loss of consciousness. The vertigo has occurred once or twice per month over the previous 6 months. The duration varies from 10 min to 1 h but, as noted above, is ordinarily 15–20 min. Witnesses have observed slurred speech and an unsteady, sometimes lurching gait. Past medical history is remarkable for insulin-dependent diabetes mellitus.

Neurologic examination is normal.

Questions:

1. What questions may elicit a diagnostic answer both from the present illness and past medical history?
2. What is the diagnosis?

Case 18 A 56-year-old nurse who works in an adjoining clinic arrives 10 min after the abrupt onset of severe vomiting, vertigo, and diaphoresis (the vestibular triad). He has had prior episodes lasting as long as several hours. On one occasion he had an abrupt fall without explanation. Past medical history is remarkable for hypertension under good control with metoprolol.

Neurologic examination: Blood pressure 140/95. Pulse is 56 and regular. Right-beating nystagmus with a slight counterclockwise rotation and an ataxic gait are noted. The Romberg test is positive. A stat CT (brain) is normal. Several hours later, MRI (brain) and MRA (head and neck) are normal.

Two hours after he is first evaluated, nystagmus beats left on left lateral gaze with a slight rotatory clockwise component. With up and down gaze the same nystagmus occurs. On right lateral gaze there is no nystagmus. The Romberg test is positive.

Questions:

1. What additional history should be obtained?
2. What diagnosis explains the features of this patient's nystagmus?

Case 19 A 67-year-old woman has the acute onset of vertigo, vomiting, and diaphoresis on a Saturday. Following treatment with over-the-counter meclizine, she feels sufficiently improved over the next 48 h to return to work. She has a residual feeling of unsteadiness and, when driving and looking over her shoulder to change lanes, cars seem to bounce. She is referred for a neurologic consultation. Past medical history is remarkable for insulin-dependent diabetes mellitus and an asymptomatic, critical right internal carotid artery stenosis treated by endarterectomy.

Neurologic examination discloses nystagmus to the right on right lateral, upward, downward, and direct forward gaze. The entire neurologic examination is otherwise normal. Non-contrast CT scan of the brain is negative. Subsequent MRI (brain) discloses several T2 and FLAIR hyperintensities in subcortical white matter, brainstem and cerebellum. The MRA reveals mild basilar artery and bilateral supraclinoid carotid artery stenoses.

Questions:

1. What bedside neuro-otologic tests are likely to be abnormal?
2. Although an L.P. is not indicated what could cerebrospinal fluid studies show?
3. What electrophysiologic test may be diagnostic?
4. What is the diagnosis and the anatomic site of pathology?

Case 20 A 62-year-old man is referred because of a single episode of severe vertigo followed by partial loss of vision O.D. He describes the loss of vision as blank or "nothing there" and specifically not black. Both symptoms lasted 3 min. There was no headache.

Past medical history includes hypertension which is being treated successfully with lisinopril. There is no history of migraine or severe headaches.

Neurologic examination: Blood pressure 130/80. Pulse 72, regular. There are no neurologic abnormalities.

Table 11.1 Duration of vertigo

BPPV	Seconds
TIA – vertebrobasilar	Few to several minutes
Migraine	5–60 min
Ménière's disease	Hours
Vestibular neuritis	Days to weeks

Questions:

1. What is the explanation of his visual symptoms?
2. What anatomic areas are affected?
3. What is the diagnosis?

The primary clue to the diagnosis of patients with vertigo [24] is the duration of symptoms (Table 11.1).

Answers:

Case 16:

1. The Dix–Hallpike maneuver is performed and elicits upbeat, torsional counterclockwise nystagmus for 10 s in the right-sided position after a latency of 3 s. This indicates the presence of otoconia (calcium carbonate particles) in the right posterior semicircular canal. The otoconia were dislodged from the tips of hair cells in the utricle by the head injury.
2. *Diagnosis*: Benign paroxysmal position vertigo (BPPV) [24].
3. A canalith repositioning procedure (modified Epley maneuver) cures the patient (Fig. 11.3).

Diagnostic key: Duration of seconds.

Case 17:

1. The patient is asked: "Do you have any discomfort around your head?" "Have you ever had severe headaches?" She responds: "My head feels sore after the vertigo subsides." "I used to have sick headaches in my 20 s."
2. *Diagnosis*: Migraine with brainstem aura (previous diagnosis – basilar migraine). Additional common symptoms which may occur include scotomata, photopsias tinnitus, perioral and limb paresthesias often manifested as a "march of paresthesias" over several seconds to 15–20 min beginning in the hand and gradually spreading up to the face. Drop attacks are uncommon and syncope is rare.

Diagnostic key: Symptom duration of 5–60 min is typical of migraine.

Case 18:

1. The patient is asked: "Do you have ringing noises or a pressure sensation in the ears?" Reply: "Yes, I have ringing in my right ear which has a full feeling and my hearing is slightly impaired on the right side."
2. Eye movement abnormalities in an acute Ménière's attack, rarely observed, may reflect irritative phenomena resulting in ipsilateral nystagmus. Shortly afterwards there is direction-fixed contralateral nystagmus which obeys Alexander's

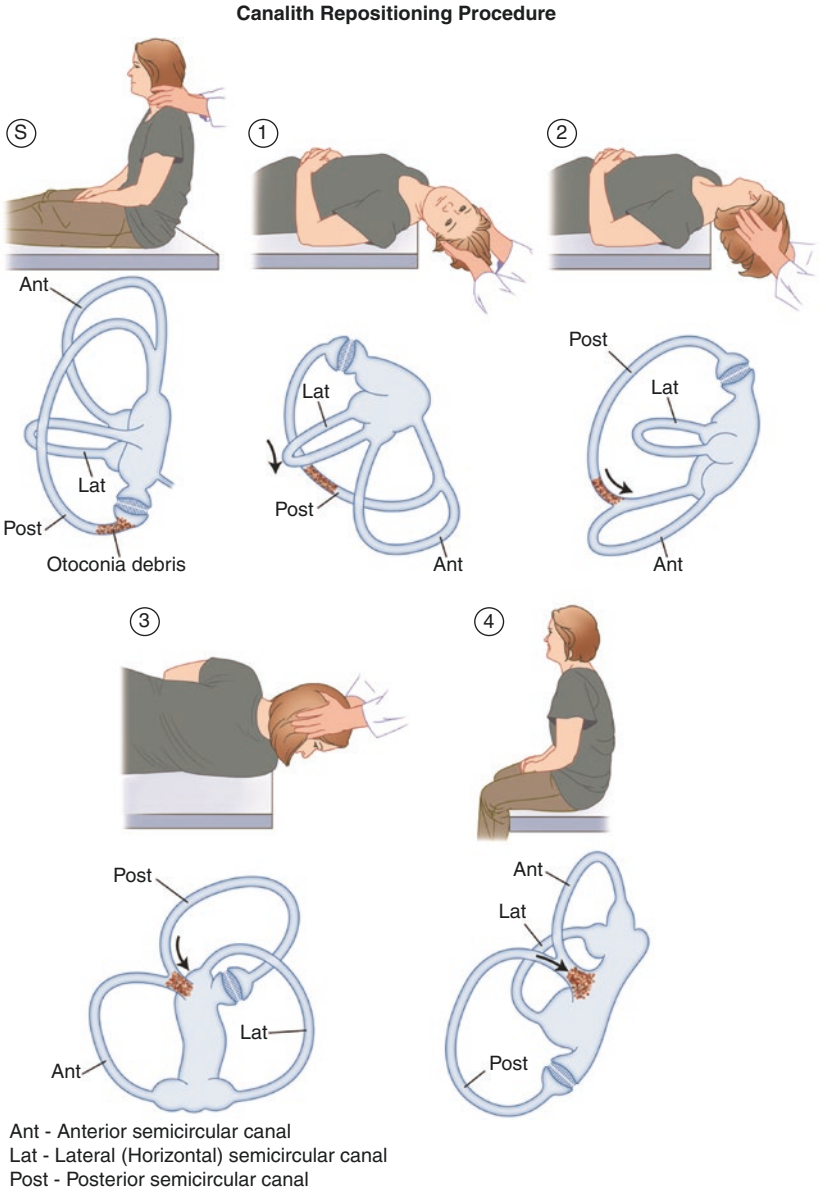

Fig. 11.3 Treatment of benign paroxysmal positional vertigo by the canalith repositioning procedure (modified Epley). In this example the left side is symptomatic. *S* starting position. *Position 1*: The patient's head is turned 45° to the left and then the patient is assisted quickly to the supine position with her head tilted back over the edge of the examining table. The patient is kept in this position for 30 s or until the dizziness stops, whichever is longer. *Position 2*: While the patient's head remains tilted back her head is rotated 45° to the right. This position is maintained for 30 s or until the dizziness stops, whichever is longer. *Position 3*: The patient is rolled over onto her right shoulder so that her head is turned 45° down. This position is maintained for 30 s or until the dizziness stops, whichever is longer. *Position 4*: The patient sits up slowly with her head rotated to the right

law. This states that nystagmus is most prominent when the eyes are deviated toward the direction of the quick phase. The sudden drop attack is known as Tumarkin's otolithic crisis or simply otolithic crisis indicating presumed acute stimulation of the otoliths from hydrops. Diuretics are usually given and an ENT referral is essential for management of Ménière's disease.

Diagnosis: Ménière's disease [17].

Diagnostic key: Duration varies and usually lasts 2–4 h. The duration, however, may range between 20 min and 24 h.

Case 19:

1. Head shake at two cps provokes oscillopsia. The dynamic visual acuity test results in a decline of visual acuity from 20/20 to 20/100. The head thrust (impulse) test [22] is abnormal from right to left as it produces a saccadic refixation from left to right.
   (See Chap. 4, Vestibular Nerve Physiology and Examination)
2. Cerebrospinal fluid studies disclose 15 lymphocytes/cu mm.
3. Electronystagmography demonstrates unilateral left-sided caloric weakness.
4. *Diagnosis*: Vestibular neuritis, left 8th nerve [23].

Comment: Although a branch occlusion of the anterior inferior cerebellar artery could theoretically cause this clinical picture, it would be quite rare and the spinal fluid findings support a viral etiology. Since Bell's palsy may be due to reactivation of a latent HSV-1 infection in the geniculate ganglion, speculations of a similar reactivation from Scarpa's ganglion could be pertinent. HSV-1 has been found in Scarpa's ganglion and vestibular labyrinth on autopsy [17]. The abnormal MRI findings are nonspecific and commonly seen in asymptomatic diabetic or hypertensive patients. Treatment options include oral prednisone, I.V. methylprednisolone, promethazine and meclizine.

Diagnostic key: Duration of symptoms varies from a few days to several weeks with a gradual resolution of symptomatology. Residual instability may last up to 3 months.

Case 20:

1. Loss of vision associated with occipital ischemia is commonly described as blank or absent. Many people with homonymous hemianopsias observe this as affecting only the eye which perceives the involved temporal field which is larger than the nasal field.
2. Brainstem dysfunction causes severe vertigo. Occipital lobe involvement explains absence rather than darkness or blackness of vision.
3. The brief episode of 3 min is compatible with a transient ischemic attack. The basilar artery supplies the brainstem plus the occipital lobe via the posterior cerebral arteries, the left being involved in this case.

Diagnosis: Transient ischemic attack secondary to basilar artery stenosis.

Comment: Vertigo and visual loss O.D. is secondary to brainstem and occipital lobe ischemia. The latter is manifested by a right homonymous hemianopsia which is misinterpreted by the patient as amaurosis O.D. An MRA (head) disclosed a high grade basilar artery stenosis.

Diagnostic key: Duration of symptoms with most TIAs is usually several minutes. In this instance, the simultaneous involvement of two separate structures in a specific vascular distribution confirms the diagnosis.

Six other cases which are less often seen but easily recognized should also be kept in mind. A seventh patient with a rare eye movement disorder will be added. Two or three case reports will be presented consecutively followed by the explanations to the posed questions. This will prevent the reader from immediately glancing at the answers.

Case 21 A 50-year-old geologist complains of dizziness and an unsteady gait which is worse in the dark. The environment seems to shift when he walks. These symptoms began 6 months ago after returning from a working trip to Venezuela where he was mapping regions for oil exploration. He developed pneumonia, was treated with unknown antibiotics and recovered quickly. Past medical history is negative.

Neurologic examination reveals easily induced oscillopsia, an abnormal dynamic visual acuity test with his acuity declining from 20/20 to 20/200 with head shake at two cps and bilateral saccadic refixations on head thrust (impulse) tests. He has a positive Romberg and a wide-based gait.

Questions:

1. Where is the lesion? Are a positive Romberg test and wide-based gait common findings with this localization?
2. What optional bedside test confirms the anatomic location?
3. What is the diagnosis?

Case 22 A 56-year-old woman has a 2-year history of periodic intense vertigo associated with blurred vision lasting 2 min each time. The episodes are identical and occur irregularly, once per month to several times per week. They have occurred supine, sitting, or standing. The frequency has been increasing. She briefly lost consciousness while in bed on one occasion when it was particularly severe.

Past medical history: Diabetes type II and hypertension.

Medications: metformin and hydrochlorothiazide.

Neurologic examination: Blood pressure 160/110 and pulse 50 and regular. The neurologic examination is normal.

Questions:

1. What elements of the symptoms are the key to the diagnosis? Is the past medical history relevant to the diagnosis?
2. What question related to the medical history is essential?

3. What physiologic test is diagnostic?
4. What is the diagnosis?
5. What etiology must always be suspected?

Answers:

Case 21:

1. Semicircular canals or 8th nerve. Yes. A positive Romberg and gait disorder are commonly present with peripheral vestibular pathology.
2. Caloric testing shows nearly absent responses bilaterally. An electronystagmogram may be used to quantify the deficit.
3. *Diagnosis*: Vestibular ototoxicity [17, 21].

Comment: The patient was treated with streptomycin, an aminoglycoside, which caused damage to the hair cells in the labyrinth. Streptomycin and gentamycin are relatively specific for causing vestibular system toxicity.

Case 22:

1. Brief duration and stereotyped features, as well as irregular occurrences. No. Concomitant medical illnesses are frequently not relevant. The history of the present illness and the neurologic examination will determine whether they are germane.
2. Since her blood pressure is high the patient was asked whether she takes her medicines regularly. She responds sheepishly that she does not.
3. Electroencephalogram (EEG). This shows a left temporal sharp and slow wave focus.
4. Focal aware nonmotor seizures (previously termed simple partial seizures). This has been called "tornado epilepsy."
5. Neoplasm.

Diagnosis: Focal aware nonmotor seizures caused by a convexity meningioma, left temporal lobe.

Comment: This patient had an extra-axial (outside brain) mass overlying the posterior part of the insula, left side. Extra-axial, well-circumscribed mass lesions are usually benign such as the meningioma which this patient had successfully resected.

Case 23 A 50-year-old man complains of disequilibrium for 6 months. At the onset he had vertigo, vomiting, and excessive perspiration which resolved over 1 week. Past medical history includes insulin-dependent diabetes mellitus, hypertension, and hypothyroidism. In addition to insulin the patient is being treated with amlodipine and thyroid replacement.

Neurologic examination: Blood pressure is 140/90 and pulse 62 and regular. Funduscopic examination O.U. reveals numerous scattered hemorrhages and exudates. Venous pulsations are seen. The visual acuity is 20/100 O.U. due to macular disease and is uncorrectable. Pupillary reactions are normal. He has a positive head

thrust test, left to right. There are no ankle reflexes, vibration sense loss is noted at the toes and ankles and a few position sense errors are made at the toes. The Romberg test is positive.

Questions:

1. What illness caused this patient's vertigo?
2. What conditions are contributing to his disequilibrium?
3. What is the significance of the funduscopic findings?
4. Are the normal pupillary reactions expected?
5. What is the diagnosis?

Case 24 A 32-year-old man complains of vertigo and right-sided neck pain after playing soccer. He successfully scored the winning goal by heading the ball into the goal from a corner kick. The following day he saw his chiropractor because of a stiff neck. On his way home, shortly after treatment by neck adjustments, he had the onset of severe vertigo, nausea, and right facial numbness. His right-sided neck pain became more intense. When eating he found it more comfortable to tilt his head to the left side.

Questions:

1. What symptom confirms the presence of CNS disease?
2. Which side of his body was likely to be numb?
3. What two neuro-ophthalmologic signs might have been found?
4. Why did he tilt his head to the left at mealtime?
5. What is the diagnosis?

Answers:

Case 23:

1. Vestibular neuritis. The account of vertigo, vomiting, and diaphoresis gradually resolving over several days is a typical history for this disease.
2. Residual of right 8th nerve disease, macular degeneration, and diabetic neuropathy. The positive head thrust test supports the presence of 8th nerve dysfunction. The positive Romberg test can be explained by both peripheral vestibular disease and diabetic neuropathy. Impaired visual acuity may be a secondary exacerbating factor.
3. They are stigmata of hypertension and diabetes. Hemorrhages are not at the disc margins and venous pulsations are present. Hence this is not papilledema.
4. Yes. Pupillary reactions are normal in patients who have macular disease.
5. *Diagnosis*: Multisensory disequilibrium [18].

Comment: Diseases affecting two or more systems may be additive and can cause a vague sense of disequilibrium. In this case the vestibular system and the peripheral neuropathy are the primary culprits. Macular degeneration is an aggravating factor.

Case 24:

1. Facial numbness. Vertigo and nausea may occur with peripheral vestibular disease.
2. The left side. Vertigo plus right facial numbness point to a right-sided brainstem lesion. The latter typically produces crossed sensory findings; right facial numbness indicates involvement of the ipsilateral spinal tract of the 5th cranial nerve and is frequently accompanied by left hemihypesthesia due to involvement of the crossed fibers of the lateral spinothalamic tract.
3. Horner's syndrome and horizontal gaze-evoked nystagmus. The Horner's syndrome is right-sided since sympathetic fibers remain ipsilateral throughout their anatomic pathway. Nystagmus is caused by damage to the vestibular nuclei and is most often horizontal gaze-evoked, to the right on right lateral gaze and to the left on left lateral gaze. Bidirectional nystagmus occurs only with brainstem/cerebellar disease or drug toxicity.
4. Probably to improve swallowing since the right soft palate is likely to be weak due to an infarction affecting the right nucleus ambiguus in the medulla.
5. *Diagnosis*: Dorsolateral medullary infarction (Wallenberg's syndrome), right side, secondary to a traumatic right vertebral artery dissection.

Comment: An abrupt violent head jerk may kink the vertebral artery injuring the arterial wall. Chiropractic manipulation of the neck carries a low but definite risk of stroke.

Case 25 A 77-year-old woman complains of episodic vertigo for 4 months. Each spell lasts 5 min and, over the last week, she has averaged eight to 10 per day. She has nausea but no vomiting. Additionally, she has noticed ringing and mild loss of hearing A.S.

Neurologic examination: There is slow large amplitude nystagmus beating left on left lateral gaze and rapid low amplitude nystagmus beating right on right lateral gaze. Rinne's test is positive on the left and Weber's lateralizes right.

Questions:

1. What cranial nerve and motor function should be evaluated carefully?
2. Is this nystagmus typical of a specific pathology?
3. What is the significance of Rinne's and Weber's tests?
4. What is the primary diagnosis to consider?

Case 26 A 45-year-old man complains of vertigo and double vision, "side-by-side." These symptoms began 2 weeks ago and are beginning to subside. Past medical history is negative.

Neurologic examination: Blood pressure is 132/88, pulse 90, regular. When the examiner uses a penlight, the patient notes horizontal diplopia on left lateral gaze. With a red glass covering O.D. the image on the far left is red. Slow, large amplitude nystagmus is noted O.S. which beats to the left. There are clumsy rapid alternating

movements of the left hand, mild weakness of left interossei and wrist extension, and a left Babinski sign.

Questions:

1. What symptom localizes the site of the vestibular dysfunction?
2. Are the findings consistent with a unilateral anatomic site?
3. What diagnosis is suspected but not proven?

Case 27 A 17-year-old female complains of perceiving a constant movement of her surroundings which seem to bounce around. These oscillations began 3 days ago and were accompanied by an occipital headache which lasted 1 day. Past medical history is entirely negative. She takes no medication and does not use recreational drugs.

Neurologic examination: The blood pressure is 90/60 and pulse 90, regular. The patient exhibits constant, chaotic saccadic eye movements on gaze in any direction with attempts at visual fixation. During sleep the eyes can be seen to be moving in a similar fashion under closed lids or with gentle elevation of the upper lids. An occasional brief jerk of either arm is seen.

Questions:

1. What is the name of this eye movement disorder? What other phenomena may occur simultaneously?
2. Where is the lesion?
3. What diagnoses should be considered.

Answers:

Case 25:

1. Fifth, 7th, and 8th cranial nerves and cerebellar function. These are structures in the region of the cerebellopontine angle (Fig. 11.4). Cerebellar function should be assessed with finger-to-nose and heel-to-shin testing, failure of check, rapid alternating movements, gait and tandem gait. The vestibular component of the 8th nerve can quickly be examined via the head thrust (impulse) test.

   Abnormal findings include impaired hearing to finger rub A.S., a positive head thrust test when moving the head from right to left, left heel-to-shin ataxia and inability to perform tandem gait.

2. Yes. This is Bruns' nystagmus characteristic of a neoplasm (schwannoma) of the 8th nerve compressing the brainstem. Remember that bidirectional nystagmus indicates brainstem and/or cerebellar pathology assuming there is no evidence for drug toxicity.
3. The patient has sensorineural hearing loss A.S. (See discussion of 8th nerve function in Chap. 4).
4. Neoplasm. An MRI confirms the presence of a well-circumscribed mass in the left cerebellopontine angle.

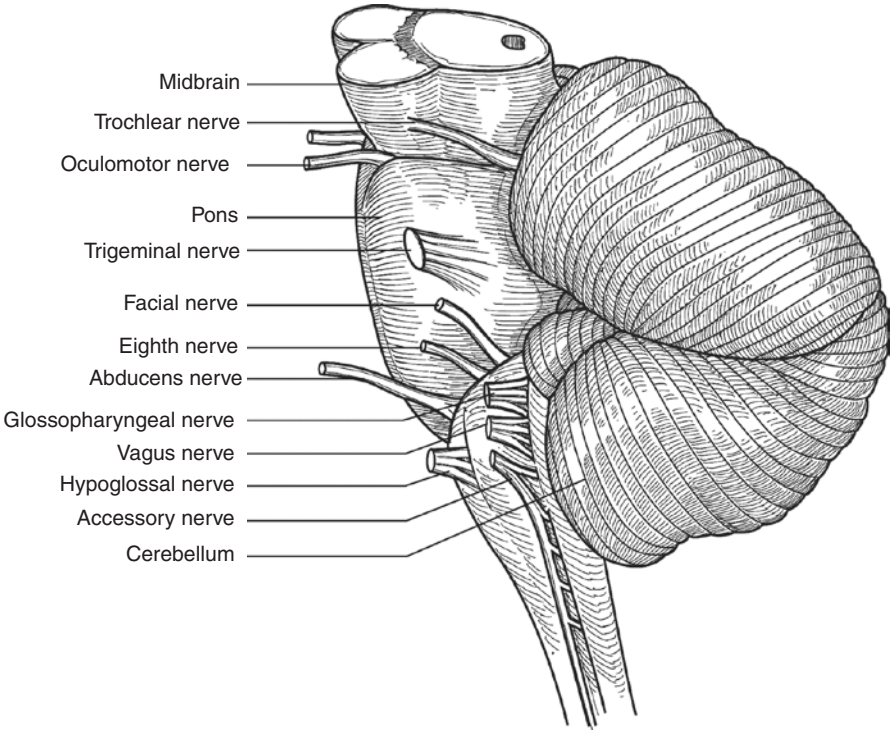

Fig. 11.4 Lateral view of the brainstem, cerebellum and cerebellopontine angle

Diagnosis: Acoustic neuroma, left 8th nerve, with brainstem compression.

Case 26:

1. Diplopia. This is a common symptom of brainstem lesions.
2. Yes. The patient has a right-sided internuclear ophthalmoplegia (INO) (lesion of the right medial longitudinal fasciculus) because of right medial rectus weakness discovered by the red glass test. Nystagmus of the contralateral eye beating away from the lesion site is a common associated sign of an internuclear ophthalmoplegia. A right pons lesion may cause left-sided motor signs, weakness, clumsiness of the left arm and left hyperreflexia due to a right-sided corticospinal tract lesion which runs in the basis pontis.
3. Multiple sclerosis. An internuclear ophthalmoplegia (INO) is a characteristic sign of multiple sclerosis. Multiple sclerosis cannot be proven, however, without two distinct attacks separated in space and time [25]. Confirmation of the diagnosis may require additional abnormalities primarily through neuroimaging by MRI and cerebrospinal fluid studies. Evoked potentials, especially visual in this case, may support the diagnosis but are no longer relied upon to confirm the pres-

ence of a lesion. An optic nerve lesion by clinical or MRI abnormalities establishes the presence of an additional anatomic lesion (separation in space).

Case 27:

1. Opsoclonus. Myoclonus and ataxia are common associated features [16].
2. Cerebellum, midbrain or pons.
3. (a) Brainstem/cerebellar viral encephalitis is probably the most common etiology.

(b) Paraneoplastic syndromes, especially associated with neuroblastoma in children, small cell lung cancer, and breast cancer.
(c) Multiple sclerosis.
(d) Vascular disease including midbrain and pontine hemorrhage or infarction.
(e) Cerebellar ataxias, hereditary.
(f) Hyperosmolar nonketotic coma.
(g) Toxic effect of drugs such as lithium, amitriptyline, cocaine.

Epilepsy

Epilepsy [29] is a chronic brain disease manifested by a tendency for recurrent seizures. A seizure is a clinical manifestation of hyperexcitable cortical neurons and may be a single lifetime event of various etiologies such as hypoglycemia. This does not warrant a diagnosis of epilepsy.
Epilepsy is defined by any of these 3 conditions.

1. At least 2 unprovoked (or reflex) seizures occurring greater than 24 h apart.
2. One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after 2 unprovoked seizures, occurring over the next 10 years.
3. Diagnosis of an epilepsy syndrome.

Epilepsy is considered to be resolved for individuals who either had an age-dependant epilepsy syndrome but are now past the applicable age or who have remained seizure-free for the last 10 years and off anti-seizure medicines for at least the last 5 years.

In 1981 The International League Against Epilepsy (ILAE) introduced a classification system which has been embedded in neurologic instruction up until 2016. After many years of contentious discussions a new classification system was introduced in 2016 and final modifications published in March 2017. The following is an abbreviated summary of the new 2016–2017 classification system [30]. Subsequent case reports will provide a diagnosis according to the new classification system and in parenthesis the older terminology.

Table 11.2 ILAE 2017 classification of seizure types

Focal onset		General onset	Unknown onset
Aware	**Impaired awareness**	**Motor** Tonic-clonic Clonic Tonic Myoclonic Myoclonic-tonic-clonic Myoclonic-atonic Atonic Epileptic spasms **Nonmotor (absence)** Typical Atypical Myoclonic Eyelid myoclonia	**Motor** Tonic-clonic Epileptic spasms **Nonmotor** Behavior arrest
Motor onset Automatisms Atonic Clonic Epileptic spasms Hyperkinetic Myoclonic Tonic **Nonmotor onset** Autonomic Behavior arrest Cognitive Emotional Sensory			
Focal to bilateral Tonic-clonic			**Unclassified**

Adapted from: [35].

Table 11.3 Descriptors of focal seizures according to degree of impairment during seizure

Without impairment of consciousness or awareness
With observable motor or autonomic components – "Focal motor" and "autonomic" can be used
Involving subjective sensory or psychic phenomena only – "aura" can also be used
Replaces the term "simple partial seizure"
With impairment of consciousness or awareness
"Dyscognitive" can also be used. It is understood that dyscognitive may not always mean altered awareness but it is used here to denote altered consciousness or awareness which may be response tested
Replaces term "complex partial seizure"
Evolving to a bilateral convulsive seizure
May include tonic, clonic or tonic and clonic components in any order
Replaces term "secondarily generalized seizure"

Epilepsy Syndromes [36]

1. Juvenile myoclonic epilepsy.
   The onset is usually in puberty with myoclonic jerks which typically occur in the morning, involve arms, legs and trunk and are not associated with loss of consciousness. Tonic-clonic seizures are common (90%) and absence occasional (30%). The EEG pattern is 4–6 Hz multiple spikes and slow wave discharges. Lifelong treatment is usually required.

Table 11.4 Examples of electroclinical syndromes and other epilepsies arranged according to age

Infancy (onset under 2 years)
Febrile seizures
Febrile seizures plus
Epilepsy of infancy with migrating focal seizures
West syndrome
Myoclonic epilepsy in infancy (MEI)
Self-limited infantile epilepsy
Self-limited familial infantile epilepsy
Dravet syndrome
Myoclonic encephalopathy in non-progressive disorders
Childhood
Febrile seizures
Febrile seizures plus (FS+)
Early onset childhood occipital epilepsy (Panayiotopoulos type)
Epilepsy with myoclonic atonic (previously astatic) seizures
Self-limited epilepsy with centrotemporal spikes (ECTS) (previously called Benign Rolandic Epilepsy)
Autosomal-dominant nocturnal frontal lobe epilepsy (ADNFLE)
Late onset childhood occipital epilepsy (Gastaut type)
Childhood Absence Epilepsy (CAE)
Epilepsy with myoclonic absences
Lennox-Gastaut syndrome
Epileptic encephalopathy with continuous spike-and-wave during sleep (CSWS)
Landau-Kleffner syndrome (LKS)
Adolescence – Adult
Juvenile absence epilepsy (JAE)
Juvenile myoclonic epilepsy (JME)
Epilepsy with generalized tonic-clonic seizures alone (GTCA)
Autosomal-dominant epilepsy with auditory features (ADEAF)
Other familial temporal lobe epilepsies
Familial epilepsy syndromes
Familial focal epilepsy with variable foci (FFEVF)
Genetic epilepsy with febrile seizures plus (GEFS+)
Generalized genetic epilepsies
Childhood absence epilepsy (CAE)
Juvenile absence epilepsy (JAE)
Juvenile myoclonic epilepsy (JME)
Epilepsy with generalized tonic-clonic seizures alone (GTCA)

Modified from Berg et al. [26]

Table 11.5 Primary changes

1. Focal aware replaces simple partial
2. Focal impaired awareness replaces complex partial
3. Focal seizures are divided into:
(a) Focal motor onset seizure
(b) Focal nonmotor onset seizure
4. Generalized tonic-clonic replaces grand mal
5. Generalized absence seizures replaces petit mal
6. New seizure types are added such as:
Myoclonic-tonic-clonic and myoclonic-atonic

Table 11.6 Epilepsy etiologies

1. Genetic, e.g. generalized genetic epilepsies.
2. Immune, e.g. anti-NMDA receptor encephalitis, anti-LGI-1 encephalitis.
3. Infectious, e.g. tuberculosis, HIV, cerebral malaria, neurocysticercosis, subacute sclerosing panencephalitis and toxoplasmosis. This does not apply to an acute infection such as meningitis/encephalitis.
4. Metabolic, e.g. porphyria, uremia, aminoacidopathies and pyridoxine dependent seizures. Metabolic/genetic may be a better term for some of these disorders.
5. Structural. This implies abnormal neuroimaging showing a structural lesion of any etiology.
6. Unknown.

2. Self-limited epilepsy with centrotemporal spikes (BECTS).
   This was previously called Rolandic epilepsy or focal epilepsy of childhood. The onset is between ages 2 and 13 and originate in a localized region of the brain. The classical description is awakening, shortly after going to sleep, with a focal motor seizure involving face and sometimes ipsilateral arm or leg. Occasionally it spreads to become tonic-clonic. Todd's phenomenon is common. They comprise 15–20% of childhood epilepsies and a positive family history is found in 15–30% of patients.

3. Childhood absence epilepsy.
   Onset is between ages 4 and 8 and is characterized by brief staring spells or lapses of consciousness commonly lasting just a few seconds but they can occur numerous times per day. There may be automatisms and myoclonus. In adolescence tonic-clonic seizures may develop and absence may diminish and disappear. The EEG pattern is 3 Hz spike-and-wave discharges which are bilateral and symmetrical.

4. Juvenile absence epilepsy.
   Onset is between ages 9 and 13 and manifested by severe and frequent absence seizures. Most patients have generalized tonic-clonic seizures typically on awakening in the morning and a few have myoclonic jerks. The EEG pattern is generalized 3 Hz spike-wave discharges.

5. Epilepsy with generalized tonic-clonic seizures, alone.
   The onset is usually in late adolescence, commonly but not always on awakening and occurring especially with sleep deprivation and excessive alcohol consumption. The EEG usually shows 3–4 Hz generalized spikes and polyspike discharges. Lifetime treatment is usually required.

6. West syndrome (infantile spasms, salaam attacks).
   This syndrome is manifested by focal epileptic spasms beginning between ages 3 and 12 months. Clinical manifestations include flexor or extensor spasms, associated with psychomotor retardation and a hypsarrhythmia EEG pattern. The latter is composed of irregular slow waves with multifocal spikes and polyspikes. Typically there are structural brain abnormalities such as would occur with hypoxic ischemic encephalopathy, intracranial infections, tuberous sclerosis, lissencephaly, chromosomal and gene abnormalities.

7. Lennox-Gastaut syndrome.
   The onset of this disorder is between ages 1 and 7. It is characterized by multiple types of intractable seizures, tonic-clonic, myoclonic, atonic and atypical absence. Development in cognition prior to the onset is usually abnormal. It has been considered an epileptic encephalopathy as the epileptic activity may contribute to additional cognitive and behavioral impairments. Structural brain abnormalities are the cause in 70% of cases and, of the remainder, genetic etiologies are likely.

Near-Syncope, Syncope, and Seizure

In the absence of head trauma, an episode of loss of consciousness is either syncope or seizure. Syncope [27] is much more common and usually easily recognized. If the event is unwitnessed and the patient is neither intelligible nor perceptive, the diagnosis may be far from apparent. Near-syncope is included in this discussion since there are illnesses and syndromes which eventuate in loss of consciousness if not recognized early and treated.

When the patient arrives at the clinic with a chief complaint of “I’m having blackouts,” the physician may shudder because this symptom often requires a lengthy history which interferes with his usual patient flow. Conversely, he may be challenged to identify the meaning of this complaint. A standard method can be useful and this will be outlined.

Since “blackout” has numerous interpretations, problem one is to distinguish between visual loss, dizziness, loss of consciousness, or other catastrophic neurologic symptoms for which the patient uses this term. Once loss or near-loss of consciousness is established, the next task is to meticulously review specific elements of the history.

General considerations:

1. What was the patient doing? Was the patient supine, sitting, standing, walking or running?
2. Was he weightlifting? Urinating? Coughing? Laughing? Receiving a neck massage? Head turning? Swallowing? Each one may indicate the mechanism and the underlying pathology.
3. What time did it occur? For example, was it at night after getting up to go the bathroom?
4. What was the time relation to meals?
5. What medicine, substance, liquid, or food was consumed and how long before this event occurred?
6. Was there any warning or symptom immediately before loss of consciousness?
7. Was the patient at home or in the hospital? The most common cause of syncope in the hospital is pulmonary embolism.

Specific questions:

1. Was there dizziness, lightheadedness, a change in vision (especially dimness), tinnitus, muffled hearing, chills, pallor, nausea, sweating or shortness of breath prior to loss of consciousness? (Typical of syncope).
2. Did this occur after urination or defecation? (Common before syncope).
3. Was there an unusual smell, taste, distortion of vision, or hearing? (Typical of seizure).
4. Was there déjà vu (familiar surroundings or experiences), jamais vu (strangeness of surroundings or experiences), forced thinking, or other psychic experience? (Typical for seizure).
5. Was there tongue biting, urinary incontinence or postictal confusion? (Typical for seizure). If confused for how long did it persist? More than 1 min, especially prolonged, is typical for seizure.
6. Were there any witnesses from whom additional history could be obtained?

Duration: Duration of each symptom is critical for making a diagnosis. For example, an unusual taste that lasts 2 h is unlikely to be due to a seizure whereas that same taste which lasts 30 s to 1 min might indicate a seizure. Consequently, the patient's reply to this question is of the utmost diagnostic significance.

Responses to any of these questions may trigger the need to pursue details. For example, the patient may say that things look "different." Follow-up questions might be: "Did they seem to be at a distance?" (teleopsia), "Did objects loom up close?" (pelopsia), "Were they small or large?" (micropsia or macropsia). These examples are illusions, a distortion of what is perceived. "Did you see things which were not actually there?" (hallucinations). If present, were they patterns or geometrical designs (occipital lobe origin) or were they animals, people or well-formed objects (temporal lobe origin)? Episodes of these visual disturbances, illusions or hallucinations are strong indicators of focal seizures with awareness if they are brief in duration (usually less than 3 min).

Auditory hallucinations of epileptiform origin can be verbal or nonverbal but not accusatory or commanding as occurs with psychoses. Examples of nonverbal noises are rumbling, machinery-like, and whistling. Indistinct voices can be heard and are often described as muffled.

Of greatest importance; was there a witness to these occurrences? [34]. A yes response requires immediate contact with that individual preferably while the patient is in the examining room or office. A delay in contacting the witness increases the chance that this person will forget a pertinent detail of the event. Finally, cardiac and pulmonary pathology must always be considered. The most common cause of syncope in the hospital is pulmonary embolism. Cardiac pathology is typically unmasked such as aortic stenosis and cardiac arrhythmia.

Psychogenic Non-Epileptic Seizures (PNES)

These seizures, also called pseudoseizures, probably comprise 10–20% of patients referred to epilepsy centers. The term pseudoseizures carries a pejorative connotation, unacceptable for many patients but certainly easier for physicians to use. Introduction of either term must be used with care and compassion.

Typical features of PNES include gradual onset, fluctuating severity, long duration (usually >2 min) and, if there is tongue biting, it is usually the tip of the tongue. Other clinical features include resistance to forcible eye opening, side-to-side head movements and undulating body movements. As a rule they are not stereotypical and, consequently, if a few are witnessed the diagnosis becomes clear.

Unfortunately, there are confounding elements. Many patients with PNES also have focal seizures with impaired awareness, motor or nonmotor (complex partial seizures). Furthermore, seizures of frontal lobe origin may exhibit features of PNES, especially the undulating body movements but they are stereotypical and thus EEG-video monitoring in a hospital epilepsy unit may clarify the diagnosis. In puzzling cases there is an emerging bias in favor of PNES which is hazardous when inaccurate. Deferring a final diagnosis to additional outpatient observations is preferable.

Psychogenic Pseudosyncope (PPS)

This disorder must be distinguished from psychiatric causes of syncope. The latter is a physiological phenomenon, discussed elsewhere in this chapter and is a vasovagal episode (neurocardiogenic syncope) triggered by witnessing an emotional or physically traumatic event or experiencing severe anxiety. This provokes bradycardia, hypotension, cerebral ischemia and loss of consciousness.

The patient with PPS typically crumples slowly to the floor and displays limp motionless limbs with eyes closed. When witnessed the diagnosis is not difficult

since vital signs show little change. Furthermore, there is no pallor or moist skin and it lasts longer than 1 min.

The neurologic examination of these patients is identical to that of a poorly responsive patient. Usually this patient is speechless and does not follow verbal commands. The next step is to apply a painful stimulus such as supraorbital or nailbed pressure, evaluating the response to visual threat, eye movement (oculocephalic maneuver), pupillary reaction to light, corneal reflexes and gag reflex. This examination is ordinarily sufficient to confirm a suspected diagnosis of PPS. The patient often resists eye opening and does not demonstrate the smooth horizontal eye movements that are elicited by the oculocephalic maneuver in patients with impaired level of consciousness. In patients with PPS visual fixation is not inhibited and thus the eye movements are commonly saccadic, focusing on different objects in the room. An additional technique is holding the patient's hand above his/her head and letting go which then results in an avoidance movement of head or hand. The ultimate answer in equivocal instances remains caloric testing, an infallible method of ascertaining the level of consciousness (described in Chap. 5).

The case reports to follow will review some of the principles, just outlined, and explore other means of making a diagnosis. These will be presented consecutively three at a time followed by the answers.

Case 28 A 17-year-old boy is referred to a neurologist as a last resort because of unexplained nausea and abdominal discomfort. The episodes began 6 months ago and are increasing in frequency to a few times per week. He has already seen his internist and two gastroenterologists. Endoscopy, colonoscopy, and thorough stool evaluations were entirely normal. A psychiatric assessment revealed a perfectly normal young man who is becoming increasingly anxious about his unpleasant symptoms.

1. What is the first question asked which virtually makes the diagnosis?
2. What is the second question which secures the diagnosis?
3. What is the diagnosis and what examinations are indicated?
4. If the examinations are normal should treatment be initiated?

Case 29 A 32-year-old man is referred by a physician's assistant because of three seizures over the past 10 days. The patient is unable to supply any detailed information. He had no warning and his last recollection is standing next to the kitchen sink. He had been in a motor-vehicle accident 6 weeks previously and suffered a brief loss of consciousness of about 1 min with subsequent confusion for a few minutes. He had no local injury and a CT scan (head) without contrast was normal.

The patient's wife witnessed all three of these spells. She reports that two episodes occurred before meals and one afterward. Two occurred when sitting and one while standing. The most recent one lasted for 10 min during which time his arms and legs jerked uncontrollably but there was no stiffening. Afterwards he seemed confused for 1 min.

1. Assuming the patient's wife is a good observer, what specific questions might uncover an accurate diagnosis?
2. If a physician is present, what examination techniques could establish a diagnosis?

Case 30 A 15-year-old girl was reported to have passed out at school. She said she was feeling dizzy and noted blurry vision after rushing to her math class for the final exam at 2:00 p.m. Her teacher observed her to fall as she was about to sit down at her desk. After the fall she stiffened and then began jerking all extremities for 10 s. Simultaneously, she lost control of her urine. In less than 1 min she was alert and oriented. Shortly afterwards general physical and neurologic examinations were normal.

1. What additional history would be useful?
2. What is the diagnosis?

Answers:

Case 28:

1. How long does the nausea and abdominal discomfort last? Response: The nausea lasts 5–10 s, rarely up to 1 min. This is a typical time course for a focal aware, nonmotor seizure (simple partial seizure).
2. Does the nausea and discomfort travel? The patient points to the epigastric region and gestures upward indicating the location and sense of movement. Rising epigastric distress, occasionally interpreted as nausea by some patients, is a relatively common ictal sensation. This focal aware seizure (simple partial seizure), previously called an aura, frequently precedes a generalized tonic-clonic seizure. The sensation arises from an epileptiform discharge in the hippocampus.
3. *Diagnosis*: Focal aware nonmotor seizure (simple partial seizure), idiopathic.

   Both an EEG and MRI (head) with and without contrast should be performed.

4. Yes. Both studies are commonly normal in patients with epilepsy. Estimates of the incidence of a normal EEG in these circumstances is approximately 25–50%. Even a normal 72-h EEG monitor, which is commonly obtained, should not delay treatment. Careful frequent follow-up visits are essential to substantiate the diagnosis.

Case 29:

1. Were his eyes open or closed? Psychogenic non-epileptic seizures (pseudoseizures) are usually associated with eye closure whereas patients who have epileptic seizures ordinarily have their eyes open and often deviated to one side. [28].
   - Was he blue or pale? Cyanosis is common with tonic-clonic seizures and pallor with syncope.
   - Did he bite his tongue? The lateral margins of the tongue not the tongue tip are bitten with generalized seizures.

- Was he incontinent? This is uncommon with pseudoseizures and common with tonic-clonic seizures. It may also occur with convulsive syncope.
- Were the three spells you witnessed identical or were they somewhat different each time? Stereotyped episodes are more likely to be seizure.
- Was he jerking, stiff, or limp? Pseudoseizures are commonly clonic but seldom tonic (stiff). Bilateral myoclonic jerks ordinarily last less than 30 s.
- Was there confusion afterwards and how long did it last. Confusion after syncope is usually less than 1 min but can be several minutes if a severe hypotensive episode occurred. Confusion after a tonic-clonic seizure is several minutes to hours.

2. • Check for tachycardia which is usually present with a seizure.
   - Is there cyanosis? This is usually present with tonic-clonic seizures.
   - Check for resistance to eyelid opening. The presence of resistance suggests a psychogenic etiology.
   - Evaluate the oculocephalic response. An alert patient has saccadic eye movements, not the smooth movements of an "intact" oculocephalic response which indicates some degree of obtundation. Smooth eye movements can be willfully produced only by visual fixation during the maneuver which is not common.
   - Are there undulating body movements? This is more common with pseudoseizures, rare with seizures. Seizures of frontal lobe origin rarely exhibit these movements.
   - Are there inappropriate emotions? If these are evident, one should suspect pseudoseizures.

Diagnoses:

1. Suspected psychogenic non-epileptic seizures (PNES).
2. Concussion.

Additional History:

The patient's wife gave further pertinent history. She stated that her husband moved his head rapidly from side to side and his eyes were closed during the seizure. Furthermore, there were no tonic elements and the duration was approximately 10 min. These manifestations support the diagnosis of PNES.

Case 30:

1. Had she slept last night or missed meals? She responded that she was studying all night, had not eaten and was very anxious. These are provoking factors for neurocardiogenic syncope (vasovagal syncope). Despite the urinary incontinence the brief (10 s) tonic-clonic event with <1 min confusion is most compatible with:
2. *Diagnosis*: Convulsive syncope, neurocardiogenic [32].
   Neurocardiogenic syncope is characterized by a slew of premonitory symptoms and signs which include: hyperventilation, lightheadedness, dimming or blurring of vision, nausea, pallor, sweating, muffled hearing, and generalized

weakness. Upward eye deviation may occur whereas, with a seizure, deviation is often lateral. Tachycardia and an elevated blood pressure may briefly precede these symptoms. Bradycardia and hypotension quickly follow. The basis for these physiologic phenomena remains controversial. Some individuals probably have a predisposition to peripheral venous pooling with consequent poor venous return. This produces vigorous ventricular contractions which activate mechanoreceptors in the aortic arch and carotid sinus which usually respond only to stretch due to hypertension. The result is paradoxical reduction in arterial resistance and reflex bradycardia caused by increased vagal discharge.

Convulsions are the brain's response to hypoxia. The degree of cerebral hypoxia determines whether convulsive activity will occur. The estimated incidence of convulsive activity in neurocardiogenic syncope is nearly 10%. Syncopal myoclonus is arrhythmic, symmetrical or asymmetrical. It affects all limbs and muscle groups equally and commonly involves the face. The duration is usually less than 30 s. Tonic muscle activity is manifested by extension of head and body and either flexion or extension of the arms. Vocalization such as moaning and complex movements such as licking the lips, chewing movements, and reaching upward have been reported and thus may confound the diagnosis. Ocular manifestations may include eye opening, downbeat nystagmus, or upward eye deviation. Visual hallucinations, both formed and unformed, and auditory hallucinations such as rushing or machinery-like sounds and vague, unintelligible voices have been described. Thus distinguishing convulsive syncope from seizure can be quite challenging.

Case 31 A 44-year-old stockbroker complains of periodic brief dizziness when using his computer. During a recent conversation with a client he lost track of the conversation for about 30 s. This lack of attention prompted his doctor to request a neurologic evaluation.

Past medical history: Insulin-dependent diabetes mellitus, heavy drinker, and smokes 1–1/2 packs of cigarettes per day.

Neurologic examination: Blood pressure 160/100. There are no ankle reflexes and vibration sense is absent at the toes.

1. Is the past medical history relevant to his symptoms?
2. What is the diagnostic test and what are the diagnoses?

Case 32 A 38-year-old woman complains of the gradual and invariable onset of feeling faint when walking more than 5 min. She describes nausea, excessive perspiration, shortness of breath, severe neck pain, and her vision darkens. She recovers promptly after sitting. She has insulin-dependent diabetes mellitus and hypertension. Current medications are metformin and hydrochlorothiazide.

Examination: Blood pressure supine is 140/80, sitting 135/85, standing at 1 min 130/90, and after 3 min 125/85. The pulse varies from 80 to 84 in all positions.

Neurologic examination reveals absent reflexes in the legs and absent vibration perception at toes and ankles.

1. Why does she have neck pain, shortness of breath, and darkening of vision?
2. What test is diagnostic?
3. What is the diagnosis?
4. What physiologic parameters should be targeted on treatment?

Case 33 A 35-year-old woman is seen 1 week postpartum because of five episodes of loss of consciousness. On the last occasion she had been sitting on the couch, then got up slowly and carefully walked to the kitchen. She felt cold, clammy, dizzy, and passed out. She was unconscious for less than a minute, according to her observations, and denies confusion. Her neurologic examination is normal.

1. What is the diagnosis?
2. What could be the pathophysiologic mechanism?

Answers:

Case 31:

1. No. Despite the importance of the past medical history the present illness must be scrutinized in its entirety prior to employing the clues provided by his medical background. The abnormal neurologic signs, however, are a consequence of his medical illnesses.
2. The diagnostic test is an EEG with photic stimulation. The EEG reveals left temporal epileptiform discharges during photic stimulation. Although epilepsy induced by reading is an additional remote consideration, the provocation by a rapidly changing screen is most likely. Additionally, an MRI (brain) with and without contrast is normal.

Diagnoses:

1. Focal aware and focal impaired awareness, nonmotor seizures, idiopathic. (previously called simple and complex partial seizures).
2. Neuropathy, diabetic and/or secondary to alcohol abuse.

Case 32:

1. Her vision becomes dark because of impaired perfusion of the retinas due to orthostatic hypotension. There is impaired perfusion of the lung apices and neck musculature causing dyspnea and neck pain.
2. Have her walk for at least 5 min or until symptoms occur; then check the blood pressure and pulse while standing. A decision about whether orthostatic hypotension is present cannot be made until the pressure has stabilized. This was not demonstrated as it was declining when recordings were prematurely discontinued. She became symptomatic after walking for 5–1/2 min at which time her blood pressure was 82/58 with a heart rate of 86.
3. *Diagnoses*:

1. Near-syncope secondary to orthostatic hypotension possibly due to diuretic use (hydrochlorothiazide is a common cause) or diabetic autonomic neuropathy.
2. Diabetic autonomic neuropathy and suspected autonomic neuropathy.

4. • Increase venous return. Elastic stockings.
   - Increase blood volume. Treat with salt, increased fluids and consider mineralocorticoids (fludrocortisone).
   - Increase peripheral resistance. Consider stimulating alpha-1 adrenergic receptors with midodrine.
   - Exercise to avoid deconditioning. This improves muscular tone which aids venous return. Using a stationary bicycle is the best choice since it allows a sitting position which is usually tolerated.
   - Raise the head of the bed to avoid supine hypertension.

Case 33:

1. *Diagnosis*: Syncope secondary to orthostatic hypotension.
2. A large blood volume and decreased vascular tone is present in pregnancy. After delivery, blood volume returns to normal but vascular tone may remain decreased for several days. Hence, immediately after delivery women are susceptible to significant drops in blood pressure when standing up.

Case 34 A 15-year-old boy is brought to the office because of three recent episodes of vertigo, ringing in the ears for several minutes and then abrupt loss of consciousness for 1–2 min. On another occasion he saw flickering blue lights for 15 min. The neurologic examination is normal.

1. What questions should be asked?
2. What is the diagnosis?

Case 35 A 32-year-old woman complains of chronic fatigue, faintness, periodic nausea, and palpitations for 2 years. She can barely walk half a block before requiring rest.

Examination Blood pressure is 90/60 sitting, 86/60 standing, and 88/58 after walking for 2 min. The pulse is 90, 110, and 124, respectively. There are no abnormal neurologic findings.

1. Do these findings explain her fatigue?
2. What is the diagnosis?

Case 36 A 15-year-old male high school student is brought to an internist because of clumsiness. At least a few times per week in the morning he drops or throws either his glass of orange juice, bowl of cereal, or an eating utensil. He is a good student, respectful, and despite intense determination on his part he has been unable to overcome this tendency. The neurologic examination is normal.

The patient's internist refers him for neurologic evaluation. The day before the appointment he has a generalized tonic–clonic seizure. The neurologist's examination is normal other than once observing the patient to stare for 3 s.

1. What phenomena are occurring?
2. What is the diagnosis?
3. How common is this condition?
4. What is the prognosis?

Answers:

Case 34:

1. Is there any headache associated with these symptoms? Does he have a prior history of headaches? The patient recollects a minimal headache after regaining consciousness. He has had a few severe pulsating headaches associated with nausea and photophobia over the last year.
2. *Diagnoses:*
    1. Migraine with brainstem aura (previous diagnosis – basilar migraine).
    2. Typical aura without headache.

Comment: This disorder is associated with symptoms referable to the brainstem which this patient experienced, namely vertigo, tinnitus, ataxic gait and syncope followed by headache. The 15-min episode of seeing flickering blue lights without headache or other symptoms is a typical aura without headache. The lengthy time (15 min) is the diagnostic key. Migraine auras are typically between 5 and 60 min.

Case 35:

1. Yes.
2. *Diagnosis*: POTS syndrome (postural orthostatic tachycardia syndrome) [31].

Comment: This syndrome is defined as an increase in heart rate of 30 beats per minute or more than 120 beats/min upon standing or with minimal exertion. With tilt table testing the increase occurs within 10 min of being upright. POTS syndrome is a well-known cause of the chronic fatigue syndrome. Treatments emphasize conditioning exercises, especially a stationary bicycle, good hydration and, lastly, a low dose beta blocker can be very helpful.

Case 36:

1. Myoclonus, absence and generalized tonic–clonic seizure. This history is typical of myoclonus, a sudden involuntary muscle contraction generated by a paroxysmal electrical discharge within the central nervous system (CNS). It can be epileptic or nonepileptic. Examples of the latter include myoclonus associated with spinal cord disease and hypnic jerks, sudden muscular contractions in drowsiness. This patient also has absence seizures (staring) and had a generalized tonic-clonic seizure.
2. *Diagnosis*: Juvenile myoclonic epilepsy.

3. This is the most common cause of genetic generalized epilepsies comprising about 10% of these disorders. Approximately 90% of these patients have generalized tonic-clonic seizures and 30–35% have absence seizures.
4. Lifelong treatment is usually required but there is an excellent response to anticonvulsants.

Case 37 A 72-year-old man requests an evaluation because of an episode of loss of consciousness after dining at his favorite restaurant. He had his usual dinner of a large bowl of pea soup, ribeye steak, mashed potatoes, and green beans. His beverage was one bottle of beer. His dessert was bread pudding and ice cream. As he was finishing dessert he felt nauseated for 1–2 min. One hour later while seated and chatting with his family after dinner he began to perspire, appeared pale, and then passed out for 1 min. There were a few brief asynchronous jerks of his extremities. On regaining consciousness he was confused for 30 s. His neurologic examination was normal.

1. Why did he lose consciousness?
2. What is the pathophysiology?
3. What is the diagnosis?

Case 38 A 27-year-old psychologist is referred for unusual and inappropriate laughter at a psychology conference. She had been depressed and under considerable stress since her boyfriend canceled their marriage plans. As the small ten-member meeting was discussing grief reactions, the patient broke out into a peal of laughter which lasted 1 min. She seemed "dazed" afterwards and was slow to respond for 2–3 min. The patient says that her friends reported three other very brief similar events over the last 2 years when out for dinner. She did not believe her friends' reports. The neurologic examination is normal.

1. Is her psychological state related to these episodes?
2. What are the two most important facts that suggest seizures?
3. How might the diagnosis be stated?

Case 39 A 38-year-old woman is referred for neurologic consultation because of a seizure in bed. She is in the 8 month of pregnancy. The night before this evaluation, while supine in bed reading a book, she felt nauseated and then lost consciousness. Her husband reports that his wife stiffened, jerked a few times, and lost control of her urine. She was moist with perspiration.

1. What additional questions should be asked of the patient and husband to determine whether this was a seizure or convulsive syncope?
2. What is the diagnosis?

Answers:

Case 37:

1. Hypotension. He had the typical premonitory symptoms and signs of nausea, pallor and diaphoresis.

2. There is failure to maintain vascular resistance during blood pooling in the splanchnic bed. Syncope may occur up to 75 min following a meal, especially a large one.
3. *Diagnosis*: Postprandial syncope.

Case 38:

1. There is no definite connection.
2. The duration of laughing was 1 min, typical for seizure phenomena. There was postictal confusion for 2–3 min. This patient has focal, impaired awareness, nonmotor seizures of gelastic character (previously called complex partial). Many patients with these seizures do not believe or reject witnesses' descriptions since there may be no preceding focal aware seizure (simple partial). Her MRI (head) disclosed a hamartoma involving the hypothalamus, a well-described cause of gelastic seizures.
3. *Diagnosis*: Focal, impaired awareness, nonmotor seizures of gelastic type secondary to a hypothalamic hamartoma.

Case 39:

1. Was the patient confused afterwards and for how long? Was there tongue biting? Husband's response: His wife was confused for 20 s and there was no tongue biting.

2. *Diagnosis:* Convulsive syncope due to hypotension.

Comment: Compression of the inferior vena cava by the fetus decreases venous return which results in poor cardiac output and cerebral ischemia.

Case 40 A 45-year-old man is referred because of sudden loss of consciousness while watching TV after dinner. His wife was unable to rouse him for 2 min. An earlier spell, 1 month ago, occurred while driving and she managed to get the car to the side of the road. Over the past year while at dinner his wife noticed that his jaw suddenly dropped open on occasion. At those times he did not respond to her for several seconds. Yet the patient can remember what his wife said. Neurologic examination, MRI (brain), and EEG are normal.

1. What additional questions might yield diagnostic information?

Case 41 An 80-year-old man is referred because of episodes of loss of consciousness associated with falling during the night. This has occurred on four occasions always when standing. He feels nauseated, dizzy (lightheaded), and short of breath before losing consciousness. There is no confusion according to the patient.

Neurologic Examination: Vital signs are normal and specifically there is no orthostatic hypotension. The blood pressure is 125/86 and pulse 78 supine, 127/80 with pulse 80 when sitting and after standing for 3 min the blood pressure is 127/87 with pulse of 80. There are no neurologic abnormalities.

1. What is the first question that should be asked?
2. What is the suspected mechanism of loss of consciousness?
3. What is the diagnosis?

Case 42 A 66-year-old woman requests an evaluation because of sudden loss of consciousness while reaching up to dust bookshelves in her living room. She was vaguely dizzy for 1–2 s before losing consciousness. She awakened on the floor in a pool of urine having remembered the time just prior to dusting and immediately after regaining consciousness. Just 2 min had elapsed. She denies tongue biting and confusion before or after the event. She suffered no injury.

Past medical history includes hypertension. Her only medicine is enalapril 10 mg q.d.

Neurologic examination (same day): There is mild weakness of the left anterior tibialis muscle associated with a slow foot tap and unsustained clonus at the left ankle. An urgent CT scan (head) and an EEG are normal. A cbc immediately afterwards shows a wbc count of 12,000/cu mm with 84% neutrophils.

Neurologic examination 2 days later: The neurologic examination is normal and a cbc is normal.

1. Did this patient have a seizure or syncope?
2. What is the significance, if any, of the transient abnormal neurologic signs?
3. Is there any other clue to support either syncope or seizure?
4. What is the diagnosis?

Answers: Case 40:

1. Was there any stiffening or jerking of the extremities, urinary incontinence, tongue biting, or confusion? The answer is no. Has he been drowsy? Yes, he is always drowsy and frequently naps. How does he respond when surprised? His legs give way occasionally.

Diagnosis: Narcolepsy with sleep attacks and cataplexy.

Comment: Two additional useful questions would include: Do you ever wake up unable to move (sleep paralysis)? Do you ever hear noises or voices, see people or animals or feel anything as you fall asleep or wake up? Hypnogogic hallucinations occur on falling asleep and hypnopompic on awakening. Sleep attacks, cataplexy, sleep paralysis and hypnogogic/hypnopompic hallucinations comprise the "tetrad" of narcolepsy.

Case 41:

1. Did you urinate or move your bowels before losing consciousness? Response: Yes, I just finished urinating.
2. Micturition or postmicturition. Bladder contraction is mediated by the parasympathetic system. A strong vagal response may produce bradycardia, reflex vasodilation, hypotension, and then syncope. Since sleep is associated with a drop in blood pressure, getting up at night to urinate is likely to add a factor of orthostatic hypotension.
3. *Diagnosis*: Postmicturition syncope [33].

Comment: An additional consideration is prostatic enlargement. Straining to urinate, especially in men with prostatic obstruction, will increase intrathoracic pres-

sure which reduces venous return followed by a subsequent drop in cardiac output, hypotension, and syncope. This mechanism occurs with straining of any type such as with defecation, weightlifting, and coughing.

Case 42:

1. The history is indeterminate with regard to the diagnosis. The 2-min lapse of time supports a diagnosis of seizure. The denial of confusion can be neither accepted nor refuted since there was no witness. Urinary incontinence is common with seizure but may also occur occasionally with syncope.
2. The transient abnormal neurologic signs are called a Todd's phenomenon, a sign of a seizure with focal elements. It can last minutes to 48 h but signifies a structural lesion even if not visible by MRI. Rarely, minimal constant twitching can occur in the affected muscles indicating focal motor status epilepticus. Status epilepticus is defined as seizures lasting more than 30 min. An EEG should be obtained promptly to see if there is ongoing epileptiform activity, focal aware motor status epilepticus requiring immediate treatment.
3. An elevated wbc count with left shift often occurs immediately after a seizure.
4. *Diagnosis*: Focal, impaired awareness, nonmotor seizure (complex partial seizure), secondary to a right cerebral lesion.

Comment: An MRI (head) with and without contrast reveals an intra-axial (within brain) mass in the right frontal parasagittal region only visible on the contrast-enhanced study. At surgery a small grade 3 astrocytoma is removed. Astrocytomas are graded from benign to malignant (1–4). Grade 4 is a glioblastoma multiformae.

Sleep Disorders

One century ago a textbook of neurology introduced an eight-page chapter on disorders of sleep with the following first sentence: "The disorders and disturbances of sleep, while mainly symptomatic, in some instances reach an important development and almost obtain the dignity of a disease."[13] Conversely, Hippocrates is reported to have said: "Sleep and watchfulness, both of them when immoderate, constitute disease." Just a few decades ago practicing physicians thought of patients with sleep disorders as occurring in two categories, the insomniac and the somnolent, the former to be bludgeoned with barbiturates and the latter to be activated with amphetamines. More attention is paid to it today since sleep comprises about one-third of our lifetime and thus rightly bears careful medical scrutiny and investigations. Treatment measures will be added to some of the discussions in this section.

Today, sleep disorders [39, 44] are known to aggravate or cause severe medical disorders as well as provide diagnostic clues to explain the source of many patient complaints. Sleep apnea predisposes to or precipitates cardiovascular and cerebro-

[13] Church A, Peterson F. Nervous and Mental Diseases. 3rd edition. London and Philadelphia, WB: Saunders; 1901.

vascular events and has other widespread adverse ramifications [43]. Sleep-related movement disorders are exceedingly common, often overlooked or misdiagnosed, and are frequent chief complaints in a general medical or neurologic clinic. This is quite unfortunate since, when severe, they are terribly distressing, life disrupting and yet eminently treatable. Restless legs syndrome (RLS), periodic leg movements of sleep (PLMS) and sleep-related leg cramps (better known as nocturnal leg cramps – NLC) warrant special attention.

There is a wide array of parasomnias many of which simulate seizures and thus are sources of diagnostic errors. A well-known REM (rapid eye movement) related parasomnia, REM behavior disorder of sleep, can be a harbinger of a neurodegenerative disorder, particularly Parkinson's disease. When violent the resulting mayhem may lead to marital discord and life altering consequences. Narcolepsy and idiopathic hypersomnia, if untreated, promote disability and are responsible for more motor-vehicle accidents than epilepsy. Chronic insomnia often provokes excessive use of sedatives eventuating in work inefficiency, a fractured family life, depression and protracted disability. Jetlag and shift work negatively influence sleep and sap the energy of those affected individuals. Lastly, sleep habits are the window into the psyche such that when organic pathologies are refuted by appropriate examinations, investigation of sleep patterns may guide the physician to an unexpected psychiatric diagnosis.

Just two to three decades ago the standard medical history either omitted or did not emphasize a sleep history. It is now, or it should be, a routine element of every history and physical examination by a primary care provider. The purpose of this abbreviated review is to acquaint the reader with common sleep disorders that have major health consequences.

The third edition of the International Classification of Sleep Disorders was published by the American Academy of Sleep Medicine in March 2014 and will provide the structure for the ensuing discussions. There are six major clinical divisions. Only the most common disorders will be reviewed.

1. Sleep-related breathing disorders.
2. Sleep-related movement disorders.
3. Hypersomnia of central origin.
4. Parasomnias.
5. Insomnia.
6. Circadian rhythm sleep-wake disorders.

Sleep-related breathing disorders, obstructive and central sleep apnea, have had a prominent impact on caring for patients with heart disease and stroke since omission of treatment may lead to catastrophic consequences [43]. Narcolepsy and idiopathic hypersomnia should be recognized by every practicing physician as adequate treatment will restore a nonfunctioning individual to a normal or near-normal life. Parasomnias such as REM sleep behavior disorder (RBD) and periodic leg movements of sleep (PLMS) are being increasingly recognized as relatively common. As previously mentioned RBD often causes nocturnal chaos and may augur the subsequent development of a neurodegenerative process. PLMS and RLS will be

discussed together because of clinical similarities; but their differences and etiologies will be contrasted. Sleep-related movement disorders such as nocturnal paroxysmal dyskinesias and bruxism warrant attention, the former because it resembles or may be a seizure disorder and the latter because of its prevalence. Lastly, insomnia, one of the most common ailments in the general public will be reviewed.

Sleep Apnea (Fig. 11.5)

Obstructive Sleep Apnea

1. The incidence of obstructive sleep apnea (OSA) in the elderly population (greater than 65 years) is believed to affect 25% of those living independently and 42% in nursing home populations.
2. Symptoms and clinical features.
   There are manifold symptoms of sleep apnea and many of them masquerade this disorder. Hence, itemization of the presenting manifestations is worthwhile. These include:

   - Daytime somnolence.*
   - Chronic fatigue.*
   - Insomnia.*
   - Snoring, choking and snorting.*
   - Frequent nocturnal urination.
   - Dry mouth.
   - Decreased libido and impotence.
   - Nocturnal sweating.
   - Morning headaches.
   - None of the above symptoms should be attributed to OSA without adequate investigation. Nevertheless, OSA should be part of the differential diagnosis. The asterisks indicate hallmark characteristics.

3. Diseases aggravated or produced by OSA:
   - Augmentation of GERD.
   - Cardiac arrhythmias.
   - Stroke.
   - Pulmonary heart disease and right heart strain.
   - Impaired cognition.

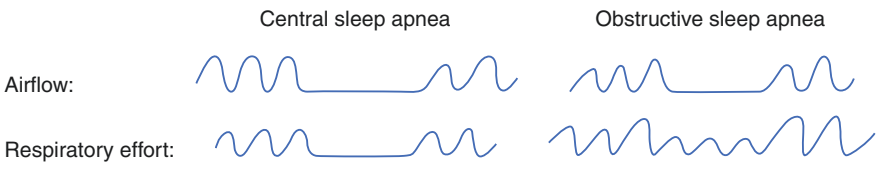

Fig. 11.5 Respiratory features of central and obstructive sleep apnea

- Hypertension.
- Sudden death.

4. Predisposing factors:
   - Obesity.
   - Nasopharyngeal abnormalities.
   - Retrognathia.
   - Micrognathia.
5. Pathogenesis
   OSA comprises about 84% of all cases of sleep apnea. It is an upper airway obstructive disorder particularly common in obese patients since pharyngeal muscles relax during sleep and they can be infiltrated by adipose tissue which results in further narrowing of the pharyngeal airway. Furthermore, in obese patients there may be enlargement of the tongue, uvula, and palate causing additional constriction of the airway passage. Other factors which play a contributing role are cigarette smoking, age, male gender, and use of alcohol or hypnotics. The age factor may correlate with the observed increase in weight of the elderly. Alcohol and hypnotics probably decrease the respiratory drive through their depressant effect on the CNS.

6. Manifestations in sleep.
   Patients with OSA may snort, gasp, choke, and snore heavily. There are body jerks and they may make flailing arm movements. They are nearly always heavy snorers which imply partial upper airway obstruction. Thus assessment of medical illnesses in patients who snore heavily warrants polysomnographic investigation.

7. Disease association.
   Hypertension and ischemic heart disease, the latter especially in men, are more prominent in heavy snorers. The prevalence of hypertension in habitual snorers is 10.5% as compared to 6.5% in non-snorers. The age-adjusted risk ratio of ischemic heart disease between often-snorers and non-snorers is 1.9. Smoking and alcohol are additive factors.

   Snoring and brain infarction are associated. The risk ratio of cerebral infarction between habitual snorers and occasional or nonsnorers is 10.3. In one study of 70 patients with cerebral infarctions during sleep, 68.6% were habitual snorers. Arterial hypertension is common in patients who have OSA but in epidemiological studies habitual snoring persisted as a risk factor for stroke even after an adjustment for arterial hypertension. Recent reports, using polysomnograms and demographic data, describe a clear association of severe sleep apnea (AHI equal or greater than 30) with increased risk of stroke or deaths from any cause. (AHI = apnea hypopnea index).

   The basis of increased cardiovascular and stroke risk may be due to increased sympathetic nervous system activity because of the work required to breathe which results in an increased heart rate and blood pressure. This increased activity can lead to an enlarged heart and arrhythmias with their attendant consequences of congestive heart failure, hypertension, and stroke.

8. Polysomnography features.
   Apnea durations often range between 20 and 40 s and must last 10 s with an associated drop in oxygen saturation to less than 90% to be considered significant. They occur in light sleep, stages 1 and 2, not deep sleep. Apnea is often associated with bradycardia and tachycardia. There must be five or more obstructive apneas per hour to confirm a diagnosis of obstructive sleep apnea. Hypopnea indicates air flow reduced by equal or greater than 30%.
   Apnea/Hypopnea Index (AHI) :

   Mild is 5–15.
   Moderate is 15–29.
   Severe is equal to or greater than 30 (Table 11.7).

Central Sleep Apnea

1. Clinical features and symptoms.
   Central sleep apnea (CSA) is relatively uncommon as it comprises about 10% of sleep apnea cases. It occurs in patients with a normal body habitus and snoring is not prominent; thus the diagnosis is often concealed. Symptoms differ somewhat from patients who have OSA. They include:

   - Chronic fatigue.
   - Insomnia, primarily difficulty maintaining sleep.
   - Daytime somnolence.
   - Morning headache.
   - Impaired cognition.
   - Depression.
   - Sexual dysfunction.

2. Diseases provoked or aggravated by CSA.

   - Hypertension.
   - Cardiac arrhythmias.
   - Congestive heart failure.
   - Pulmonary hypertension.

3. Predisposing factors, causes.
   - Congestive heart failure.
   - High altitude.
   - Neurologic disorders that affect central control.

4. Pathogenesis.
   The pCO_2 is the primary determinant of ventilation during sleep. Conversely, large fluctuations in the pO_2 around the normal range have little effect on ventilation efforts. CSA is probably due to an altered sensitivity to hypercapnia.

5. Manifestations in sleep.
   Gasping, choking, frequent body movements, and cyanosis.

Table 11.7 Diagnostic criteria for obstructive sleep apnea, adult. (Adapted from ICSD-3)[a]

(A and B) or C satisfy the criteria
A. The presence of one or more of the following:
1. The patient complains of sleepiness, non-restorative sleep, fatigue or insomnia symptoms.
2. The patient wakes with breath holding, gasping or choking.
3. The bed partner or other observer reports habitual snoring, breathing interruptions or both during the patient's sleep.
4. The patient has been diagnosed with hypertension, a mood disorder, cognitive dysfunction, coronary artery disease, stroke, congestive heart failure, atrial fibrillation or type 2 diabetes mellitus.
B. Polysomnography (PSG) or out-of-centre sleep testing (OCST) demonstrates:
1. Five or more predominantly obstructive respiratory events [obstructive and mixed apneas, hypopnoeas or respiratory effort-related arousals (RERAs)] per hour of sleep during a PSG or per hour of monitoring (OCST).
Or
C. PSG or OCST demonstrates:
1. Fifteen or more predominantly obstructive events (apneas, hypopnoeas or RERAs) per hour of sleep during a PSG or per hour of monitoring (OCST).

[a]American Academy of Sleep Medicine [37]

6. Disease association.
   Any disease which affects the medulla can cause CSA. Thus, patients with autonomic dysfunction such as in multiple system atrophy, neoplasms infiltrating or compressing the medulla, poliomyelitis and syringobulbia can suffer from CSA. Post-polio syndrome can affect medullary neurons earlier than spinal cord neurons and thus CSA can be the initial presenting problem.
7. Polysomnographic characteristics.
   Apnea lasts for 10–30 s followed by 10–60 s of hyperventilation. It usually occurs between wakefulness and sleep and when the patient is supine. One or more of these events are present:
   - Frequent arousals with apnea.
   - Bradycardia/tachycardia.
   - O_2 desaturations with apnea.

Criteria for diagnosis is an AHI equal or greater than 5 per hour; 5–15 is mild; 15–29 is moderate; equal or greater than 30 is severe (Table 11.8).

Sleep Stages

A brief summary of the staging of sleep is now timely. There are two broad sleep stages, rapid eye movement (REM) and non-REM (NREM). The latter is composed of N_1, N_2 and N_3 with N_3 as deep sleep, a combination of stages 3 and 4 in previous classifications. As sleep progresses the duration of REM increases and N_3 decreases. N_3 shortens with age. There are 4–6 cycles of REM and NREM sleep with each averaging 90–100 min. The staging is based on electroencephalographic (EEG) patterns. Details of these patterns are beyond the scope of this text:

Table 11.8 Diagnostic criteria for central sleep apnea (Adapted from ICSD-3)

Criteria A–D must be met.
A. The presence of at least one of the following:
1. Sleepiness.
2. Difficulty initiating or maintaining sleep, frequent awakenings or non-restorative sleep.
3. Awakening short of breath.
4. Snoring.
5. Witnessed apneas.
B. PSG demonstrates all of the following:
1. Five or more central apneas and/or central hypopnoeas per hour of sleep (PSG).
2. The number of central apneas and/or central hypopnoeas is >50% of the total number of apneas and hypopnoeas.
3. Absence of CSB.
C. There is no evidence of daytime or nocturnal hypoventilation.
D. The disorder is not explained more clearly by another current sleep disorder, medical or neurological disorder, medication use or substance use disorder.

CSB Cheyne-Stokes breathing, *PSG* polysomnography

1. N_1 lasts 5–10 min and comprises 5% of total sleep. Hypnic jerks (sleep starts) may occur.
2. N_2 lasts 10–25 min, considered light sleep and is 55% of total sleep.
3. N_3 lasts 20–40 min, is associated with a decrease in blood pressure and pulse and parasomnias. Examples of the latter include night terrors (pavor nocturnus), sleep talking (somniloquy), sleep walking (somnambulism) and sleep eating.
4. REM sleep comprises 20–25% of total sleep. Associated features include:
   (a) Rapid saccadic horizontal eye movements.
   (b) Muscle atonia.
   (c) EEG desynchronization (patterns change from slow to fast rhythms).
   (d) Dreaming.
   (e) More prominent late in sleep.
   (f) SOREMP. This stands for sleep onset REM period. It is pathologic if it occurs within 15 min of sleep onset. This finding is present in patients with narcolepsy.

Sleep-Related Movement Disorders

There is much confusion among clinicians about the most common of these four disorders. Each has unique characteristics and management/treatment differs. Periodic leg movements of sleep (PLMS) and hypnic jerks (HJ) are motor system disorders whereas, restless legs syndrome (RLS) and nocturnal leg cramps (NLC) are both sensory and motor with a prominent sensory component.

PLMS have wide ramifications. Prevalence in the elderly is nearly 50%. The movements are stereotyped, slow, and manifested by extension of the big toe with flexor movements at ankle, knee, and infrequently hip. They can begin with a myo-

clonic jerk but last up to 5 s and may occur two to three times per minute. They emerge in stage 1 or 2 sleep, not REM sleep. Partial arousal often occurs; thus sleep fragmentation with insomnia and daytime somnolence can result. Underlying disorders include iron and folate deficiency, anemia, renal failure, neuropathy, and radiculopathy. They may occur with other sleep disorders such as CSA, OSA, RBD, and narcolepsy.

RLS occurs prior to sleep onset and is characterized by an irresistible urge to move both legs. They are most common just after lying down at night. Patients may also awaken during the night severely symptomatic. It may be prevalent in daytime hours, especially when the patient rests. The arms may be affected. Patients describe "creeping," crawling, and tingling sensations in the calves, often asymmetric, lasting minutes to hours. They are relieved by movement; thus the patient often gets out of bed and walks around. The differential diagnosis includes akathisia but this disorder is not relieved with movement.

Features that support the diagnosis of RLS include the presence of PLMS which are evident in 80% of patients, a positive family history (autosomal dominant), and a good response to the standard treatment with dopamine agonists, pramipexole, or ropinirole. Dyskinesias do not emerge since nigrostriatal neurons are intact obviating denervation supersensitivity.

Disorders which precipitate or are associated with RLS include iron deficiency anemia, uremia, dialysis, rheumatoid arthritis, peripheral arterial disease, congestive heart failure, neuropathy, and Parkinson's disease. Incidence in pregnancy is quite high, 15% after the 20th week. Iron deficiency anemia, particularly with low ferritin levels, is important to recognize as iron supplements can be an effective remedy.

There are numerous alternative treatments should dopamine agonists be ineffective or iron supplements not indicated. These include clonazepam, gabapentin, baclofen, tramadol, pregabalin and, as a last resort, opioids.

NLC ("charleyhorses") are common, painful, involuntary muscle contractions which primarily affect calf and thigh musculature, last several minutes and are relieved by stretching. Plantar flexion is the most common manifestation. They awaken the patient and usually do not return immediately after stretching relieves the muscle contractions. These may be the underlying basis for chronic insomnia. The incidence increases with age and estimates of the prevalence are over 50% of people over age 50 although they may be isolated infrequent events.

The source of the cramps is most likely a high frequency discharge in the anterior horn cells. This may be related to our sedentary lifestyle with insufficient stretching of muscles and tendons. Perhaps this is analogous to release hallucinations, both visual and auditory, that may emerge from severe visual and auditory deprivation. Excessive exercise and muscle fatigue are likely additional provoking factors. Natural/environmental factors and diseases include pregnancy, alcoholism, dehydration, cancer and cancer chemotherapy, liver cirrhosis and hemodialysis. Patients with chronic renal disease treated with hemodialysis have been studied in more detail and, of particular interest, there is a correlation with high phosphorus and higher parathormone levels with nocturnal leg cramps. Altered calcium levels, high or low, do not show a definite association.

Medicines strongly associated with NLC include I.V. iron sucrose, conjugated estrogens, treatment with parathormone and raloxifene. Numerous reports have implicated other causes but most are not substantiated by high-quality studies. Perhaps the most important are the statins, diuretics (especially hydrochlorothiazide) and bronchodilators. Current useful treatments are few but these are most common: gabapentin is most successful and may require relatively high doses such as 600–800 mg. 1 h before bedtime, the calcium channel blockers verapamil and diltiazem, orphenadrine, magnesium and questionably vitamin B12. Quinine is no longer recommended since it decreases the excitability of the motor endplate which may result in a risk for cardiac arrhythmias. Additional numerous toxic side effects of quinine include thrombocytopenia, thrombotic thrombocytopenic purpura, interstitial nephritis and the hemolytic uremic syndrome.

HJ are sudden single muscle contractions in the legs occurring at onset of sleep and hence have been called sleep starts. Infrequently, the arms and head are involved. HJ are nearly universal experiences in the general population. Caffeine and other stimulants provoke them. The only medical care required is reassurance and avoidance of pharmacotherapy.

Parasomnias

These are normal or abnormal movements and behaviors occurring during sleep. They need to be understood and identified so that they can be differentiated from seizures. They may be related to either REM or non-REM sleep.

REM-Related Parasomnias

REM Sleep Behavior Disorder (RBD)

REM sleep comprises about 20–25% of sleep. Features include episodic bursts of REM, EEG activation with beta activity (greater than 13 Hz), and it is most prominent in the latter one-third of sleep. During REM sleep there is loss of muscle tone so that dreaming, which occurs during this sleep period, is unaccompanied by physical activity. In REM sleep behavior disorder, muscle atonia is absent and thus violent dreams are likely to be accompanied by violent physical activity. This disorder occurs primarily in the elderly population, especially beginning in the sixth or seventh decades, and about 80% of the patients are male.

The abnormal behavior can be simple or complex motor, and/or verbal. Manifestations of simple behavior include laughing, swearing, crying as well as limb and body jerking. Complex behavioral features are often aggressive such as reaching out to grab the bed partner, kicking, punching, jumping out of bed, and running.

Clinical criteria for the diagnosis, as described above, are insufficiently specific. Other diagnoses such as night terrors (pavor nocturnus in children, incubus in

adults), nightmares, sleepwalking (somnambulism), obstructive sleep apnea, post-traumatic stress disorder, confusional arousal, and nocturnal seizures can produce similar behavior. Polysomnography provides the required evidence to document the diagnosis since the abnormal sleep behavior must occur during REM sleep.

RBD occurs in diseases associated with alpha-synuclein deposition. The most common is Parkinson's disease but it may also occur in multiple system atrophy, Lewy body disease and progressive supranuclear palsy. The incidence of development of such a disorder after RBD onset may reach 40% over a 10-year period.

Specific medicines can aggravate or induce RBD. These include tricyclics, MAO inhibitors, SSRIs or SNRIs, tramadol and bisoprolol. Caffeine, nicotine and alcohol may aggravate RBD and should be avoided. Current treatments are clonazepam and melatonin.

Nightmare Disorders

Nightmares or threatening dreams occur in the last third of the night during REM sleep. The patient recalls the dream and when awakened has normal cognition.

Sleep Paralysis

This often occurs with narcolepsy but can be a sole symptom. During this period, usually a few minutes, there is a flaccid paralysis with areflexia but retention of eye and chest movements. The patient is severely anxious and may have a sense of suffocating. A touch or sound may terminate the episode which occurs commonly at the end of a REM sleep period.

Non-REM-Related Parasomnias

1. Sleep terrors (pavor nocturnus in children, incubus in adults).
   These are manifestations of extreme fright with concomitant autonomic discharges manifested by diaphoresis, pupillary dilatation, tachycardia, and tachypnea. The phenomena are initiated by a piercing scream and erupt from slow wave sleep (N_3) in the first third of the night. A common provoking scenario is attempting to arouse a child. There is complete amnesia for the event.

2. Sleepwalking (somnambulism)
   This occurs during slow wave sleep and when awakened the patient is often confused. It can be associated with somniloquy (sleeptalking). Inappropriate behavior is not unusual such as urinating in a corner of a room.

3. Confusional arousal.
   Physical violence can be precipitated by sleep drunkenness. This typically occurs with forced awakening from slow wave sleep in the first third of the night. Upon

arousal the patient is disoriented and thinking is slow. The duration varies from several minutes to several hours. Restraining the patient can provoke aggression. This is most common in children.

4. Nocturnal paroxysmal dystonia.
   During non-REM sleep, N_2 or N_3, the individual exhibits complex motor behavior, especially dystonic but occasionally ballistic or choreoathetoid. These are either brief, less than 1 min, or prolonged attacks lasting up to 1 h. The brief spells simulate frontal lobe seizures and have been described as extrapyramidal seizures. Although they are most common in infants they have been reported to begin in middle age. They respond to anticonvulsant treatment.

5. Sleep bruxism.
   This is a common stereotyped movement disorder manifested by grinding and crunching of the jaws. Bruxism is most prevalent during N_1 and N_2 sleep. It is often associated with anxiety and is common in children with mental retardation and cerebral palsy. Complications include excessive wear on the teeth, temporomandibular joint pain, and periodontal disease. The diagnosis can be particularly important since the noise of bruxism may raise the question of seizures.

Other Parasomnias, Sleep-Wake Transition

1. Rhythmic movement disorders.
   These are stereotyped repetitive movements mostly occurring in infants and children usually at sleep onset. The movements primarily involve the head, neck, and body. Head banging against the wall (jactatio capitis nocturna) can easily be misinterpreted as a seizure particularly when heard but not witnessed. Rarely there are skull injuries. Prolonged, repetitive, forward and backward body rocking is another manifestation.

2. Sleeptalking (somniloquy).
   The individual speaks briefly or utters sounds without emotional content. It occurs in all sleep stages but most often with REM sleep.

Chronic Primary Insomnia

Chronic primary insomnia (CPI) [42] is an accurate diagnosis provided two conditions are met; there is nonrestorative sleep which interferes with work or social life and the insomnia is not secondary to drug use, medical disease, psychiatric illness, or another sleep disorder. Thus sleep apnea, parasomnias, and circadian dysrhythmias

cannot be present. Acute insomnia is less than 1 month, subacute 1–6 months and chronic greater than 6 months duration.

Common medical conditions that interfere with sleep include asthma, chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), gastroesophageal reflux disease (GERD), rheumatic disorders, endstage renal disease (ESRD), and hyperthyroidism. Common substances that interfere with sleep are caffeine, nicotine, alcohol, and illegal drugs. Perhaps the most important illness to consider is depression since sleep disorders are an integral part of the depressive diathesis as well as its common predecessor.

Treatment approaches for CPI focus on behavior, sleep hygiene, and lastly, pharmacotherapy. Behavioral techniques and education should take precedence. Some of the principles are self-evident:

1. Go to bed when sleepy.
2. Use the bedroom only for sleep and sex.
3. Avoid prolonged daytime naps.
4. Avoid TV or i-phone use in bed since exposure to bright light has an arousing effect.
5. Include regular exercise in daytime activities.
6. Get out of bed at the same time daily, irrespective of the amount of sleep.
7. Avoid caffeine, alcohol, nicotine, and stressful activities in the evening.

There are different opinions on pharmacologic therapy. My view is to use medications that have a short half-life such as zaleplon and zolpidem which have half-lives of 1 and 2.5–3 h, respectively. These are agonists at the benzodiazepine receptor component of the GABA receptor complex and are less likely to interfere with sleep architecture. Short-term treatment is the goal. An extremely effective benzodiazepine is alprazolam. Although this medicine is notoriously addictive, a dose of 0.125–0.5 mg given only at bedtime is a lifesaver for many patients. Intermittent use is always the goal. Trazodone, a weak SSRI, is often quite helpful. Standard SSRIs are additional options but their successful use implies the presence of depression or generalized anxiety disorder as the underlying etiology. Psychological intervention should be considered and the topic at least broached with patients although many are resistant. Mirtazapine is a very potent sedating antidepressant and particularly efficacious. The adverse effects of increased appetite, weight gain, and daytime somnolence associated with a long half-life of 20–40 h makes its successful long-term use unlikely. Lastly, quetiapine 25–50 mg at bedtime, with a half-life of only 6 h, may be very useful.

Problematic drugs, especially in the elderly, should be recognized. The tricyclic compounds such as amitriptyline, nortriptyline, and doxepin should not be initiated, if at all, because of their anticholinergic side effects. These include cardiac arrhythmias, impaired cognition, somnolence, orthostatic hypotension, aggravation of glaucoma and prostate disease, decreased sexual function, and exacerbation of psychosis. A general principle is to avoid their use in elderly patients. Antihistamines, an ingredient of over-the-counter drugs, are used with success in younger individuals

but in the elderly often cause grogginess and impaired cognition the following day. Specifically, diphenhydramine (Benadryl) should be avoided. Sedatives which have a longer half-life such as flurazepam and, to a lesser extent temazepam, are useful only if there is concomitant chronic anxiety which can be ameliorated the following day. They are rarely, if ever, indicated.

The serious adverse consequences of hypnotics in general, but particularly those with long half-lives, include aggravation of depression, daytime somnolence, impaired cognition, and increased risk of falls.

Central Disorders of Hypersomnolence

Narcolepsy and Cataplexy

The excessive daytime somnolence (EDS) of narcolepsy has several unique characteristics. There is an irresistible urge to sleep but the naps are short, refreshing, and typically last only 15–20 min. The sleep attacks commonly occur at inappropriate times such as driving, eating or in the midst of conversations. Automatic behavior, perhaps due to "microsleeps," may occur after which patients have no recollection of what has transpired. They may describe them as blackouts or memory lapses. Reported behaviors have included putting vegetables in the dishwasher or taking incomprehensible notes at a lecture. Differentiating these events from focal motor or nonmotor seizures with impaired awareness (complex partial seizures with automatisms) is critical. Nocturnal sleep is usually disturbed in narcoleptic patients. There are frequent awakenings some of which may be due to RBD and PLMS.

The main criterion for the diagnosis of narcolepsy is the presence of cataplexy [38], a sudden loss of muscular tone typically provoked by a surprise or sudden, forceful, emotional event. Ordinarily it lasts less than 2 min. It is often manifested by a fall, head drop, or jaw opening. Falls can be associated with injury or put the patient at risk. One such alarming incident described by a patient was an abrupt collapse while crossing a street when observing a car approaching her at an unexpectedly rapid speed. The famous tetrad of narcolepsy adds two other common but not required phenomena. These are sleep paralysis, an occurrence upon awakening or falling asleep, a complete loss of motor function with retention of eye and respiratory movements lasting seconds to several minutes. This may be an isolated phenomenon and hence is not diagnostic of narcolepsy. Hypnagogic and hypnopompic hallucinations may occur, the former at sleep onset and the latter on awakening. These can be auditory, visual, or somesthetic. The latter is a sense of feeling touched or an out-of-body experience. To some patients the hallucinations appear so real that the specter of schizophrenia is raised (Table 11.9).

Table 11.9 Diagnostic criteria for narcolepsy types 1 and 2 (adapted from ICSD-3)

Criteria A and B must be met.
Narcolepsy type 1
A. The patient has daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for at least 3 months.
B. The presence of one or both of the following:
1. Cataplexy (as defined under "Essential features") and a mean sleep latency of ≤8 min and two or more sleep-onset REM periods (SOREMPs) on an MSLT performed according to standard techniques. A SOREMP (within 15 min of sleep onset) on the preceding nocturnal polysomnogram may replace one of the SOREMPs on the MSLT.
2. CSF hypocretin-1 concentration, measured by immunoreactivity, is either ≤110 pg mL^{-1} or < 1/3 of mean values obtained in normal subjects with the same standardized assay.
Criteria A-E must be met.
Narcolepsy type 2
A. The patient has daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for at least 3 months.
B. A mean sleep latency of ≤8 min and two or more sleep-onset REM periods (SOREMPs) are found on a MSLT performed according to standard techniques. A SOREMP (within 15 min of sleep onset) on the preceding nocturnal polysomnogram may replace one of the SOREMPs on the MSLT.
C. Cataplexy is absent.
D. Either CSF hypocretin-1 concentration has not been measured or CSF hypocretin-1 concentration measured by immunoreactivity is either ≤110 pg mL^{-1} or < 1/3 of mean values obtained in normal subjects with the same standardized assay.
E. The hypersomnolence and/or MSLT findings are not explained more clearly by other causes such as insufficient sleep, obstructive sleep apnea, delayed sleep phase disorder or the effect of medication or substances or their withdrawal.

CSF cerebrospinal fluid, *REM* rapid eye movement, *MSLT* Multiple Sleep Latency Test

Physiology of Sleep and Narcolepsy

Diagnostic Criteria for Narcolepsy

A brief discussion of the physiology of narcolepsy is warranted. Hypocretins (also called orexins) are produced and secreted by neurons located in the posterior hypothalamus. Ninety percent of narcoleptic patients have low CSF levels [41]. Hypocretin neurons excite brainstem neurotransmitter systems, locus ceruleus (norepinephrine), dorsal raphe of pons (serotonin), substantia nigra (dopamine), and lateral dorsal tegmental (LDT)/pedunculopontine tegmental (PPT) area (acetylcholine). During REM sleep there is activation of the LDT/PPT neurons and inactivation of other brainstem neurotransmitter systems. Additionally, the basal forebrain (acetylcholine) and tuberomammillary nucleus (histamine) neurons are activated. Conversely, neurons in the anterior hypothalamus (GABA-producing) promote non-REM sleep via projections to the thalamus and brainstem nuclei.

Hypocretin-producing neurons are reduced in number in the posterior hypothalamus [40]. This has been documented by proton MR spectroscopy. N-acetylaspartate

(NAA) is the neuronal marker which can be used to measure the number of neurons. The number is reduced in the hypothalamus of narcoleptic patients with or without cataplexy. The etiology is unknown but there is an autoimmune hypothesis supported by successful treatment with intravenous immunoglobulin of a patient at the onset of the illness.

Treatment of cataplexy includes sodium oxybate, SSRIs, and SNRIs. Sodium oxybate is used immediately before bed and stimulates GABA receptors. To reiterate, GABA-producing neurons in the anterior hypothalamus promote non-REM sleep. Narcolepsy can be treated with modafinil, methylphenidate, or amphetamines. Modafinil is the first choice since it is long-acting, has little abuse potential and has been proven efficacious in a double blind, placebo-controlled study. Methylphenidate and amphetamines increase dopamine and norepinephrine release at the synapse and block their reuptake.

The Epworth's Scale is a particularly good screening test for narcolepsy. It is quick and easy to administer. Perhaps the most accurate diagnostic measure for narcolepsy in the near future will be the measurement of CSF hypocretin-1 (orexin) concentration but this is not currently easily available. MR spectroscopy may also become a prime diagnostic test in equivocal cases. Polysomnography and the multiple sleep latency test will remain the gold standard for the diagnosis of narcolepsy for the foreseeable future.

Epworth's Sleepiness Scale (ESS)

A measurement of the general level of daytime sleepiness.

Epworth Sleepiness Scale (ESS)

This questionnaire will help your physician to measure your general level of daytime sleepiness.

How likely are you to doze off or fall asleep in the situation described below, in contrast to feeling just tired?

This refers to your usual way of life in recent times.

Even if you haven't done some of these things recently, try to work out how they would have affected you.

Use the following scale to choose the most appropriate number for each situation.

0 = *would never doze* **1** = *slight chance of dozing* **2** = *moderate chance of dozing* **3** = *high chance of dozing*

Situation	Chance of dozing			
Sitting and reading	0	1	2	3
Watching TV	0	1	2	3
Sitting, inactive in a public place (e.g. a theater or a meeting)	0	1	2	3

Situation	Chance of dozing			
As a passenger in a car for an hour without a break	0	1	2	3
Lying down to rest in the afternoon when circumstances permit	0	1	2	3
Sitting and talking to someone	0	1	2	3
Sitting quietly after lunch without alcohol	0	1	2	3
In a car, while stopped for a few minutes in traffic	0	1	2	3
Total your score in each column Combine column totals				

If your score is 10 or higher, you should discuss these results with your doctor
Epworth Sleepiness Scale used under license. © 1990–1997 MW Johns

Additional Narcolepsy Symptoms

Please take a minute to answer the following questions to determine if you may suffer from narcolepsy.

1. I sometimes experience muscle weakness or a loss of muscle strength when I laugh or get angry.	*YES*	*NO*
(a) If yes to #1, I sometimes avoid emotional situations because of these episodes of muscle weakness/loss of muscle strength.	*YES*	*NO*
2. I have no problem falling asleep at night, but have trouble sleeping through the night.	*YES*	*NO*
3. I sometimes experience a brief period upon waking or falling asleep where I want to get up but cannot move a muscle or speak.	*YES*	*NO*
4. I often have very vivid and/or frightening dreams when I sleep.	*YES*	*NO*

If you answered YES to one or more of the situations, we recommend you consult your doctor
Your doctor can determine if you should be screened or tested for narcolepsy

Idiopathic Hypersomnia

Idiopathic hypersomnia comprises 5–10% of patients evaluated at sleep disorder clinics. The clinical features are considerably different than those of narcolepsy. Patients are usually less than age 25 at onset. The condition is marked by long periods of sleep, normal nocturnal sleep and yet, patients remain drowsy throughout the day. They have prolonged naps of 1–2 h which are composed of non-REM, non-refreshing sleep instead of the brief 15–20-min naps of patients with narcolepsy who feel rejuvenated. MSLT discloses short latencies of less than 10 min but a normal latency of REM sleep. Associated symptoms may include Raynaud's syndrome, syncope and orthostatic hypotension all of which suggest concomitant autonomic dysfunction. Headache disorders are common. Treatment is the same as for narcolepsy other than avoiding sodium oxybate. Adverse reactions to medical treatment are more common compared to patients with narcolepsy (Table 11.10).

Table 11.10 Diagnostic criteria for idiopathic hypersomnia (Adapted from ICSD-3)

Criteria A–F must be met.
A. The patient has daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for at least 3 months.
B. Cataplexy is absent.
C. An MSLT performed according to standard techniques shows fewer than two sleep onset REM periods or no sleep onset REM periods if the REM latency on the preceding polysomnogram was ≤15 min.
D. The presence of at least one of the following:
1. The MSLT shows a mean sleep latency of ≤8 min.
2. Total 24-h sleep time is ≥660 min (typically 12–14 h) on 24-h polysomnographic monitoring (performed after correction of chronic sleep deprivation), or by wrist actigraphy if the patient has daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for at least three associations with a sleep log (averaged over at least 7 days with unrestricted sleep).
E. Insufficient sleep syndrome is ruled out (if deemed necessary, by lack of improvement of sleepiness after an adequate trial of increased nocturnal time in bed, preferably confirmed by at least a week of wrist actigraphy).
F. The hypersomnolence and/or MSLT findings are not explained more clearly by another sleep disorder, other medical or psychiatric disorder or use of drugs or medications.

REM rapid eye movement, *MSLT* Multiple Sleep Latency Test

Other Central Disorders of Hypersomnolence

1. Kleine-Levin Syndrome. Episodic hypersomnolence, hyperphagia and hypersexual behavior.
2. Hypersomnia due to a medical disorder, medicine or substance.
3. Hypersomnia associated with a psychiatric disorder.
4. Insufficient sleep syndrome.

General Criteria for Circadian Rhythm Sleep-Wake Disorder

Circadian dysrhythmias are a misalignment between the natural endogenous circadian clock which is 24.2 h and the social/physical environment. The circadian clock is located in the suprachiasmatic nucleus of the hypothalamus. Light is the stimulus which affects this rhythm. Melatonin, produced by the pineal gland, is the modulator of this system. Its secretion is controlled by neurons in the suprachiasmatic nucleus. The two most commonly recognized of these disorders are jet lag and shift work. The physiology of this symptom and management techniques are beyond the scope of this text (Table 11.11).

Other Transient Neurologic Symptoms

The majority of transient neurologic symptoms have been covered. But there are additional neurologic occurrences which may be more challenging to diagnose. This section will contain a cursory review of important symptoms and a few rare

Table 11.11 General criteria for circadian rhythm sleep-awake disorder. (Adapted from ICSD-3)

Criteria A–C must be met.
A. A chronic or recurrent pattern of sleep-awake rhythm disruption due primarily to alteration of the endogenous circadian timing system or misalignment between the endogenous circadian rhythm and the sleep-wake schedule desired or required by an individual's physical environment or social/work schedules.
B. The circadian rhythm disruption leads to insomnia symptoms, excessive sleepiness or both.
C. The sleep and wake disturbances cause clinically significant distress or impairment in mental, physical, social, occupational, educational or other important areas of functioning.

conditions. The purpose of including rare phenomena is to stimulate an interest in carefully listening to and observing patients as well as to avoid discarding descriptions as either inconceivable or psychogenic. A misdiagnosis may cause long-lasting harm to both patients and their families. Three case reports will be presented consecutively followed by the answers.

"Drop Attack" (The Sudden Inexplicable Fall)

Case 43 A 42-year-old man complains of several falling episodes without warning. His physician questions him about what he was doing at the instant of falling. Did he briefly lose consciousness and does he remember hitting the ground? Did he have chest pain, palpitations, sweating, nausea, dizziness, visual disturbance, sudden weakness, or numbness of one or more extremities? The patient replies that while shopping at the supermarket he unexpectedly ran across an old college friend he had not seen for 15 years. Neurologic examination is normal.

What questions were omitted that could have easily led to the diagnosis?

Case 44 A 58-year-old woman has fallen on several occasions over the past year. She brings her daughter who is invited to share her observations. She has observed her mother to collapse abruptly sometimes striking her head and never able to break the fall. The patient feels as though she is thrown to the ground. She denies headache, visual disturbances, vertigo, altered speech and memory, nausea, sweating, numbness or weakness of the extremities, and impaired balance. The neurologic examination is normal.

What questions were omitted that might lead to the diagnosis?

Case 45 A 37-year-old male, a high-achieving mechanical engineer, is brought to his internist by his wife because of several abrupt falls which occurred without evident provocation over the previous 3 months. The patient reports tripping but his wife says the sidewalks are smooth and without obstacles. Moreover, he denies all neurologic complaints and exhibits no overt signs of fear or anxiety. His wife reports that she believes her husband was unsteady on those occasions. Neurologic examination is normal including a thorough mental status examination.

Problem: How does one distinguish pathological denial (anosognosia) from willful prevarication, ignorance, or a behavioral quirk such as fear of physicians?

Anosognosia is usually generalized to all questions and accompanied by dementia such as Alzheimer's disease or a nondominant hemisphere lesion. These disorders are easily exposed after additional history followed by an assiduous neurologic examination. The normal patient who is anxious and brought in under duress, after a few moments of adjustment, ordinarily replies truthfully to other questions. The patient described above fits the category of prevarication.

What part of the history should be meticulously and dexterously handled?

Answers:

Case 43:

Do you feel drowsy during the day? Other related questions might include: Has this occurred to you on other occasions when you were surprised? Do you wake up at night and find that you are unable to move? Do you have visual hallucinations when you are falling asleep or waking up?

The patient responds yes to all questions and adds that he frequently dozes at inopportune times such as momentarily when driving or when stopped at a red light.

Diagnosis: Narcolepsy.

Comment: This patient has the full tetrad of findings, sleep attacks, cataplexy, sleep paralysis, and hypnagogic hallucinations. The patient's sudden fall was due to cataplexy provoked by the surprise of meeting an old college friend.

Case 44:
The patient is asked: Do you have a loss of hearing or ringing in the ears? She responds: I have poor hearing and ringing in my right ear.

Diagnosis: Ménière's disease.

Comment: The condition is called an otolithic crisis or Tumarkin's otolithic crisis [50]. The etiology is presumed to be a sudden disturbance of otolithic function due to hydrops. This affects the vestibulospinal system and precipitates loss of postural tone.

Case 45:
The social history must be thoroughly investigated. Alcohol abuse or use of drugs must be suspected. Questions might include: "How many days per week do you have an alcoholic beverage and what is the average number of drinks on those days?" "What would be the maximum number?" The latter is most likely to be the average number. Look at the patient's wife who often winces in disagreement when her husband underestimates his alcohol consumption but she remains quiet to prevent an anger outburst from him. Patients often demand some objective confirmation of excessive consumption. The examination of vibration sense is the most useful. For how long does the patient perceive vibration at the toes? Commonly, it is decreased to adaptation and someone else in the room senses vibration when the tuning fork is transferred to their toes after not being perceived by the patient.

Macrocytic blood indices are common and may persuade some patients to take their alcohol consumption seriously. Liver functions and thiamin levels are usually normal in patients who function well.

Diagnosis: Alcoholism with prevarication.

Case 46 A 45-year-old retarded woman is brought to her family physician because of many sudden falls over the last year. She is the product of a complicated breech delivery, delayed developmental milestones, and numerous seizures in childhood. These were myoclonic, atypical absence, rarely focal motor or nonmotor with impaired awareness (complex partial), and generalized tonic–clonic. Treatment with valproate and zonisamide reduced the frequency of generalized tonic-clonic seizures to 2–3 per year and just a few myoclonic jerks daily. Her neurologic examination is unremarkable other than mental retardation manifested by the attainment of only a fourth grade level of education.

What is the etiology of these falls?
Do you know the name of this syndrome?

Case 47 A 63-year-old man suddenly collapsed on the floor in the airport without warning. He denied loss of consciousness. He looked pale, felt cold, and his skin was moist when he was examined by a physician who rushed over to attend to him arriving only 2 min after the fall. His pulse was strong and regular at 72 beats per minute. A medical examination performed 10 min later in the airport clinic was normal. He reported that an identical event occurred on one previous occasion at home. General physical and medical examinations were also normal performed a few hours after this first episode.

What is the most likely diagnosis and what specific test is indicated?

Case 48 A 77-year-old woman has fallen without warning on three occasions over the past 2 weeks. She reports that her legs suddenly gave way and she could not break her falls. She has a longstanding history of hypertension and smoked one pack of cigarettes per day until 10 years ago. Several years ago she had three episodes of double vision lasting about 10 min each. She recalls that they were associated with a striking tilt of the environment of about 45°. Neurologic examination is normal.

What is the most likely diagnosis?

Answers:

Case 46:

These falls are likely to be caused by astatic (atonic) seizures. The etiology is sudden loss of muscular tone or sudden tonic spasms with abrupt falling. They are often accompanied by myoclonus.

Diagnosis: Lennox–Gastaut syndrome.

Comment: This syndrome usually begins between ages 1 and 8 years and is manifested by the triad of multiple seizure types, retardation, and EEG findings of slow spike-wave discharges (less than 3 Hz). The latter were recorded in this patient.

Underlying etiologies, present in most patients, include congenital malformations, neurocutaneous disorders such as tuberous sclerosis, hypoxic-ischemic encephalopathy and CNS infections.

Case 47:
Pallor, moist and cold skin occurs with syncope. Cardiac arrhythmia is suspected since there were none of the usual premonitory signs of hypotension. Since this is the patient's second episode a critical cardiac arrhythmia is most likely.

Diagnosis: Probable cardiac syncope.

Comment: Other cardiac diseases must be considered such as aortic stenosis and obstructive hypertrophic cardiomyopathy as well as pulmonary embolism. A 24-h Holter monitor followed, if normal, by a 30-day monitor should be performed. A prompt cardiology consultation is mandatory.

Case 48:
This patient had double vision which may occur with brainstem, cranial nerve or neuromuscular junction pathology. The short duration is most compatible with transient brainstem ischemia although an aneurysm with intermittent compression of a cranial nerve is a remote consideration. Myasthenia gravis may present itself with transient diplopia, especially late in the day, when the patient is fatigued. The visual illusion of a tilted environment occurs with vestibular dysfunction, peripheral or central (brainstem). Sudden loss of strength affecting both legs suggests involvement of the corticospinal tract although, as previously noted in preceding case reports, an astatic (atonic) seizure and otolithic crisis may provoke a similar event. Thus the only anatomic localization compatible with all three symptoms, double vision, tilt of the environment and leg weakness, is the brainstem. The short duration supports a transient ischemic attack (TIA). An MRA (head and neck) revealed a high-grade mid-basilar artery stenosis and the MRI (brain) disclosed ischemic changes in the basis pontis, the location of the corticospinal tracts.

Diagnosis: Transient ischemic attack secondary to basilar artery stenosis.

Confusion/Amnesia

Case 49 A 52-year-old man asks his wife what concert they were planning to attend. They had just finished dinner and discussed the event 2 min before. His startled wife reminded her husband. They got into their car with the patient driving. He asked his wife "Where are we going?" His question came after 15 min of highway driving. He appeared puzzled and she insisted that they return home. He drove home uneventfully. She excused his behavior as due to overwork, lack of sleep and believed that a nap would restore him to normal. After a nap of 45 min she awakened him. He appeared annoyed and asked the identical question "Where are we

going?" She replied, "To the Emergency Room." When the Emergency Room physician walked into the examining room the patient became alarmed and said "How did I get here? I don't remember anything since dinner except briefly driving into the garage" on their return home earlier that evening. He complained of a dull, generalized headache. The neurologic examination including a detailed mental status evaluation was normal.

What is this syndrome called and what is a currently proposed etiology?
What other neurologic disorder is this syndrome associated with?

Answers:

Diagnosis: Transient global amnesia [47].

Comment: This is a well-known although uncommon syndrome which often prompts an Emergency Room visit as the patient suddenly becomes aware that he has lost his memory for the preceding hour to several hours and may find himself in an unexpected location. During the period of amnesia, most often 2–8 h, rarely longer, the patient can appear to function normally except for asking the same questions repeatedly due to absence of short-term recall. There may be islands of memory such as this patient had as he recalled driving into his garage.

Studies have shown dysfunction of neurons in the hippocampus [49]. Diffusion-weighted imaging MRI studies have disclosed hyperintensities in this region for a few days afterwards. Etiologic speculations include glutamate release producing metabolic stress on the susceptible neurons, venous flow abnormalities and transient epileptic amnesia (TEA).

There is a strong association with migraine and many patients do complain of headaches afterwards, although often mild and nonspecific. Some precipitating factors include: sexual intercourse, Valsalva maneuver, exposure to hot or cold water, traumatic emotional experiences and use of marijuana and scopolamine.

Transient Visual Impairment

Case 50 A 38-year-old woman complains of frequent "blackouts" affecting either eye which last seconds. These have occurred numerous times usually affecting the left eye, rarely the right or bilateral. When they began 4 months ago they occurred about twice weekly but now several times per day. The past medical history is entirely negative and the patient takes no medications. She has been on the Adkin's diet for obesity and now weighs 190 lb. at 5′3″ tall. She weighed 240 lb. 1 year ago. An MRI scan of the brain is normal.

1. What additional questions would lead to the diagnosis?
2. What part of the neurologic examination is most important?
3. What test confirms the diagnosis?

Case 51 A 65-year-old man complains of a gray curtain being drawn across his right eye from right to left lasting 30 s and completely obliterating his vision. The visual loss persists for 3–4 min. These episodes have occurred 10–15 times over the last 6 weeks. The most recent occurrence was 10 min ago while in the waiting room. He has type II diabetes controlled with metformin.

1. What may be seen on funduscopic examination?
2. What is the etiology?
3. Is the manner of the loss of vision horizontal or vertical (like a curtain descending) of diagnostic significance?
4. What is the diagnosis?

Case 52 A 52-year-old woman complains of repeated episodes of brief loss of vision O.S. when walking into a brightly lit environment. This has occurred daily for 3 months and is increasing in frequency such that she expects loss of vision every time she leaves the house on a sunny day. Her past medical history is remarkable for hypertension and smoking two packs of cigarettes per day.

Neurologic examination: Blood pressure is 140/90. There are no carotid bruits. The entire neurologic examination is normal other than the funduscopic exam. This shows dot and blot hemorrhages in the midperiphery region associated with dilated retinal veins and arteriolar narrowing.

1. What does this funduscopic picture suggest?
2. Why does the patient lose vision in bright light?
3. What is the most likely cause?

Case 53 A 28-year-old woman complains of loss of vision O.S. when she looks to the left. This symptom has been present for 1 month. She has no illnesses. The neurologic examination is normal except for diminished color perception O.S. Visual acuity is 20/20 O.U. She has a left RAPD (relative afferent pupillary defect).

1. What causes decreased color perception?
2. What could be the etiology of this rare condition?

Answers:

Case 50:

1. Do you have headaches? The history of brief visual loss affecting either eye alone or rarely both eyes simultaneously is typical of papilledema. She replies that she has had daily generalized throbbing headaches for 2 weeks. Have you experienced double vision? Yes, if she looks far to the left.
2. Funduscopic examination. The three cardinal signs of papilledema are blurred optic disk margins, absence of venous pulsations (usually lost when intracranial pressure exceeds 200 mm H_2O), and hemorrhages at the disk margin. Only the presence of hemorrhages secures the diagnosis as the other two elements can occur as a normal variation. It must be emphasized that, apart from these events,

most patients with papilledema have normal vision. This formerly morbidly obese patient has papilledema and normal vision. When looking to the left she has horizontal diplopia even though there is no obvious ocular paresis. Red glass testing is used with the glass covering O.D. the most lateral image is white which confirms a left lateral rectus or 6th nerve lesion, a common sign of increased intracranial pressure.

Diagnosis: Pseudotumor cerebri (idiopathic intracranial hypertension).

Comment: A lumbar puncture confirms the diagnosis as the opening pressure is 280 mm H_2O. Normal opening pressures are <200 mm H_2O. However, 200–250 mm H_2O is considered borderline.

Case 51:

1. Gray particles, which are platelet-fibrin emboli, may be seen passing through the retinal arterioles. Hollenhorst plaques are yellow, glistening, lodge at vessel bifurcations, arise and embolize from plaques in the aorta or carotid arteries. They are commonly seen in asymptomatic patients. Chalky white plaques which are composed of calcium originate and embolize from calcified aortic or mitral valves.
2. The etiology is usually embolism from extracranial carotid atheromatous disease.
3. No.
4. *Diagnosis*: Transient ischemic attacks secondary to a severe left internal carotid artery stenosis with embolism to the ophthalmic and central retinal artery.

Comment: The most common mechanism of TIAs associated with critical (>95%) carotid stenoses remains embolism. Good collateral circulation is not protective and definitive treatment by endarterectomy or stent should be employed.

Case 52:

1. Chronic low perfusion. The slowed circulation time causes focal dilation and congestion of retinal veins. There is a breakdown of capillary walls producing infarctions with hemorrhage. This is venous stasis retinopathy [51].
2. Exposure to bright light requires increased retinal metabolism which cannot be sustained because of chronic retinal ischemia.
3. Critical stenosis or occlusion of the ipsilateral internal carotid artery. Angiography revealed a nearly occluded left internal carotid artery with a few but insufficient collaterals arising from a patent external carotid artery. Bruits are not always present with severe carotid artery disease.

Diagnosis: Transient ischemic attacks of hemodynamic origin due to a high-grade stenosis of the left internal carotid artery associated with venous stasis retinopathy [51].

Comment: This is a rare clinical syndrome but well-documented. Endarterectomy or stenting should be curative.

Case 53:

1. Optic nerve pathology.
2. An orbital mass lesion produced torsion and stretching of the optic nerve with leftward eye movement.

Diagnosis: Orbital metastasis from carcinoma of the breast.

Comment: An early sign of optic nerve pathology is usually impaired light and/or color perception which precedes a decline in visual acuity.

Transient Visual Illusions and Hallucinations

Case 54 A 95-year-old woman requests an evaluation for visual hallucinations. She sees idyllic country scenes which include farmers and cattle moving about in brownish-green pastures. The hallucinations occur frequently, are present for a few minutes, and appear most often in a dimly lit environment. She is not frightened but rather curious about them.

Neurologic examination discloses bilateral, positive, central scotomas plus visual acuities of 20/200 O.U. The pupils are normal. Specifically, there is no afferent pupillary defect.

1. What is a positive central scotoma and what is its anatomic source?
2. What is the etiology of the hallucinations and what name is attached to them?

Case 55 A 48-year-old man complains of frequent visual hallucinations occurring simultaneously with smelling "rotten eggs." The hallucinations are composed of seeing little men, wearing overalls and working on machinery, in his left visual field. They are only a few inches tall and they approach him without any visible sign of hostile intent.

The neurologic examination reveals a left superior homonymous quadrantanopsia.

1. What is the name of these hallucinations?
2. What single question will determine the mechanism of these events?
3. Where is the lesion?

Case 56 *An unusual phenomenon*

A 47-year-old man was referred for neurologic evaluation because of persistent visualization of a television scene after turning away from the TV set to answer a question from his wife who stood on his left side. He observed the same picture he just saw on the TV superimposed on his wife. It lasted nearly 3 min, occurred 1 month ago, and he has had 5 similar episodes since then. Past medical history is negative for any illnesses. He takes no medicines or recreational drugs.

Neurologic examination discloses a left homonymous inferior quadrantanopsia and poor rapid alternating movements of the left arm. Sensory testing is remarkable

for normal vibration perception, position sense loss affecting all fingers of the left hand, inability to identify numbers written on the left palm or a rubber band placed in the left hand.

1. What is the name of the visual phenomenon that the patient describes?
2. What are the names of the impaired identifications?
3. Is it unusual to retain perception of vibration with this degree of sensory impairment?
4. Where is the lesion and what is the suspected diagnosis?

Case 57 *A rare phenomenon*

A 91-year-old woman arrives in the Emergency Room because of severe vertigo and double vision of 5 h duration. She has a longstanding history of hypertension and hypercholesterolemia.

Neurologic examination:

Blood pressure is 150/100. The pupils are normal. She has horizontal gaze-evoked nystagmus. There is paresis of left superior rectus, inferior oblique, inferior rectus, medial rectus, right superior rectus, and she has bilateral ptosis due to weak levator palpebrae superioris muscles.

Hospital course:

The patient recovers after 2 more hours but then reports visual hallucinations. She describes beautiful scenes of gardens with pink and green flowers lasting a few hours. These persist intermittently for several days.

1. Do you know the name of these hallucinations? Where is the source, cerebral or brainstem?
2. How can the eye signs be explained and what could be the etiology of the hallucinations?
3. What is the most likely diagnosis?

Answers:

Case 54:

1. Positive central scotomas are dark or brownish due to pathology in the macula as opposed to absence or blurriness of vision which is common with optic nerve disease.
2. Sensory deprivation of the occipital cortex causes increased spontaneous activity resulting in these hallucinations which are called release hallucinations.

Diagnosis: Charles Bonnet syndrome (CB) [52].

Comment: Hallucinations of CB are commonly composed of small people or animals and are recognized as unreal by the patient. They are most often due to bilateral severe macular degeneration or other severe bilateral eye pathology which can be cataracts, glaucoma, diabetic retinopathy, retinitis pigmentosa, central retinal

artery occlusions as well as severe bilateral optic neuropathies and extensive occipital cortex infarctions. The prevalence of CB in low vision clinics has been estimated to be as high as 15–20%.

Case 55:

1. Lilliputian. This name was used in a novel by Jonathan Swift, *Gulliver's Travels*, for an imaginary race of men of minute proportions.
2. How long do the visual and olfactory hallucinations last? They last about 2 min and thus are consistent with the definition of focal, aware, nonmotor seizures (simple partial seizures).
3. Temporal lobe. The olfactory cortex is in the orbitofrontal and adjacent temporal cortex. Formed visual hallucinations are usually derived from temporal lobe lesions whereas unformed hallucinations most often originate from the occipital lobe. The conjunction of brief olfactory and formed visual hallucinations is characteristic of seizures due to a temporal lobe lesion. The fact that the visual hallucinations were in his left visual field and that the examination disclosed a left superior homonymous quadrantanopsia indicates that the site of the lesion is in the right temporal lobe. The CT (head) and MRI (head) with and without contrast are abnormal showing a calcified lesion typical of cysticercosis.

Diagnosis: Focal, aware, nonmotor seizures (simple partial seizures) secondary to a right temporal lobe cysticercosis cyst.

Case 56:

1. This patient has palinopsia (or palinopia), the perseveration of a visual image [45]. The repeated stereotyped brief symptoms indicate the likelihood of focal, aware, nonmotor seizures (simple partial seizures).
2. Inability to identify numbers is impaired graphesthesia and difficulty identifying objects such as a rubber band is astereognosis.
3. No. This is common with cerebral lesions.
4. Patients usually have a right parieto-occipital lesion with impaired vision in the left peripheral field. This patient has a visual field defect, impaired rapid alternating movements and sensory loss manifested by astereognosis, impaired graphesthesia, and abnormal position sense. These findings are all consistent with a right parietal lesion. The repeated stereotyped symptoms of short duration suggest focal, aware, nonmotor seizures. Neoplasm, intra-axial (within brain) is suspected, such as glioma or metastatic disease. An extra-axial (outside brain) mass such as a meningioma is not likely to produce these rare visual illusions. Other etiologies such as demyelinating disease, progressive multifocal leukoencephalopathy, infectious disorders, arteriovenous malformations and neurodegenerative diseases are all diagnostic possibilities. An MRI (head) with and without contrast discloses an extensive high-grade, intra-axial neoplasm infiltrating the corpus callosum and crossing the midline. The biopsy reveals a malignant neoplasm.

Diagnosis: Astrocytoma grade 4 (glioblastoma multiformae), right parietal lobe.

Case 57:

1. This patient has peduncular hallucinosis. The conjunction of vertigo and diplopia indicates brainstem localization.
2. The exam reveals a left 3rd nerve lesion plus right superior rectus paresis which is expected when the lesion is in the oculomotor nucleus. There is contralateral innervation of the superior rectus muscle, a peculiar anatomic fact. The patient has bilateral ptosis as neurons which supply the nerves to the levator palpebrae superioris muscles are located in a single midline nuclear structure. There is no pairing of the nuclei. The only other crossed innervation among the cranial nerves is the 4th nerve. The pathology is in the midbrain. This is the usual location of the lesion which produces peduncular hallucinosis although thalamic lesions have also been documented in a few patients. The precise cause of peduncular hallucinosis is unknown but it may be due to reticular formation damage. This can prevent ascending inhibitory information from reaching the lateral geniculate nucleus. Thus the resulting excitation of neurons in this nucleus may be the source of peduncular hallucinosis. The mechanism may be similar to the release hallucinations which occur in Charles Bonnet syndrome.
3. *Diagnosis*: Midbrain infarction secondary to small vessel intracranial arterial disease associated with peduncular hallucinosis [48].

Comment: Findings on MRI and MRA (head and neck) confirm the diagnosis as the MRI (diffusion-weighted imaging) discloses an ischemic lesion in the expected location of the left oculomotor nucleus in the midbrain. The MRA (head and neck) reveals normal large vessels. A thorough cardiology evaluation is normal. The chance of an infarction in this region being due to cardioembolism is extremely low.

Transient Motor and Sensory Disturbances

Case 58 A 66-year-old woman reports an episode of clumsiness of the left hand lasting 10 min. She was getting dressed at that time and could not button her blouse. She gives no history of pain, numbness, or tingling. Neither her face nor her legs were affected. Her past history is remarkable for a one pack per day smoking habit for 45 years. She has always been normotensive and there is no history of diabetes.

The neurologic examination reveals a blood pressure of 110/70 in both arms, pulse 70, regular. There are bilateral carotid and supraclavicular bruits. She has slightly impaired rapid alternating movements of the left hand.

1. Where is the lesion? What is the most likely etiology?

Case 59 A 25-year-old man reports an episode of intermittent numbness and painful tingling of the entire left leg lasting 6 h one week ago. This occurred once previously about 2 months ago but was less severe although more prolonged, about 10 h. The patient had optic neuritis 2 years ago at which time an MRI (brain) with and without contrast was normal. A thorough neurologic examination was entirely normal.

Cerebrospinal fluid studies included a normal IgG index and no oligoclonal bands were found.

1. What is the significance of this history?
2. What additional questions and bedside techniques might reveal the anatomic source of these symptoms which would permit an accurate diagnosis?

Answers:

Case 58:

1. Brief clumsiness of the left hand with residual impairment of rapid alternating movements could be due to either right corticospinal tract or left cerebellar system pathology. The brief duration of 10 min is characteristic of a vascular event. Focal ischemic events involving cerebellar pathways in brainstem or cerebellar hemisphere causing clumsiness of one hand are exceedingly rare whereas they are common with internal carotid artery distribution TIAs. Pontine ischemia involving the corticospinal tract is a second possibility. If the patient was at all dysarthric the lacunar syndrome of clumsy hand-dysarthria would be suspected and support the possibility of pontine ischemia. But an embolus from a right internal carotid artery plaque is the most likely etiology especially since the patient is a lifelong smoker. Smoking is a common cause, if not the most common, of extracranial vascular disease. Cardioembolism is much less likely in the absence of known cardiac disease.

Diagnosis: Right cerebral ischemia and probable infarction secondary to right internal carotid artery high grade stenosis with embolism.

Comment: This is confirmed by four-vessel angiography. Carotid Dopplers were not performed since angiography or CT-angiography were indicated whether or not the carotid Dopplers were abnormal. An MRI (brain) was normal.

Case 59:

1. The anatomic basis for brief single diffuse limb sensory symptoms could be cerebral, unlikely to be brainstem or spinal cord, very likely root and less likely nerve. The patient has no symptoms or signs of brainstem involvement. A spinal cord lesion almost invariably gives bilateral persistent symptoms and pain as an initial symptom is unexpected. Since the entire limb is involved, single nerve compression or entrapment cannot explain the symptoms. Consequently, a contralateral cerebral or ipsilateral lumbar root lesion is most likely. Multiple sclerosis relapses are defined as greater than 24 h. An ischemic vascular event ordinarily lasts less than 10 min, exceedingly rare in this age group, anyway. Since the tingling is painful lumbar root pathology is suspected.
2. When queried in detail the patient says his symptoms were most severe when sitting, typical of lumbar root pathology, especially a herniated disk. He has lumbar radiculopathy supported by a positive straight leg raising test, the specific diagnostic examination technique. Lumbar root symptoms are commonly diffuse. An MRI (lumbar spine) discloses a herniated disk at L4–L5 compressing the left L5 root.

Diagnosis: Lumbar radiculopathy secondary to a herniated disk.
Comment: When the diagnosis is in question an MRI is indicated. Otherwise conservative management is employed for at least 2–4 weeks, unless significant weakness or intolerable pain occurs. Only these developments should prompt an MRI (lumbar) to be performed.

Case 60 A 77-year-old man complains of nonradiating cold, tingling and gripping sensations of the left calf and foot. These are stereotyped, began 4 months ago and occur whether supine, sitting or standing. He denies back pain, weakness, restlessness or aggravation of symptoms with either prolonged sitting or walking.

The neurologic examination is normal other than mild left anterior tibialis weakness.

1. Where can the lesion be?
2. What additional information could be obtained which would lead to the diagnosis?

Case 61 A 27-year-old woman complains of tingling sensations involving the left arm and face. They begin in the left hand and gradually travel up the left arm to eventually deposit on the left cheek. The movement of the paresthesias up to the face develops over 40 min and the cheek is involved for 5 more minutes. Her neurologic examination is normal.

1. What question should the patient be asked?
2. What is the diagnosis?

Answers:

Case 60:

1. As in the previous case cerebral and lumbar root pathology are most likely. RLS could be considered but the patient is not restless nor does he have a need to get up and walk. Claudication, vascular or neurogenic, may produce gripping sensations but it is not expected to occur at rest. Nerve root compression is commonly exacerbated with prolonged sitting, not present with this patient. Weakness of anterior tibialis is compatible with nerve root or CNS pathology.
2. The diagnostic question is "What is the duration of the symptoms?" The answer? It varies from 30 s to 2 min, never more. This duration with stereotypical symptoms indicates focal, aware, nonmotor seizures (simple partial seizures). An MRI (head) reveals a parasagittal meningioma, right parietal lobe.

Diagnosis: Parasagittal meningioma, right parietal lobe, associated with focal, aware, nonmotor seizures (simple partial seizures).

Case 61:

1. The patient should be questioned about headache. The history is typical of the "march of paresthesias" which is a common aura of migraine. The duration of symptoms is characteristic for migraine, 5–60 min. This patient reports a mild headache beginning when the paresthesias reach their peak. From her perspective, the headache is of no concern compared to the severe paresthesias.
2. *Diagnosis*: Migraine with aura (cheiro-oral paresthesias).

Paroxysmal Motor Phenomena

The following three case reports describe rare disorders but they are representative of a large group of patients. The purpose of a cursory discussion of these conditions is merely to expose the reader to the existence of these paroxysmal disorders of involuntary movements and paralysis. Dismissing these illnesses as solely a psychogenic condition can have catastrophic consequences for the patient and the patient's family.

Case 62 A 19-year-old college student is referred because of periodic involuntary movements for 6 months. He notes the movement on getting out of his chair quickly after working on his computer or reading for a few hours. The involuntary movements are either rapid, affecting the hands, or of a sustained posture such as inversion of a foot. They last between 30 and 60 s and can be provoked if he is surprised.

1. What types of movements are they?
2. Do you know the name of this rare condition?

Case 63 A 19-year-old college student complains of several spells, over a few months, of paralysis during the night. He may awaken at 2:00 a.m. and be unable to move any extremity until 4:00 or 5:00 a.m. Speech, breathing and swallowing are unaffected. The episodes occur most often early Sunday morning or the night prior to examinations. The neurologic examination is normal.

1. Why might this occur early Sunday morning or before an examination?
2. Any thoughts about the diagnosis?

Case 64 A 17-year-old girl is referred because of brief episodes of slurred speech, double vision and loss of balance. She has had these spells since age 10 and her mother attributed them to stress at school. During the summer vacation she has had an occasional day when several episodes occurred. Another embarrassing problem is frequent eyelid twitches which are severe enough to prompt her boyfriend to make comments about it.

Past Medical History: The patient has a history of two tonic-clonic seizures at age 14 treated with levetiracetam for 2 years. Two EEGs and an MRI (brain) were normal.

Family History: The patient's father was killed in a motorcycle accident at age 22. He had a seizure disorder.

Neurologic Examination: Her examination is normal other than eyelid myokymia. These are rippling movements seen in normal individuals under stress or after excessive coffee consumption. This patient has them constantly with fluctuating severity. When discussing her illness immediately after the examination the

patient complains of sudden vertigo associated with nausea. Her examination discloses horizontal gaze-evoked nystagmus, dysarthria, finger-to-nose and heel-to-shin ataxia and a wide-based ataxic gait. Her myokymia becomes more severe. Her examination returns to normal in 1 min with the exception of persistent eyelid myokymia.

Questions:

1. Where is the lesion?
2. What name would you give for the diagnosis?

Answers:

Case 62:

1. The rapid distal involuntary movements are choreiform. A sustained abnormal posture, inversion of the foot, is dystonia.
2. *Diagnosis:* Paroxysmal kinesigenic choreoathetosis [46].

Comment: This is a rare disorder which can be primary or secondary. The former are typically autosomal dominant and begin between ages 1 and 20. The movements can be choreiform, athetoid, ballistic or dystonic and usually last less than 1 min. Precipitating factors can be sudden movements (kinesigenic), startle, hyperventilation and movement after a prolonged period of rest. Anticonvulsants can quickly eliminate these episodes. The secondary form can occur rarely with multiple sclerosis, stroke, pseudohypoparathyroidism, hypocalcemia, hyperglycemia and hypoglycemia.

Other forms of paroxysmal dyskinesia are nonkinesigenic, exertion-induced and hypnogenic. Paroxysmal nonkinesigenic choreoathetosis (PNKD) often occurs without a trigger, lasts 2 min to 4 h and has the same motor manifestations. The exertion-induced form, which occurs after prolonged exercise, lasts 5–30 min. The hypnogenic form occurs during non-REM sleep, lasts 15–45 s and a seizure disorder must be ruled out.

The presumed etiology of paroxysmal dyskinesias is dysfunction in the basal ganglia. An ictal origin must be strongly considered since patients respond to anticonvulsants.

Case 63:

1. The occurrence of paralysis early Sunday morning suggests a provoking activity the preceding night. A common activity for a college student on a Saturday night is alcohol consumption and before exams there is a factor of emotional stress. Both are known to precipitate an attack of periodic paralysis.
2. *Diagnosis:* Hypokalemic periodic paralysis [53].

Comment: This hypokalemic type of periodic paralysis can manifest itself as rarely as a few occasions in a lifetime or as often as daily. The attacks are usually nocturnal, last a few hours and can be manifested by quadriplegia with areflexia. Common precipitating factors, noted in the case report, include alcohol consumption and

emotional stress. This is a calcium channelopathy related to a mutation on chromosome 1q.

The hyperkalemic form lasts 15 min to 4 h, is precipitated by rest after exercise or ingestion of potassium-rich foods. Weakness is mainly proximal but there is commonly a quadriparesis with normal sensation and absent reflexes.

These paralyses are autosomal dominant or sporadic, primary or acquired. The major differential diagnoses of the acquired form are thyrotoxicosis and potassium loss from gastrointestinal or renal disease.

Case 64:

1. Cerebellum.
2. Episodic ataxia or paroxysmal cerebellar ataxia.

Diagnosis: Episodic ataxia (EA1) [17].

Comment: This illness is an autosomal dominant potassium channelopathy with attacks lasting seconds to minutes. The attacks are provoked by startle, fatigue, anxiety, sudden movements and menstruation. Seizures are present in some patients.

To recapitulate the clinical correlation of the neurologic signs: horizontal-gaze-evoked nystagmus means right beating nystagmus on right lateral gaze and left beating nystagmus on left lateral gaze. Bilateral directionality is diagnostic of brainstem or cerebellar system pathology and drug toxicity. Myokymia is noted with lesions affecting facial nuclei but this is not a pathognomonic association. Dysarthria is a nonlocalizing sign and the other findings indicate cerebellar system pathology which could be within the cerebellum or cerebellar pathways in the brainstem. Treatment with acetazolamide is usually helpful. There are several episodic ataxias but a full discussion of these are beyond the scope of this book. Genetic testing is required to confirm the diagnosis.

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Chapter 12
Diagnostic Dilemmas

The aim of this chapter is to review categories of neurologic diseases not covered in preceding sections. The method will be case studies with a focus on clinical-neuroanatomic correlation followed by a differential diagnosis. Analysis of laboratory data, especially cerebrospinal fluid, will be included. There will be a potpourri of diseases, many uncommon, yet all likely to be encountered at one time in a general neurologic and some medical practices. The requirement to be conversant in internal medicine will be apparent in several case reports. These case analyses and differential diagnoses are likely to go beyond the level of most readers of this text but challenges often pique curiosity and stimulate the medical student or physician to think beyond the mundane, rote requirements of daily practice. The discussions are meant to be only an introduction to each disease. The references will provide an opportunity to further explore the manifestations and pathogenesis of each illness in detail.

Case 1 A 76-year-old man complains of impaired memory, loss of balance, falling, and a stiff neck. There was an insidious onset of these symptoms beginning 7 months ago. They are steadily increasing in severity.

The past medical history includes type II diabetes, hypertension, and coronary artery disease. Medications are metformin, ramipril, clopidogrel, and atenolol.

Neurologic Examination Blood pressure is 140/100 in the right arm and 125/90 in the left arm. There are bilateral carotid bruits. Mental status examination is normal other than bradyphrenia and poor short-term recall. Downgaze is absent and upgaze is paretic. Upward saccades are slow and optokinetic testing does not elicit any vertical quick phases. The vertical oculocephalic maneuver, performed with difficulty because of nuchal rigidity, elicits incomplete up gaze but no down gaze. The patient exhibits mild bradykinesia, truncal instability with retropulsion, cogwheel rigidity, and has a positive pull test.

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Case 1 Questions

1. Can a focal lesion explain the symptoms and signs?
2. Is the past medical history relevant in making the diagnosis? Are the blood pressure findings and carotid bruits helpful?
3. Where is the pathology?
4. Does the history help to exclude some types of pathology?
5. What is the diagnosis?

Case 1 Analysis

1. No. The abnormal mental status manifested by bradyphrenia and short-term memory loss indicates cerebral pathology and vertical gaze paresis, absent down gaze and slow upward saccades, is a sign of midbrain involvement.
2. No to both questions. Many elderly people have multiple illnesses, especially type II diabetes and hypertension. The mild blood pressure asymmetry in the arms may indicate a mild left subclavian stenosis but there is no history of transient ischemic attacks to suggest a subclavian steal syndrome and most subclavian stenoses are asymptomatic. The presence of bruits may indicate internal or external carotid artery disease and, if present, are not symptomatic in this patient with a history of progressive neurologic dysfunction.
3. A lesion in the rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF) in the midbrain results in impaired vertical gaze but with preservation of the vertical oculocephalic maneuver. Deficient cognition indicates bilateral cerebral involvement.
4. The history of progressive multifocal neurologic impairments and the absence of discrete focal events of neurologic dysfunction is indicative of a degenerative process and virtually rules out vascular etiology.

5. *Diagnosis*: Progressive supranuclear palsy (PSP) [19, 57].

Comment The clinical presentation of PSP has 4 core features which include ocular motor dysfunction, postural instability with frequent falls, akinesia and cognitive impairment. The disease occurs sporadically in patients over age 40 and is characterized by a gradually progressive course. The salient features are the eye signs which are slow or absent saccades, primarily vertical and downward > upward, yet retention of oculocephalic responses, macrosquare wave jerks (horizontal saccadic intrusions displacing the eyes from primary position), and eyelid opening apraxia which is the inability to initiate eyelid opening after a variable period of passive eye closure. The major pathology is located primarily in the subthalamic nucleus, midbrain, and superior cerebellar peduncle. It is a tau-positive disorder in which the tau protein is derived from one gene on chromosome 17. Hyperphosphorylated tau is the primary component of neurofibrillary tangles.

PSP is one of the Parkinson-plus syndromes which include multiple system atrophy (MSA), Lewy body disease (DLB) and corticobasal degeneration (CBD). MSA encompasses previously described conditions which include olivopontocerebellar atrophy, striatonigral degeneration, and Shy-Drager syndrome. MSA and DLB will be discussed in forthcoming case reports.

CBD is a rare disorder manifested by asymmetric rigidity, myoclonus, tremor, apraxia, sensory disturbances such as astereognosis, and an alien limb syndrome. The latter is a peculiar, involuntary, independent and inappropriate movement of one limb. The patient may manipulate objects within his reach despite no intention to do this. MRI scans often show marked basal ganglia and asymmetric cortical atrophy involving parietal much more than frontal lobes.

Case 2 A 32-year-old woman requests an evaluation because of double vision, right facial weakness, impaired taste, stiff legs, and shortness of breath of 2 weeks duration. She has a past medical history of insulin-dependent diabetes mellitus and migraine.

Neurologic Examination Blood pressure 120/78, pulse 88, and regular. Pertinent findings include dysconjugate gaze with the left eye deviated down and to the left. Pupils are 4 mm O.D. with a 4 + / 4 light reaction and 4.5 mm O.S. with a 2 + / 4 light reaction. Consensual responses to light are the same. Downgaze elicits intorsion O.S. There is mild weakness of right frontalis, orbicularis oculi, and orbicularis oris muscles. Taste is impaired on the right side of the tongue. Leg strength is 4 + / 5 bilaterally except for 4/5 anterior tibialis on the right and 3/5 on the left. Tone is spastic in both legs and she has bilateral Babinski signs.

A lumbar puncture discloses normal opening pressure with ten lymphocytes/cu mm and protein 70 mg/dl. There is an elevated IgG index and oligoclonal bands are present. An MRI scan of the brain is normal.

Case 2 Questions

1. Where are the lesions most likely located?
2. What diagnosis should be considered but discarded and why?
3. What simple examination may be diagnostic?
4. What do the cerebrospinal fluid findings indicate?
5. What is the diagnosis?

Case 2 Analysis

1. Left third nerve, right seventh nerve, and spinal cord. Intorsion O.S. indicates preservation of fourth nerve function.
2. Multiple sclerosis. Dyspnea and impaired taste are not presenting symptoms. Loss of taste occurs with peripheral facial nerve lesions. Peripheral nerve disease does not occur with multiple sclerosis. The spinal fluid protein is almost invariably normal. Lyme disease should be considered but it rarely causes a myelopathy.
3. The chest X-ray shows hilar adenopathy. Subsequently drawn, an angiotensin-converting enzyme level is elevated. This patient has sarcoidosis which commonly affects cranial nerves, especially the facial nerve, and may be associated with a myelopathy.
4. They indicate inflammation such as occurs with immune disorders. Numerous illnesses which may produce oligoclonal bands or an elevated IgG index are Lyme disease, systemic lupus erythematosus, herpes simplex encephalitis, neurosyphilis, Sjögren's disease, subacute sclerosing panencephalitis, primary cen-

tral nervous system lymphoma, meningeal carcinomatosis, multiple myeloma, Guillain-Barré syndrome, autoimmune encephalitis, and infrequently neuromyelitis optica.

5. *Diagnosis*: Neurosarcoidosis with cranial neuropathy and myelopathy [51].

Comment Neurosarcoidosis often presents with protean medical and neurologic manifestations and should be part of many differential diagnoses. The presence of peripheral nervous system disease removes multiple sclerosis as a possible etiology. The presence of shortness of breath and cranial nerve involvement implicates the likelihood of an underlying medical disorder with neurologic complications. Neurosarcoidosis fits this description. Prednisone is usually efficacious and frequently returns the patient to a normal or near-normal state.

Case 3 A 58-year-old woman is referred by a psychiatrist because of suspected mild cognitive impairment. She has refused neuropsychological testing. Two years ago she sought treatment for depression, but over recent months she has exhibited inappropriate behavior which has included stealing antiques from a friend's home, no longer bathing regularly and exhibiting loss of initiative or interest in any activity.

Past medical history is remarkable for hypothyroidism, hypercholesterolemia, and small cell lung cancer resected successfully 3 years ago. Medications are venlafaxine, thyroid replacement, and atorvastatin.

Neurologic Examination Blood pressure 140/95, pulse 92 with an occasional irregular beat. She is right-handed. Her spontaneous speech is limited and answers to questions are brief. Echolalia is noted occasionally and naming is impaired. The Mini-Mental State Exam score is 27/30. Two errors made in this examination are those of naming and repetition. She has bilateral grasp and palmomental reflexes.

Case 3 Questions

1. Does this patient have symptoms which suggest focal pathology?
2. Does this patient have clinical signs which suggest focal pathology?
3. What diagnoses should be considered?
4. What additional history should be reviewed?
5. What is the diagnosis?

Case 3 Analysis

1. Yes. The behavioral changes suggest frontal lobe disease.
2. Yes. Paucity of speech and dysnomia are indicative of aphasia and therefore left cerebral pathology, especially frontal and temporal lobes. Echolalia is most often seen in patients with aphasia but there are exceptions. Paucity of speech implies a nonfluent aphasia in contrast to a fluent aphasia where speech production is rather good although filled with paraphasias. Grasp reflexes are often found in patients with frontal lobe pathology. Palmomental reflexes are commonly present in patients with dementia, but they can be seen in the normal population.

3. Considerations are degenerative disease, neoplasm, both metastatic such as from carcinoma of the lung and benign neoplasms such as meningioma. A paraneoplastic syndrome such as limbic encephalitis is an unlikely but possible etiology. Limbic encephalitis may produce psychiatric disorders, seizures, memory loss, agitation, and altered mental status but it is a subacute disorder. Vascular disease is unlikely to present as a slowly progressive disease. The degenerative disease that is the primary consideration is frontotemporal dementia.
4. The patient's family history is critical since frontotemporal dementia is autosomal dominant and, therefore, a positive family history for dementia is in the range of 40–50%. The patient's mother had abnormal behavior followed by dementia beginning in her early 60s, a typical sequence of events in frontotemporal dementia which is the second most common dementia in patients less than age 65.

   This patient has frontotemporal dementia, most often tau-positive (there are tau-negative forms which are ubiquitin-positive, another pathogenic protein). It is due to a progranulin mutation on chromosome 17.

5. *Diagnosis*: Frontotemporal dementia [1, 20].

Comment There are three forms of this disease.

1. Behavioral variant frontotemporal dementia is described in this case. Another uncommon manifestation is the Klüver–Bucy syndrome, a behavior disorder characterized by hyperreactivity to visual stimuli, hyperoral, and hypersexual behavior.
2. Semantic dementia. This disorder is manifested by deficient expressive and receptive vocabulary which develops insidiously. Dysnomia, lack of emotional responses and inability to use utensils or common tools (apraxia) are common. These patients have poor recall of names and identification of faces. MRI scans reveal anterior temporal lobe atrophy.
3. Nonfluent progressive aphasia. The typical characteristics are phonemic paraphasias, poor repetition, dysnomia, halting speech, alexia, and agraphia but, initially, preservation of word meaning.

Case 4 A 58-year-old accountant is referred for neurologic evaluation because of severe tremor, poor handwriting, unstable gait, leg weakness and several recent falls. His illness began 6 years ago with an intention tremor. A diagnosis of essential tremor was made and treatment with propranolol, primidone and topiramate was ineffective. Four years ago his work performance declined; he became depressed and exhibited poor short-term recall. This past year he had sporadic episodes of vaguely described dizziness witnessed by friends at the dinner table. They observed no unusual movements or behavior. His tremor later became so severe that he used both hands to hold a glass of water and required a soup spoon to eat.

Neurologic Examination Blood pressure supine is 130/85, sitting 120/80, standing at 1 min 88/60 and the patient complains of dizziness. Heart rates are 58, 60 and 60, respectively. A Mini-Mental State Exam score is 25/30. He appears apathetic, depressed and exhibits bradyphrenia. Errors are disorientation to month, year and 0

recall of 3 words after 1 min has elapsed. Neuropsychological testing also revealed poor executive function and speed of information processing. He has prominent ocular dysmetria, hypomimia, failure of check, severe finger-to-nose ataxia, moderate heel-to-shin ataxia, mild resting tremor and is unable to perform tandem gait. Leg strength is minimally decreased at 5−/5 in all muscles and he has mild spasticity in both legs.

Case 4 Questions

1. What questions for the patient and the witnesses of his dizzy spells might elicit diagnostic information?
2. What additional abnormal findings on examination might be found?
3. What medical illness might explain his apathy, cognitive impairment and cerebellar ataxia?
4. What motor systems are involved and what findings are they responsible for?
5. What are the two major diagnostic considerations?

Case 4 Analysis

1. Did the dizziness occur at the end of the meal and did he appear pale? The answer to both questions is yes. The patient reported that dizziness was a lightheaded sensation which occurred when standing up and often after a heavy meal. This history points toward postprandial near-syncope due to hypotension, a result of blood pooling in the splanchnic bed.
2. The patient should be checked for cogwheel rigidity since he has a resting tremor and hypomimia. He might also have a positive glabellar response. All of these findings support the diagnosis of a parkinsonian syndrome.
3. Hypothyroidism. It is not well-known that cerebellar ataxia can be an early sign of hypothyroidism.
4. (a) Cerebellar: Ocular dysmetria, failure of check, limb ataxia and poor tandem gait.
   (b) Extrapyramidal: Hypomimia and resting tremor.
   (c) Corticospinal: Spasticity and leg weakness.
5. Multiple system atrophy and fragile X-associated tremor/ataxia syndrome (FXTAS).

Diagnosis Fragile X-associated tremor/ataxia syndrome (FXTAS) [30].

Comment This illness usually begins in males over age 50 who initially have normal intellect. The cardinal features are cerebellar gait ataxia, intention tremor, and impaired executive function. Frequent associated features are parkinsonism, psychiatric symptoms, autonomic dysfunction and neuropathy. MRI imaging reveals global brain atrophy and T2/FLAIR hyperintensity in cerebral white matter, cerebellum, middle cerebellar peduncle and pons. This is an X-linked dominant syndrome with trinucleotide repeat expansions of CGG in the permutation range (55–200) in the fragile X mental retardation 1 gene. Genetic testing is diagnostic.

Case 5 A 67-year-old male lawyer was brought to the Emergency Room because of confusion. While speaking to a client, he noted the sudden onset of total loss of vision and could no longer remember the elements of a contract he had just composed. His speech was incoherent and he became agitated.

Past medical history includes coronary artery disease, three myocardial infarctions, and congestive heart failure. Current medications are digoxin, furosemide and clopidogrel.

Neurologic Examination Blood pressure 140/80 and pulse 82 with an occasional extra beat. After the agitation subsided, about 1 h later, the patient could be examined and he was disoriented to month and year. When shown a picture of a volleyball game he was able to identify and describe each player, but could not comprehend the action that was being portrayed. He was unable to generate saccadic eye movements to command. There was paresis of upgaze, eyelid retraction, and convergence-retraction nystagmus. Each quick phase of nystagmus produced convergence and retraction of the globes. This was easily elicited by moving an optokinetic tape downward. Pupils were 6 mm, equal, round, and fixed to light. He was unable to reach a target that he could clearly see.

Case 5 Questions

1. What syndrome is present?
2. What are its elements?
3. Where is or where are the lesions on the MRI scan?
4. Does this explain the confusion and agitation?
5. What is the differential diagnosis and the probable diagnosis?
6. What screening tests should confirm it?

Case 5 Analysis

1. Balint's syndrome [18].
2. The primary elements are:
   (a) Simultanagnosia. This is demonstrated by the patient's ability to identify each element of a scene, but inability to appreciate its meaning.
   (b) Oculomotor apraxia. This is the inability to generate saccades on command.
   (c) Optic ataxia. This is the inability to reach or touch a target which is clearly seen.
3. Diffusion-weighted imaging (DWI) on the MRI scan shows bilateral ischemic lesions in the parieto-occipital and pretectal regions. An MRA (head and neck) is normal. Convergence-retraction nystagmus, eyelid retraction, upgaze paresis, and large, round, fixed pupils occur due to bilateral lesions of the pretectum and involvement of the posterior commissure.
4. Acute confusion and agitation occurs with acute bilateral ischemic changes, especially involving parieto-occipital regions. Acute, unilateral, nondominant parietal lesions have rarely been associated with this behavioral change.

5. The abrupt onset indicates vascular disease. Encephalitis could be considered but prodromal symptoms ordinarily occur.
6. A 24-hour Holter monitor and a 2D echocardiogram revealed a normal cardiac rhythm and a left ventricular aneurysm. Thus, this patient had a source for cardioembolism to the distal portion of the basilar artery with resultant ischemia in both posterior cerebral artery distributions. This is one manifestation of "top-of-the-basilar syndrome" [9].

Diagnosis

Multiple cerebral (bilateral parieto-occipital) and brainstem (midbrain) infarctions secondary to cardioembolism to the distal portion of the basilar artery.

Case 6 A 55-year-old man is brought to the Emergency Room because of the sudden onset of left-sided weakness and accelerating severity of headache. A pulsating headache began 2 days before admission. Yesterday, the patient had two episodes lasting 15–20 s of brief loss of vision affecting each eye independently.

The patient has had periodic low back pain and anorexia for 3 months with a weight loss of 18 lb. He has a 2-month history of chronic fatigue.

Past Medical History The patient has a five-year history of type II diabetes and has been treated with metformin. Approximately 10 months ago he was started on atorvastatin because of an LDL of 200 mg/dl.

Neurologic Examination Pulse is 52 and the blood pressure 150/105. Funduscopic examination shows blurred disk margins on the superior and inferior portions of both optic disks. Venous pulsations are not seen. A single splinter hemorrhage is noted on the disk margin O.S. Pupils, visual fields, and eye movements are normal. He has a left arm pronator drift with diminished rapid alternating movements and finger tap on the left side. Strength of the left arm is 4 + / 5 except for interossei at 4/5.

CT scan of the head is normal. Hematocrit is 32%. Routine metabolic screen is normal.

Hospital Course The next morning the patient has a 1-min right focal motor seizure involving arm, face, and leg associated with nystagmoid jerks to the right. Afterwards he has a right hemiparesis with strength 3/5 except for 2/5 interossei and wrist extensors. At this time, the left arm has returned to normal.

Case 6 Questions

1. What caused the two brief episodes of loss of vision affecting each eye independently?
2. Does this patient have cerebral or brainstem pathology? Why?
3. What do the funduscopic changes reveal?
4. What disease causes an alternating hemiparesis and these funduscopic changes?
5. Why did a seizure occur?

6. What is the relevance of the back pain, weight loss, and anorexia?
7. What are the diagnoses?

Case 6 Analysis

1. Increased intracranial pressure. Brief episodes of visual loss, unilateral or bilateral, may occur in association with papilledema, often many times per day.
2. Cerebral. Focal seizures do not occur with brainstem lesions.
3. Papilledema. Blurred disk margins often begin over superior and inferior margins of the optic disk. Venous pulsations may be absent in 5–10% of the normal population, but the single splinter hemorrhage at the disk margin O.S. confirms the diagnosis of papilledema.
4. Alternating hemipareses are a classic although uncommon presenting manifestation of superior sagittal sinus thrombosis which frequently causes papilledema.
5. Patients with superior sagittal sinus thrombosis have hemorrhagic infarctions and hemorrhage is a cortical irritant.
6. This patient has cancer of the pancreas which may cause a coagulopathy and is associated with venous sinus disease as well as its better-known connection to deep venous thrombosis in the legs. Back pain, anorexia, weight loss and fatigue are frequent early symptoms.
7. *Diagnoses*:
   (a) Carcinoma of the pancreas causing a coagulopathy [46].
   (b) Superior sagittal sinus thrombosis with bilateral hemorrhagic cerebral infarctions [4].
   (c) Right focal motor, aware seizures (simple partial seizures) secondary to a hemorrhagic left cerebral infarction.

Case 7 A 60-year-old man is brought to the clinic by his wife because of frequent falls over the previous 3 months. The patient believes that he has been clumsy on these occasions and has simply tripped. From his viewpoint he feels entirely well and he denies all neurologic symptoms.

Past medical history is remarkable for peptic ulcer disease, GERD and alcohol abuse (reported by his wife on a written note). He denies alcohol abuse. He smokes one pack of cigarettes per day. Medications are omeprazole and multivitamins.

Neurologic Examination Pulse 60 and regular and blood pressure 110/70. There are bilateral carotid bruits. He has several large ecchymoses on both arms and one leg. The patient's mental status examination is normal and this includes short-term recall. Palpebral fissures are asymmetric, left much greater than right. Pupils are 3 mm, equal, and briskly reactive to light. He has impaired finger tap on the left side. When seated on the edge of the table, he falls backwards. He cannot perform tandem gait.

Case 7 Questions

1. What part of the present illness localizes the disorder?
2. What is the meaning of the asymmetric palpebral fissures? Does this specific finding fit with the history?

3. Does inability to perform tandem gait indicate cerebellar dysfunction in this patient?
4. When there is retropulsion (falling backwards) what anatomic structures are often affected?
5. Can the past medical history help to explain the clinical presentation? What is the differential diagnosis?

Case 7 Analysis

1. Denial. Despite the obvious presence of several large bruises, he dismisses the significance of his falls. This syndrome is called anosognosia although anosodiaphoria might be more apt. This latter term refers to dismissing the significance rather than the complete denial of the falls.
2. Since the pupils are equal and reactive, the asymmetric palpebral fissures must be due to weakness of the left orbicularis oculi which is innervated by the right cerebral hemisphere via corticobulbar fibers which cross in the pons to synapse at the left facial nucleus and provide innervation via the left facial nerve. Patients with right cerebral hemisphere lesions often have left facial weakness, which includes eye closure and lower facial movement, but only rarely the frontalis muscles which are bilaterally innervated. Asymmetrical palpebral fissures are common with cerebral lesions but often ignored by the examining physician.
3. No. Tandem gait is impaired in many disorders, especially those with severe sensory loss, particularly involving position sense, vestibular disorders, mass lesions with midline shift, and any of the three motor systems, cerebellar, extrapyramidal, and corticospinal.
4. Retropulsion is common with midline or degenerative pathologies which include lesions involving the cerebellar vermis, obstructive or communicating hydrocephalus, Parkinson's disease, and a shift of midline structures.
5. Yes. One must presume that the patient suffered a head injury as a result of at least one of his falls which are likely due to alcohol intoxication. The differential diagnosis, therefore, includes primarily trauma and neoplasm. Neoplasm, if present, could be benign but more likely malignant because of the rapid development of neurologic deficits.

Diagnoses

1. Chronic subdural hematoma, right side, due to head trauma.
2. Alcoholism.

Comment Chronic subdural hematomas may cause focal neurologic signs, progressive dementia or remain stable for many years resulting in mild cognitive impairment. Any patient with cognitive impairment as well as focal signs requires at least a CT (brain) to rule out this treatable lesion.

Case 8 A 27-year-old woman complains of a left temporal headache and impaired speech of 5 h duration. Other than endometriosis she is entirely well. She has a past medical history of ulcerative colitis and was in a motor-vehicle accident 2 months ago, her car being struck from the rear. There was no loss of consciousness.

Neurologic Examination Blood pressure 130/100 and a regular pulse of 80. Her speech is halting, nonfluent, and naming is impaired. Repetition is normal. Other abnormal neurologic findings include asymmetric pupils which are 4 mm O.D. and 3 mm O.S. with a 3 + / 4 reaction to light bilaterally. There is an equal reaction to near. The right palpebral fissure is greater than the left. The patient has right Hoffmann's and Babinski signs. There are 5 beats of clonus at the right ankle and 2 at the left.

Case 8 Questions

1. What kind of aphasia does this patient have?
2. What is the meaning of the pupillary asymmetry? What additional bedside test can be useful when there is a pupillary asymmetry? Why are the lids asymmetric?
3. Is the pupillary asymmetry helpful in the differential diagnosis? What artery could be affected? Which part of that artery?

Case 8 Analysis

1. The patient has a transcortical motor aphasia which is nonfluent speech along with usually normal comprehension and good repetition. In Broca's aphasia repetition is impaired.
2. A pupillary asymmetry of greater than 0.5 mm must be considered abnormal. The lid asymmetry is either due to a right orbicularis oculi weakness, left third nerve lesion or a left Horner's syndrome. A right third nerve lesion would impair reactivity to light. A left cerebral lesion would not cause a pupillary asymmetry. Thus a Horner's syndrome is the most likely etiology. The pupillary findings can be rechecked in dark and, with a sympathetic lesion, the asymmetry increases when the pupils are measured after 5–15 s have elapsed. In this case the normal right pupil increases to 5 mm and the left to 3.5 mm, an increase in the asymmetry by 0.5 mm.
3. The sympathetic pathway runs through the carotid artery sheath and is commonly injured with carotid dissections. Dissections of extracranial arteries are far more common than intracranial dissections. They may be spontaneous or traumatic with the trauma often quite trivial. Usually blood dissects between the intima and the media causing stenosis but, if between media and adventitia, pseudoaneurysms may develop. Dissections are typically located at the C2–C3 level. Angiograms demonstrate a tapered high-grade stenosis resulting in an extended thin column of contrast called the "string sign."

Diagnosis Left cerebral infarction, frontal lobe, secondary to a traumatic extracranial dissection of the left internal carotid artery [17, 23].

Comment The prognosis is good for both clinical recovery and spontaneous resolution of the dissection over 3–6 months. Standard treatment is warfarin, although some neurologists now advocate clopidogrel.

Case 9 A 55-year-old man is brought to the Emergency Room after a tonic–clonic seizure. His postictal state lasts about 1 h. When awake and alert the following information is obtained. He has noticed a decline in his memory over the last 2 months and has had occasional involuntary jerky movements of his extremities causing him to drop his dinner plate and eating utensils. His walking is unsteady. His wife adds that his behavior is odd as he has been withdrawn and taciturn, a sharp departure from his usual ebullient nature.

Neurologic Examination Blood pressure 120/70 and pulse 96 and regular. The patient is afebrile. A Mini-Mental State Exam score is 24/30. The patient has paresis of upgaze, bilateral heel-to-shin and finger-to-nose ataxia, and a wide-based ataxic gait. He has moderate bradykinesia and failure of check in both arms. Fasciculations are prominent over left thigh musculature. He has a left Babinski sign.

Case 9 Questions

1. Where is the pathology located?
2. What motor systems are involved?
3. What tests should be ordered and what do they show?
4. What is the diagnosis and the etiology?

Case 9 Analysis

1. There is cerebral hemisphere involvement because of dementia, generalized tonic-clonic seizure and abnormal behavior. Dementia confirms bilateral cerebral involvement. A posterior commissure lesion explains upgaze paresis. Limb ataxia, failure of check and a wide-based gait indicate cerebellar system dysfunction. He has myoclonic jerks which are likely to be of cerebral origin although myoclonus may occur with brainstem or spinal cord disease. Anterior horn cell disease is signified by the presence of fasciculations. The Babinski sign indicates corticospinal tract pathology but is nonlocalizing within this pathway.
2. Corticospinal, extrapyramidal, and cerebellar. The Babinski sign is the quintessential hallmark of corticospinal tract disease. Bradykinesia is a manifestation of extrapyramidal disease. Failure of check, limb and gait ataxia indicate cerebellar system involvement.
3. Abnormal results in this patient are:
   (a) Electroencephalogram: This shows periodic, bilateral, sharp, triphasic complexes of 1 Hz, characteristic of Creutzfeldt-Jakob disease.
   (b) Cerebrospinal fluid: This reveals the presence of 14–3-3 protein, often found in patients with Creutzfeldt-Jakob disease but with a false positive rate of 5–10%.
   (c) MRI: This discloses T2/FLAIR hyperintensities in caudate and putamen nuclei.
   (d) New promising testing was not performed but includes nasal brushing [7] which is reportedly 97% sensitive and 100% specific in an initial study and

urine testing [33] which has revealed evidence of prion protein (Pr P) in about 40% of urine specimens.

4. *Diagnosis*: Sporadic Creutzfeldt–Jakob disease (sCJD) [24].

Comment Sporadic Creutzfeldt-Jakob disease is caused by an abnormal transmissible (by brain or CSF) prion protein which is most often due to a mutated gene for normal Pr P which produces a misfolded protein. This rapidly progressive disease has a median survival time of approximately 4 months. Other prion diseases are Kuru due to ingested, infected, human brains in Papua, New Guinea, fatal familial insomnia, Gerstmann–Sträussler–Scheinker disease, and bovine spongiform encephalopathy (mad cow disease).

Case 10 A 45-year-old man complains of the sudden onset 1 week ago of horizontal double vision when looking to the left. The double vision is slowly resolving. He has no other neurologic symptoms. He did have one episode of blurred vision affecting the right eye 3 years ago. His ophthalmologist found a normal eye 1 week after the episode resolved.

Past medical history is remarkable for hypertension for which he takes atenolol and enalapril.

Neurologic Examination Blood pressure 130/90 and pulse 100, regular. The patient has normal pursuit eye movements in all directions. His saccadic eye movements show a decreased velocity of right eye saccades to the left. There is decreased perception of light and color O.S., but 20/20 visual acuity in both eyes. The left pupil shows a better consensual reaction than direct response to light.

Case 10 Questions

1. What eye movement syndrome does this patient have?
2. Is there more than one lesion?
3. What diagnosis is virtually certain?
4. What studies may help to confirm the diagnosis?

Case 10 Analysis

1. Internuclear ophthalmoplegia or MLF (medial longitudinal fasciculus) syndrome. The MLF is mainly a quick system pathway; thus an evaluation assessing saccades is much more sensitive than examining ocular pursuit. Nystagmus may or may not be present in the contralateral abducting eye. Convergence is usually preserved but not invariably and, consequently, its assessment is of little diagnostic assistance.
2. Yes. There is an optic nerve lesion O.S. since the patient perceives less light and color with this eye. Visual acuity is a less sensitive test. The better consensual response to light O.S. objectively confirms the presence of optic nerve pathology.

3. *Diagnosis*: Multiple sclerosis [52].

Comment There are two symptomatic lesions separated in space and time. A normal ophthalmologic evaluation one week after the symptoms abated neither negates the history nor the current findings on examination.

Since there are two attacks by history and neurologic examination, additional supporting data are not required. Moreover, his examination demonstrates clinical findings of optic nerve disease despite absence of related symptoms. A baseline MRI (head) with and without contrast is still indicated. A normal result would still not refute the diagnosis. A contrast-enhancing lesion would indicate active ongoing disease.

4. Cerebrospinal fluid studies of interest would include:

   (a) Cell count. Multiple sclerosis CSF often shows a modest lymphocyte pleocytosis in the range of 6–20 wbc/cu mm.
   (b) Protein. This is expected to be normal. If it is increased other etiologies should be considered.
   (c) IgG index. This is commonly but not always increased and not pathognomonic for multiple sclerosis.
   (d) Oligoclonal bands. These are commonly but not always present and not pathognomonic for multiple sclerosis.

Evoked potentials. Visual-evoked potentials may support the diagnosis of an optic neuropathy but are often normal when there are mild clinical signs. An abnormal visual-evoked potential alone is not sufficient to qualify as a lesion.

Case 11 A 14-year-old girl complains of headache, fever, and neck pain of 3 days duration. For 3 months she has had fatigue and migratory joint and muscle pain. Two months ago she developed mild left facial weakness while traveling with her family in Mexico during summer vacation. A diagnosis of Bell's palsy was made, treatment with prednisone was given but no changes in the facial weakness have been noted since then. Over the past 2 weeks she has had shooting pains and tingling down the left leg.

Neurologic Examination The patient has a temperature of 100 °F. Blood pressure is 90/60, pulse 88 and regular. There is mild nuchal rigidity and left facial weakness which involves frontalis, orbicularis oculi, orbicularis oris, and platysma.

Cerebrospinal fluid studies show 88 wbc/cu mm and all are mononuclear. Protein is 110 mg/dl and glucose 70 mg/dl. The IgG index is elevated and oligoclonal bands are present.

Case 11 Questions

1. What part of the general physical examination could be diagnostic?
2. Does geography matter?
3. What are the two main diagnostic considerations?
4. What tests may distinguish between these diagnoses?
5. What is the most likely diagnosis?

Case 11 Analysis

1. Careful inspection of the skin may reveal an erythematous ring-like lesion with a clear central area, erythema migrans.
2. Yes. This family lives in New Jersey, a state with a high prevalence of Lyme disease.
3. Sarcoidosis and Lyme disease. Both diseases can cause polyarthralgia, polymyalgia, peripheral facial paresis, meningeal inflammation and abnormal spinal fluid. The cerebrospinal fluid findings, which may occur in both diseases, include a mononuclear pleocytosis, elevated protein, increased IgG index, and oligoclonal bands. In contrast, although multiple sclerosis patients frequently have an increased IgG index and oligoclonal bands, there is a normal CSF protein and mild, if any, pleocytosis.
4. For Lyme disease, serologic tests of blood and spinal fluid are useful. For sarcoidosis, angiotensin-converting enzyme levels may be increased, chest x-ray may show hilar adenopathy and gallium scans can be abnormal. Biopsy of lymph nodes or muscle are occasionally required for the diagnosis of sarcoidosis.

5. *Diagnosis*: Lyme disease [37].

Comment Lyme disease is caused by Borrelia burgdorferi bacteria, a spirochete, which is carried by deer, small mammals (especially mice) and birds. Erythema migrans is the prototypical initial skin manifestation often with a "bulls-eye" rash. The highest prevalence is in the northeastern states. The most common neurologic complications are the triad of meningitis, radiculitis and cranial neuritis.

Case 12 An 88-year-old woman complains of a 1-week history of severe bilateral occipital headache and jaw pain when chewing. She has type II diabetes and chronic obstructive pulmonary disease, the latter a result of a one pack per day smoking history for 55 years. She stopped smoking 5 years ago. She takes metformin and uses an Albuterol inhaler.

Neurologic examination is normal. Laboratory tests are performed and she is started on prednisone 60 mg q.d.

Over the next 6 months, the patient's dose of prednisone is gradually reduced to 10 mg q.d. Her blood tests are now completely normal, but her headache returns and increases in intensity to a level of 9/10. She is readmitted to the hospital.

Neurologic examination reveals a temperature of 101 °F, blood pressure 140/90, and a regular heart rate of 90. She has severe photophobia and phonophobia. Her eyeballs are tender to palpation. Examination otherwise is normal. Pertinent laboratory tests reveal a hematocrit of 39%, white count of 16,000/cu mm with 80% neutrophils, and she has a normal metabolic panel. The sedimentation rate (ESR) is 20 mm/h. An MRI scan of the brain shows a few scattered T2/FLAIR hyperintensities which are not unusual in number and size for age.

Case 12 Questions

1. What tests were performed when she was first seen which established the original diagnosis?

2. What finding on the second neurologic examination helps to determine the next test?
3. What is the next test?
4. What could this examination show?
5. What is the diagnosis?

Case 12 Analysis

1. The tests performed were an ESR which was 96 mm/h and a CRP (C- reactive protein) was 20 mg/L. The patient refused a temporal artery biopsy. The headache with temporal arteritis may be unilateral or bilateral and located anywhere on the head. Any person over the age of 50 who has a persistent headache must have an ESR and CRP drawn. Jaw claudication is due to ischemia of jaw musculature which is a result of inflammatory involvement of the internal maxillary artery, a branch of the external carotid artery.
2. Eyeball tenderness may occur with meningeal irritation. This finding in addition to fever and photophobia raises the distinct possibility of a chronic meningitis or subarachnoid hemorrhage. Infection must be suspected in any patient with fever who is taking prednisone.
3. Lumbar puncture.
4. The patient has turbid cerebrospinal fluid with 700 wbc/cu mm of which 90% are mononuclears. The protein is 102 mg/dl. There is a positive India ink preparation and cryptococcal antigen is present.

5. *Diagnoses*:

   (a) Cryptococcal meningitis [44].
   (b) Temporal arteritis.

Comment Diabetes mellitus and immunosuppression predispose patients to infections, commonly fungal. Evaluation of the CSF must be considered in all patients under treatment for temporal arteritis who have recrudescence of symptoms.

Case 13 An 82-year-old man is admitted to the hospital because of acute confusion, fever, cough, and hypotension. Past medical history is unknown and there are no family members available.

Neurologic Examination Blood pressure 80/50, pulse 60, temperature 101 °F.

The neck is supple and there is no adenopathy. There is a grade 3/6 systolic murmur at the apex; rales, decreased fremitus and breath sounds are present at the left base. The spleen is palpable.

Case 13 Questions

1. What diagnosis is suspected and proven?
2. What examinations are abnormal?

Treatment is initiated. The patient improves over the course of 1 week. The patient's mental status returns to normal. On the seventh hospital day the patient

asks for a “boke” instead of “coke.” On the eighth hospital day the patient complains of a sudden severe headache, joint pain, clumsy right hand and stiff neck.

Neurologic Examination Blood pressure is 120/70, temperature 99.6 °F, pulse 100. Speech is fluent but he makes phonemic paraphasias such as requesting a “goose paper” instead of a newspaper. He makes position sense errors at the right fingers. Within 8 h he complains of neck pain and is found to have a positive Brudzinski’s sign. A stat CT scan (head), noncontrast, is normal.

Case 13 Additional Questions

3. What test is performed?
4. What are the most likely results?
5. What diagnosis should be high on the list?

Case 13 Analysis

1. This patient has acute bacterial endocarditis. He has the murmur of mitral insufficiency, signs of a left lower lobe pneumonia, and an enlarged spleen.
2. He has hematuria, positive blood cultures with streptococcus viridans and a mass on the mitral valve seen on echocardiogram.
3. Lumbar puncture. He has nuchal rigidity and a positive Brudzinski’s sign.
4. The CSF is bloody and the supernatant is xanthochromic. There are 250 wbc/cu mm with 90% neutrophils and rbc’s too numerous to count. Gram stain is positive for cocci in chains. A normal CT scan (brain) does not rule out subarachnoid hemorrhage. About 5–10% of CT scans will be negative for blood.
5. Mycotic aneurysm. A repeat CT (brain) performed 2 days later, because of worsening of aphasia, discloses a 2 cm intracerebral hematoma within the left posterior temporal lobe. Angiography demonstrates an aneurysm in a distal branch of the left middle cerebral artery, a typical location for mycotic aneurysm. The first symptom of an embolic event were the phonemic paraphasias which would be the optimal time for neurologic investigations.

Diagnoses

1. Intracerebral hematoma, left posterior temporal lobe and subarachnoid hemorrhage secondary to a ruptured mycotic aneurysm [43].
2. Acute bacterial endocarditis.

Case 14 A 52-year-old woman is referred to the neurology clinic because of a 1-week history of severe, diffuse headache, impaired vision on the left side, and a clumsy left hand. She is currently being treated with cyclosporine for aplastic anemia. The initial neurologic examination reveals a blood pressure of 180/110. Abnormal findings include disorientation to month and year, difficulty performing simple addition such as 14 + 7, and 0 recall of 3 words after 3 min have elapsed. She has a left homonymous hemiachromatopsia, poor rapid alternating movements of the left arm, and position sense loss at the left fingers.

She is admitted to the hospital, has a grand mal seizure on the night of admission and, when questioned afterwards, says that her vision is normal. Neurologic exami-

nation discloses an alert patient, disoriented to place and date. She is unable to count fingers with either eye but can perceive light flashes. Pupils are 4 mm equal and reactive to light at 4 + / 4. She has a left arm pronator drift, absent position sense at the left fingers, and impaired rapid finger tap on the left. There is sensory extinction of the left side with double simultaneous stimulation.

An MRI shows large T2 hyperintensities, mainly parieto-occipital white matter, right greater than left.

The patient is treated with labetalol and phenytoin. Blood pressure returns to normal after 2 h to 116/80. Cyclosporine is withheld. Forty-eight hours later, the patient has a normal mental status and vision returns to normal. The left arm is no longer clumsy, but she still makes a few position sense errors at the fingers. Vibration sense is normal. A repeat MRI (head) 3 days later is normal.

Case 14 Questions

1. What clinical syndrome did this patient have?
2. Is it common to have normal strength but impaired finger tap?
3. Is it common to have impaired position sense and normal vibratory perception?
4. What is the diagnosis?
5. What conditions are associated with this disorder?
6. What could be the pathogenesis?
7. What are the treatment considerations?

Case 14 Analysis

1. Anton's syndrome. This is denial of blindness which may occur with bilateral occipital lobe lesions. Pupillary responses are intact since the light reflex pathway leaves the optic tract, travels through the brachium of the superior colliculus, then to the pretectum, Edinger–Westphal nucleus, third nerve, ciliary ganglion, sphincter pupillae.
2. Yes. Functional testing such as finger tap, foot tap and rapid alternating movements is more sensitive to uncover impaired motor function and should be the initial focus with an evaluation, particularly if there is central nervous system disease.
3. Yes. This is frequent with cerebral lesions but not with brainstem, spinal cord or peripheral nerve disease in which case vibration loss precedes deficits in position sense.

4. *Diagnosis*: Posterior reversible encephalopathy syndrome (PRES) [29] due to cyclosporine toxicity. This is also known as hyperperfusion encephalopathy.

5. Other illnesses associated with posterior reversible encephalopathy syndrome [28, 29].

   (a) Pre-eclampsia and eclampsia.
   (b) Hypertensive encephalopathy.
   (c) Postcarotid endarterectomy with ipsilateral hyperperfusion especially with prior severe, critical stenoses. Occasionally, this may be bilateral.
   (d) Postsurgical treatment of arteriovenous malformations.
   (e) Lupus nephritis.

(f) Drug overdose or toxicity.
(g) Chemotherapy for malignancy.
(h) Renal disease.

6. Altered cerebral autoregulation. Cerebral vessels supplying the occipital lobe have less sympathetic innervation and are therefore less protective for hypertensive events.
7. Avoid steroids which may produce endothelial dysfunction, discontinue provoking drugs and treat with beta blockers such as labetalol or calcium channel blockers.

Case 15 A 47-year-old male certified public accountant is referred by an ophthalmologist because of visual disturbances. The patient describes four episodes over the last 2 weeks of altered color vision. His entire visual field turned a deep red on each occasion for 2–4 min. Additional symptoms include chronic fatigue and a gradual decline in his performance at work over 1 year. He feels unmotivated and seldom contributes to discussions in group meetings. He has to struggle to recall details of contracts he has drawn up. He has no illnesses nor does he take any medicine.

Neurologic Examination Blood pressure 130/80, pulse 76 and regular, temperature 98.6 F.

Abnormal findings include inability to perform serial seven subtractions and poor short-term recall. He has a left homonymous inferior quadrantanopsia to rapid finger count. Optokinetic slow phases to the right are impaired and quick phases to the left appear slow. He has a right arm pronator drift upwards and loss of position sense at the right fingers and wrist.

MRI (head) shows two T2 hyperintensities, right parieto-occipital and left parietal. There is no contrast enhancement on a T1 study.

Case 15 Questions

1. What is the name of the visual syndrome?
2. What are the four salient features of the present illness?
3. What is the localizing value of each abnormal finding?
4. What is the differential diagnosis?
5. What tests were positive and diagnostic?
6. What other disorders occur with this disease?

Case 15 Analysis

1. Illusory spread of color, more specifically erythropsia (red) in this case [11]. This phenomenon is occasionally an epileptiform event. It is usually associated with a nondominant parieto-occipital lesion.
2. The patient has a 1-year history of chronic fatigue, visual disturbances, cognitive impairment, and multifocal signs.
3. The inability to perform serial sevens and the impaired short-term recall are nonlocalizing findings which together indicate bilateral cerebral hemisphere disease. It should be recognized that inability to perform serial seven subtractions is common amongst the general public but not with the patient's education and successful work history as a certified public accountant. The left homonymous inferior

quadrantanopsia to rapid finger count indicates a lesion affecting the optic radiations in the right parietal lobe. Conversely, a temporal lobe lesion which interrupts optic radiation pathways would produce a superior homonymous quadrantanopsia. Optokinetic slow phases to the right are impaired and quick phases to the left appear slow. This is also compatible with a right cerebral, especially parietal lesion. Furthermore, the right arm pronator drift upwards and loss of position sense at the right fingers and wrist also indicates a left parietal lesion. Of note is the intact vibration perception which is commonly preserved with cerebral lesions.

4. The differential diagnosis includes infection, demyelinating disease, neoplasm and paraneoplastic syndrome as the primary considerations.

A primary neoplasm such as a glioma is nearly always unilateral. Metastatic neoplasm could be a reasonable explanation, but neither illness is likely to have been so slowly progressive over 1 year. Lack of enhancement of the lesions with contrast nearly excludes neoplasm. Conversely, a paraneoplastic syndrome is a consideration. Demyelinating disease is likely by MRI criteria. Multiple sclerosis, the epitome of a demyelinating disorder, presents initially with optic nerve, brainstem, or spinal cord involvement, at variance with this clinical presentation. An infectious etiology whether fungal, bacterial, viral, or parasitic are diagnostic possibilities. All of them are likely to be acute and devastating, incompatible with this alert, mildly dysfunctional individual.

Diagnosis Progressive multifocal leukoencephalopathy associated with human immunodeficiency virus (HIV) [53].

5. This patient has positive diagnostic tests, HIV serology and PCR for JC virus in the spinal fluid. Additionally, he may have HIV dementia, typically subcortical, as he exhibits memory impairment and abulia which is manifested by his loss of initiative, apathy, and paucity of speech.
6. HIV predisposes to any opportunistic central nervous system infection whether bacterial, protozoan, viral, or fungal. Neoplasms, especially primary central nervous system lymphoma and metastatic Kaposi sarcoma, are complications. Additional associated diseases include vacuolar myelopathy, sensory polyneuropathy, and myopathy.

Comment This is a demyelinating disorder caused by the JC virus (John Cunningham – named after a patient) which is carried by more than 90% of the population in latent form in the kidney. The virus infects the oligodendrocyte, the glial cell responsible for myelination. It has a predilection for parieto-occipital white matter. Although the natural course is usually subacute there are chronic cases.

Case 16 A 54-year-old woman is admitted to the hospital because of fever and cough productive of yellow sputum. Six months ago she had a left hemiglossectomy and radical neck dissection for carcinoma of the tongue. She has been anorectic, lost 26 lb after surgery, currently weighs 82 lb, and is dehydrated. Her pneumonia is treated successfully with antibiotics and she is rehydrated. On the

third hospital day, she complains of dizziness and the nurses find that her level of consciousness varies from alert to lethargic with occasional brief episodes of unresponsiveness.

Neurologic Examination Blood pressure 94/50, pulse 100, temperature 98.6 F.

The patient is lethargic but is rousable and then completely oriented with normal speech, naming, and repetition. She spells, adds, and reverses words correctly. There is horizontal gaze-evoked nystagmus, paresis of the left inferior oblique, both superior rectus and right superior oblique muscles. She has moderate bilateral heel-to-shin and finger-to-nose ataxia and an ataxic, wide-based gait.

Case 16 Questions

1. Where is the lesion? Why?
2. What does each eye movement sign signify? Why is there ataxia?
3. What is the diagnosis?
4. What treatment restores the patient to a normal neurologic examination within 48 h?

Case 16 Analysis

1. Midbrain. The altered sensorium indicates pathology affecting the upper pontine, midbrain or thalamic reticular formation. The eye signs which indicate third and fourth nerve dysfunction associated with cerebellar system abnormalities support the presence of midbrain localization.
2. Horizontal gaze-evoked nystagmus means nystagmus to the right on right lateral gaze and nystagmus to the left on left lateral gaze. Nystagmus present in two directions is always of central nervous system origin (brainstem or cerebellum) or a toxic effect of drugs on the central nervous system. Horizontal gaze-evoked nystagmus does not have a precise localizing value. One exception would be the infrequent patient with congenital nystagmus, although ordinarily pendular, who usually informs the examiner that his eye findings are of longstanding. The left inferior oblique and superior rectus pareses indicate a partial left third nerve palsy due to a lesion affecting adjacent third nerve fascicles. The right superior rectus weakness is due to the lesion involving the left third nerve nucleus since fibers emanating from this nucleus cross to innervate the contralateral superior rectus muscle. The superior oblique weakness O.D. indicates a right fourth nerve lesion or a left trochlear nucleus lesion. The latter is likely in this case since the left third nerve nucleus is also involved. The ataxia is a result of damage to the brachium conjunctivum (superior cerebellar peduncle).

3. *Diagnosis*: Wernicke's encephalopathy [54].

Comment The patient has the triad of this disorder, altered sensorium, eye signs and ataxia. The patient was obviously poorly nourished, cachectic, and evidently deficient in stores of the B vitamins, primarily B_1. Hydration with D_5W or saline solutions without vitamin supplementation resulted in depleting whatever B_1 stores remained with subsequent precipitation of this syndrome.

4. Vitamin B_1 100 mg. given IV and then by mouth daily restored the patient to normal neurologic function.

Case 17 An 82-year-old woman complains of dizziness only when walking. This has progressively increased over the last 3 months. She feels well otherwise.

Past medical history includes repair of an ascending aortic aneurysm, hypertension, and resection of colon carcinoma 1 year ago. She had bacterial meningitis at age 62 and recovered quickly without sequelae.

Neurologic Examination Blood pressure is 130/76 with a regular pulse of 106. The patient has an abnormal gait manifested by difficulty initiating a step after getting out of a chair. After she does take a first step, her subsequent gait is shuffling and she takes extra steps when turning. When seated on the examining table she falls backwards and must be supported by a nurse standing behind her.

Case 17 Questions

1. What is the name of this gait disorder?
2. What other symptoms should the patient be questioned about?
3. What is the significance of falling backwards?
4. Is the past medical history relevant?
5. What is the differential diagnosis and the final diagnosis?

Case 17 Analysis

1. Gait apraxia.
2. Questions that might yield diagnostic responses relate to memory loss, bladder function, tremor, handwriting, and initiating movements such as turning in bed or getting out of a chair. In other words, does this patient have a cognitive disorder associated with extrapyramidal dysfunction or an extrapyramidal disorder such as Parkinson's disease?
3. Falling backwards, retropulsion, may occur with Parkinson's disease, communicating hydrocephalus and, rarely, mass lesions affecting midline structures or causing a midline shift.
4. Yes. The patient had meningitis 20 years ago.
5. The differential diagnosis is hydrocephalus, Parkinson's disease, and mass lesion affecting midline structures.

Diagnosis Communicating hydrocephalus, remote complication of meningitis.

Comment The symptoms and signs of communicating hydrocephalus commonly include the triad of gait apraxia (not ataxia), dementia and urinary incontinence. There is free flow of cerebrospinal fluid from the lateral ventricles to the lumbar subarachnoid space. The gait apraxia nearly always occurs first. When the syndrome begins with dementia, degenerative disease is much more likely. A resting tremor, micrographia and bradykinesia would support a diagnosis of Parkinson's disease. Hydrocephalus may be a sequela of meningitis and subarachnoid hemorrhage as

well as due to the idiopathic syndrome of normal pressure hydrocephalus (NPH). This patient has communicating hydrocephalus due to bacterial meningitis which likely caused adhesions and partial obstruction of spinal fluid resorption into the venous sinuses. The disorder may develop slowly over decades, but it is more often a subacute complication.

A useful standard test to confirm the diagnosis in patients with suspected NPH is evaluating gait before and after a lumbar puncture with drainage of 40–50 cc of CSF. A marked improvement of gait the following day supports the diagnosis. An additional technique is the TUG (timed up and go) test [36]. This measures the time it takes for a seated patient to stand, walk 3 meters and return to a seated position. This is done before and one day after the lumbar puncture. An improvement of 5 s predicts an improvement of more than 10 s one year post-shunt.

Case 18 A 40-year-old bachelor, living alone, is brought to the Emergency Room by a neighbor because of progressive confusion first noted 1 week ago. His neighbor initially thought he was drunk since he had obviously been inebriated on several occasions during the preceding 6 months. His past medical history is otherwise unknown.

Neurologic Examination Blood pressure is 120/70, pulse 86, regular, and he is afebrile. The patient is alert and has fluent, rapid, and unintelligible speech. Naming and repetition are impaired. He states his name and follows two but not three-step commands. Perseveration is common. He has a right Hoffmann's sign and the right plantar response is neutral whereas the left is flexor.

Case 18 Questions

1. Where is the lesion? Explain the abnormal neurologic signs.
2. What are the diagnostic considerations?
3. What tests should be performed?
4. What is the etiology?

Case 18 Analysis

1. Fluent, rapid, unintelligible speech with poor repetition and poor comprehension is compatible with a fluent aphasia, Wernicke's type. Perseveration, repeating the same response to a new request, is a common accompaniment although not a pathognomonic sign of an aphasia. The reflex asymmetries support localization to the left cerebral hemisphere.
2. Neither an ischemic nor hemorrhagic stroke is likely to present with a steadily although rapidly progressive decline in language function over several days. An ischemic infarction with secondary edema or an intracerebral hematoma with recurrent bleeding or edema could be the etiology, but they are usually acute. Neoplasm, especially metastatic with secondary hemorrhage, is an additional possibility. An infection, mainly herpes simplex encephalitis (HSV-1), fits the clinical presentation and is the etiology.

3. The electroencephalogram shows periodic lateralized epileptiform discharges in the left temporal leads. The MRI reveals T2 and FLAIR (fluid attenuated inversion recovery) hyperintensity in the left temporal lobe. Cerebrospinal fluid contains 90 lymphocytes/cu mm and 300 rbc/cu mm, indicating the presence of a hemorrhagic encephalitis. PCR (polymerase chain reaction) of CSF discloses HSV-1 DNA.

4. *Diagnosis*: Herpes simplex encephalitis [48].

Comment HSV-1 resides in latent form in the trigeminal ganglion (gasserian) located under the temporal lobe and thus there is a predilection for temporal lobe involvement. The infection may spread to infect the nose and olfactory tract. Additional early symptoms and signs may therefore include anosmia, gustatory and olfactory hallucinations, focal impaired awareness seizure (complex partial seizure) and psychotic behavior. Complications can include cerebral edema and uncal herniation. The patient is treated successfully with acyclovir.

Case 19 A 22-year-old male college student is found on the street, unresponsive. The patient's family was contacted and they report no known illnesses nor does he take any medications. There is neither a history of drug or alcohol abuse nor signs of trauma.

Neurologic Examination Blood pressure is 150/70, pulse 100, temperature 100.2° F, and the neck is supple. The patient responds to pain with movement of all extremities. The oculocephalic maneuver elicits full horizontal and vertical eye movements. Caloric testing with cold water A.S. produces ipsilateral deviation with contralateral nystagmus and vice versa A.D. The right pupil is 6 mm with a 2 + / 4 reaction to light and the left pupil is 3 mm with a 2 + / 4 reaction to light.

Laboratory Data CT scan (head) is normal. CBC reveals a hematocrit of 42%, 13,000 white cells /cu mm with 82% neutrophils. A lumbar puncture discloses 27 wbc/cu mm of which 80% are neutrophils. The protein is 30 mg/dl and glucose 70 mg/dl. Gram stain, fungal smear, and acid-fast smear are normal. The cryptococcal antigen and VDRL are negative. A subsequent MRI scan of the brain is normal.

Case 19 Questions

1. What test is now done immediately?
2. What could it show?
3. What clinical and laboratory findings does this patient have which are consistent with the eventual diagnosis?

Case 19 Analysis

1. Electroencephalogram. An electroencephalogram is the only commonly used neurologic test that evaluates function, not structure. MRI (head) is often normal in a comatose patient as in this case.
2. The EEG discloses continuous generalized sharp and slow wave discharges indicating status epilepticus which explains his unresponsive state.
3. Low grade fever, unilateral mydriasis, and abnormal caloric testing because of ocular deviation. Unilateral mydriasis can be present in the absence of focal

pathology. The mild leukocytosis with left shift and the CSF pleocytosis are well-known occurrences in patients after an acute seizure.

Diagnosis Nonconvulsive status epilepticus [27].

Comment Nonconvulsive status epilepticus is frequently overlooked if there are no witnesses at the onset of the seizures. Unilateral mydriasis, in this case, is especially puzzling since the CT (head) is normal, but it is a known inexplicable and rare occurrence after a seizure. One speculation is secondary spread of initial focal epileptiform activity to the ipsilateral hypothalamus causing sympathetic overactivity.

Laboratory abnormalities such as an increased white blood cell count with left shift and, especially, CSF pleocytosis easily obscure the cause of the patient's stupor or coma. Naturally, the initial diagnosis is often encephalitis. The diagnostic key is an electroencephalogram which should be performed on an emergency basis. This reveals continuous spike and wave abnormalities.

The patient is treated with intravenous valproate and returns to normal after 2 h have elapsed.

Case 20 A 67-year-old man arrives at the Emergency Room with intense paroxysmal abdominal pain. This is his fourth visit over the previous 3 months. In the last 3 years, he has had an appendectomy, cholecystectomy, and two exploratory laparotomies. He has periodic dizziness and an unsteady gait. He has difficulty initiating urination and, additionally, has sporadic urinary incontinence.

Past medical history includes osteoarthritis with an enlarged deformed left ankle. He was a cocaine addict for many years.

Neurologic Examination Blood pressure 130/80 sitting and 90/50 standing. The pulse is 72 and 76, respectively. Pupils are 2.5 mm, irregular and with a 2 + / 4 reaction to light, but 4 + / 4 to near. Visual acuity is 20/30 O.D. and 20/40 O.S., but with pinhole it is 20/20 O.U. There is no central scotoma.

Case 20 Questions

1. What part of the history is unique?
2. What other parts of the neurologic examination could yield diagnostic information?
3. What is the name given for this type of pupillary reaction? Is this a pathognomonic sign?
4. What is the name of this patient's pupillary abnormality and the disease this patient is suffering from?
5. What is the name of the deformed, enlarged joint?

Case 20 Analysis

1. Intense paroxysmal abdominal pain due to dorsal root irritation.
2. The sensory and gait examinations are most useful. The patient has vibration sense loss at toes and ankles and no position sense at the toes. The Romberg test is positive.

3. Light-near dissociation. This is not a pathognomonic sign. It may occur with midbrain and, when there is associated visual impairment, optic nerve lesions.
4. The patient has Argyll–Robertson pupils which are usually small, irregular, symmetrical, and poorly or nonreactive to light, but there is a good reaction to the near stimulus. The diagnosis does not require total absence of a light reaction but there is unequivocal asymmetry between light and near stimuli.

Diagnosis Tabes dorsalis, tertiary syphilis [41].

Comment The pathology is in the dorsal roots with secondary degeneration in the posterior columns. The autonomic nervous system is commonly involved and, in this case, includes orthostatic hypotension and impaired parasympathetic innervation of the bladder. The latter results in urinary retention and overflow incontinence.

4. The patient has a Charcot joint which is associated with sensory loss, cartilage rupture, and bone overgrowth. The same findings may occur in patients with diabetes.

Case 21 A 68-year-old man requests an evaluation for memory loss of 6 months duration. This primarily involves recall of names. He has been depressed since his retirement 1 year ago. He has a history of ulcerative colitis which is quiescent. He was a heavy smoker of two packs per day until 5 years ago when he was hospitalized for 1 week because of pneumonia at which time he was able to quit smoking. At about the same time he noted loss of his sensation of taste. Additionally, he has insomnia with early morning awakening.

Neurologic Examination Blood pressure 150/90. There are bilateral carotid bruits. The pulse is 96 and irregularly irregular. The patient has a flat, depressed affect. His Mini-Mental State Exam score is 26/30. This includes recalling one of three words after 3 min have elapsed, knowing the month but not the date and he makes one error when reversing five-letter words.

Case 21 Questions

1. Could the carotid bruits tie in with his memory loss?
2. Could the cardiac arrhythmia be a factor and what should be done about it?
3. What part of the cranial nerve examination might yield a diagnostic clue?
4. What diagnoses should be considered?

A workup for dementia is indicated with a cbc, TSH, B_{12}, glucose, calcium, electrolytes, BUN, creatinine, liver functions and RPR. An MRI is performed. The patient is seen by a cardiologist and is treated with atenolol and warfarin. Sertraline is added.

Re-evaluation 2 Months Later The patient feels much better. He sleeps well and no longer feels depressed. His wife is present but she is still disturbed by his inertia. He prefers to stay at home and watch television when he used to be urging his wife to go out to dinner and to the movies.

Neurologic Examination The blood pressure is 124/70 and the pulse 64 and irregularly irregular. A Mini-Mental State Exam score is 28/30 (improved).

Case 21 Additional Questions

5. What were the most likely results of the studies performed?
6. What abnormal signs should be searched for with the motor and reflex examination?
7. What examination is likely to be the most valuable in this clinical setting?

Re-Evaluation 4 Months Later The patient reports that his memory is now normal. His wife says he is getting lost when driving in the neighborhood. He no longer goes for daily walks and he exhibits no emotion.

Neurologic Examination Examination is remarkable for a Mini-Mental State Exam score of 20/30.

Case 21 Additional Questions

8. What name can be given for the patient's assessment of his memory?
9. What condition is his wife describing?
10. Although neuropsychological testing shows evidence for a degenerative cause for dementia, namely Alzheimer's disease [34], his wife requests an additional study to support this conclusion. What routine procedure could be useful? What other noninvasive test may be useful?
11. What is the diagnosis?

Case 21 Analysis

1. No. This patient has not had transient ischemic attacks or multiple strokes. Furthermore, memory loss indicates bilateral cerebral pathology and thus may occur only with bilateral cerebral infarctions assuming a vascular etiology.
2. No. This patient has not had transient ischemic attacks or stroke but an urgent EKG reveals atrial fibrillation and a prompt cardiology consultation is indicated.
3. Sense of smell. The patient complains of loss of taste, but the sense of smell provides most of the nuance of taste.
4. Mild cognitive impairment, pseudodementia of depression, Alzheimer's disease.
5. Normal.
6. Paratonic rigidity and grasp reflexes.
7. Neuropsychological testing. This disclosed evidence of a degenerative dementia.
8. Anosognosia.
9. Abulia.
10. Lumbar puncture. There are three useful biomarkers in the CSF, $A\beta_{42}$ (beta-amyloid 42), p-tau and t-tau protein. Patients with Alzheimer's disease have a marked decrease in levels of $A\beta_{42}$ possibly correlated with an increased number of amyloid plaques in brain (the amyloid sink hypothesis). Tau maintains

stability of microtubules in neurons. Hyperphosphorylated tau becomes detached from tubules, polymerized to insoluble paired helical filaments (PHF) which then contribute to neurofibrillary tangles (NFT). NFT formation results in significant disruption of neuronal architecture and tau protein would then be released into the CSF. T-tau is a sensitive test but p-tau CSF concentration is more sensitive and specific in discriminating Alzheimer's disease from normal aging than either t-tau or $A\beta_{42}$ [5].

An Amyvid scan, which measures amyloid plaques, strongly correlates with this diagnosis and is currently the preferred noninvasive test.

Diagnoses

(a) Alzheimer's disease [12].
(b) Depression, often an early sign of Alzheimer's disease.

Case 22(A) A 55-year-old woman living on a farm in a rural community complains of double vision, neck, and low back pain of 10 days duration. She notes that the double vision is horizontal, present only when focusing on distant objects and perhaps more evident when looking to the left. The neck pain bothers her when she puts on her shoes. Her back pain is constant, unchanged by any position and occasionally radiates around to the navel on the left side. Two days ago, she suffered a burn on her right leg when testing the temperature of her bath water.

Past Medical History The patient has hypertension, chronic renal insufficiency with a BUN of 48 mg/dl and creatinine 2 mg/dl. She has chronic bronchitis associated with a one pack per day smoking habit for 35 years.

Neurologic Examination Blood pressure 140/95, pulse 72, temperature 98.6 °F. She has horizontal diplopia only on left lateral gaze when looking at an object beyond 15 ft. The left palpebral fissure is wider than the right. There is a right T10 sensory level to temperature and pin (up to the navel). Temperature testing with a cold tuning fork is often the most sensitive method of finding a sensory level and correlates with the history.

Case 22(A) Questions

1. What is the significance of diplopia at distance?
2. The history mandates an evaluation for and comment about what neurologic signs?
3. Can a single lesion explain the neurologic symptoms and signs? What are the anatomic considerations?
4. A CT (head), noncontrast because of renal insufficiency, is normal. This small community hospital has no MRI unit. What is the next study indicated?

Case 22(A) Analysis

1. Diplopia at distance occurs with sixth nerve palsies. This patient has a left sixth nerve lesion since diplopia is more evident when looking to the left. At distance, the eyes must diverge and thus a lateral rectus paresis is easier to detect.

2. Since head flexion (putting on shoes) causes neck pain, meningeal irritation may be present. A comment about nuchal rigidity or Brudzinski sign should be made. This patient does have nuchal rigidity.
3. No. The patient has a left sixth and seventh nerve paresis. The latter is surmised because of the wider left palpebral fissure implying weak left eye closure (orbicularis oculi). This is likely to be a cranial neuropathy, although a lesion at the facial colliculus in the pons where the seventh nerve fibers loop around the sixth nucleus cannot be excluded. Thoracic radiculopathy is likely to explain the pain radiating around to the navel. Since she burned her right leg a myelopathy affecting the spinal cord on the left side is evident as the lateral spinothalamic tract is crossed. Nuchal rigidity indicates meningeal involvement.
4. Lumbar puncture.

Case 22(B) The cerebrospinal fluid protein is 80 mg/dl. The CSF glucose is 18 mg/dl. A simultaneous serum glucose is 62 mg/dl. CSF glucose is ordinarily about 2/3 of blood glucose. The CSF wbc count is 220 /cu mm with 50% neutrophils. The IgG index is abnormal and oligoclonal bands are present.

Case 22(B) Questions

1. What other spinal fluid test should be performed? Are the abnormal IgG index and the presence of oligoclonal bands compatible with a diagnosis of neoplasm?
2. Is another examination indicated?
3. What diagnosis is most likely?
4. Why is the glucose so low?
5. If all of these additional studies are normal, what should be done next?

Case 22(B) Analysis

1. Cytology with a 10 cc aliquot of fluid, acid-fast smear and culture, gram stain, cryptococcal antigen, fungal smear, and culture. The cytology is negative. Abnormal IgG and the presence of oligoclonal bands may occur with metastatic disease.
2. Yes. An MRI (cervical and thoracic) with and without contrast is indicated. The entire spinal cord requires imaging despite a discrete sensory level. A right T10 epidural lesion is found.

3. *Diagnosis*: Leptomeningeal carcinomatosis due to small cell (oat) carcinoma of the lung [10, 32] and thoracic myelopathy due to an epidural metastasis with spinal cord compression at T10.

Comment

4. There are at least two possible explanations. The tumor cells may utilize glucose and/or there may be defective glucose entry into the cerebrospinal fluid. IV glucose given to patients with leptomeningeal carcinomatosis does not increase CSF glucose levels, whereas, in normal controls, CSF glucose is increased. Thus defective glucose entry into the CSF is probable but does not exclude additional tumor cell utilization of glucose.

5. A repeat lumbar puncture with another 10 cc of cerebrospinal fluid should be sent for cytology. This should further increase the yield of positive cytology to over 90% and it is positive in this case. Infrequently, a third lumbar puncture yields positive findings.

Case 23 A 62-year-old man was admitted to the hospital after an 8-min episode of halting, effortful speech. He has a history of type II diabetes and hypertension. Medicines are metformin and losartan. Examination in the Emergency Room was normal other than decreased right finger tap and a right Babinski sign. An MRI (brain) was normal and an MRA (head and neck) revealed a high-grade stenosis of the M1 segment of left middle cerebral artery. He was discharged on clopidogrel and atorvastatin therapy.

Two weeks later the patient was readmitted because of confusion, diplopia, fatigue and "purple splotches" on both arms. Examination disclosed a heart rate of 90 beats per minute, blood pressure 96/60 and numerous purpura on his arms and chest. Neurologic findings included disorientation to month and year; he followed 3- but not 4-step commands and he could not reverse a 5-letter word. He exhibited paresis of left lateral gaze, weakness of adduction O.S., nystagmus O.D. to the right on right lateral gaze. He had left finger-to-nose ataxia, decreased right finger tap and a right Babinski sign.

Case 23 Questions

1. What type of language disorder was his first symptom? What was the likely lesion location?
2. Is it possible to have a normal MRI despite these symptoms and signs?
3. Is there more than one lesion? Explain.
4. What is the name of the syndrome that explains the eye findings? Is ataxia part of it? Do the findings of decreased right finger tap and right Babinski sign fit with the lesion localization?

Laboratory Data Hematocrit 28%, platelet count 40,000, positive Coombs test, creatinine 2.1 mg%, total bilirubin 3 mg/dl with direct fraction 2 mg%, LDH 700 U/L.

Case 23 Additional Questions

5. What etiology is suspected in view of the laboratory data? What are the associated conditions or illnesses?

Case 23 Analysis

1. Nonfluent aphasia. Frontal lobe with Broca's or transcortical motor aphasia is manifested by halting effortful speech.
2. Yes. Although it is extremely unlikely.
3. Yes. Confusion indicates bilateral cerebral dysfunction. Halting speech which lasted 8 min suggests a transient nonfluent aphasia and thus supports a left frontal or anterior temporal located cerebral pathology. The abnormal eye signs indicate brainstem dysfunction.

4. The one-and-a-half syndrome which in this case affects the left MLF and left PPRF. Ataxia is not part of it and is probably a result of a lesion affecting the left middle cerebellar peduncle (brachium pontis). Yes. The decreased right finger tap and the right Babinski sign are compatible with a left pontine lesion involving the left corticospinal tract in the basis pontis.
5. The patient has a hemolytic anemia, thrombocytopenia with purpura, renal insufficiency and multiple cerebral and brainstem infarctions. A repeat MRI (head) confirmed the presence of multiple infarctions involving the left temporal lobe, left pons and left brachium pontis (middle cerebellar peduncle).

Diagnosis Thrombotic thrombocytopenic purpura (TTP) associated with a left pontine infarction due to microthrombi within small intracranial arteries [15].

Comment TTP has been associated with pregnancy, cancer, systemic lupus erythematosus, HIV, infections and medications. There is also an autosomal recessive genetic form. In this case the etiology is clopidogrel and other culprits include cyclosporine, hormone therapy, chemotherapy and quinine. The etiology is usually auto-antibody mediated inhibition of the enzyme ADAMTS13 which prevents clotting. Treatment is plasma exchange and steroids.

Case 24 A 52-year-old man is admitted to the hospital because of severe headaches and confusion developing over 3 days. On admission, he is disoriented to place and date, but speech content and fluency are normal. He has poor short-term recall. MRI (head) without contrast is normal. Three days after admission, his speech becomes incomprehensible but fluency remains normal. He uses occasional nonsensical words. He has a 20-year history of hypertension controlled with medication. A cbc, ESR, metabolic panel, liver functions, and ANA are all normal. A neurologic consultation is requested.

Neurologic Examination Blood pressure 140/100, pulse 100, regular. There are no carotid bruits. The patient is afebrile and his neck is supple. His speech is rambling, fluent, relatively rapid, and he makes numerous paraphasias such as "flindow" instead of "window," "sty" instead of "fly." He calls a watch a "vintel" and a shoe, "flatsar." Repetition is normal. He does not respond to visual threat in the right visual field when testing each eye alone. He has a slow right finger tap and impaired rapid alternating movements of the right arm.

Case 24 Qustions

1. What two types of paraphasias does he exhibit?
2. What type of aphasia is this and what is its localizing value? Can impaired motor functions and abnormal reflexes be found with lesions in this location?
3. Does this patient have unilateral or bilateral disease?
4. If an MRI (head) and an MRA (head and neck) are normal, what diagnoses should be considered?
5. A repeat MRI (head) performed after the speech abnormality occurred shows three acute infarctions; one is subcortical in the right centrum semiovale, a

second is in the right temporal lobe, and the third is in the left parietal region. An MRA (head and neck) is normal. What diagnoses should be considered?
6. With either a normal or abnormal MRI (brain) what test should be next? What results could be anticipated?
7. After reviewing the nondiagnostic CSF results what is the next indicated procedure?

Case 24 Anaysis

1. Phonemic paraphasias, such as "flindow," and neologisms, "vintel" and "flatsar." A neologism is making up a new word for an object.
2. Transcortical sensory aphasia. This is a fluent aphasia similar to Wernicke's aphasia, but with intact repetition. The lesion is usually outside the perisylvian region in the left parietal cortex. Yes. Abnormal motor function and reflexes are often present. Motor and sensory systems overlap in frontal and parietal lobes.
3. Bilateral because of a confusional state at the onset.
4. Infection, neoplasm and vascular disease.

   (a) Infection. Viral encephalitis is a consideration, especially herpes simplex encephalitis which often presents with an aphasia because it has a predilection for the temporal lobe. The MRI is usually abnormal. Another viral encephalitis is possible. Meningitis is not likely as the neck is supple. Fungal disease causing an associated vasculitis and human immunodeficiency virus (HIV) should be considered.
   (b) Neoplasm, especially primary central nervous system lymphoma. An MRI (head) should show the lesions, however, even before all the symptoms emerge.
   (c) Vascular. MRI scans are usually abnormal but may not be specific with regard to the etiology.

   Vasculitis such as primary angiitis of the central nervous system. Other types such as polyarteritis nodosa or systemic lupus erythematosus usually have systemic signs.

   Cardioembolism, especially subacute bacterial endocarditis, is a consideration except for the absence of systemic signs.

   Reversible vasoconstriction syndrome [16]. Etiologies to consider are migraine, illicit drug use, and over-the-counter medicines for colds that include pseudoephedrine or other similar compounds. It may occur during the puerperium. CSF is normal in these disorders as vasoconstriction is the etiology of these symptoms.

5. Vascular etiologies as described under 4(c).
6. The next test is a lumbar puncture which shows: 110 wbc/cu mm of which 95% are lymphocytes, 200 rbc/cu mm, protein 94 mg/dl, glucose 77 mg/dl with a simultaneous blood sugar of 110 mg/dl. Cytology, gram stain, India ink prep, cryptococcal antigen, VDRL, AFB smear, and PCR for herpes simplex are negative.

7. A brain and leptomeningeal biopsy should be performed to obtain a specimen from the tip of the nondominant temporal lobe. Angiography is optional although it may support a diagnosis of vascular disease as it may reveal beading of vessels indicating a probable inflammatory process such as vasculitis. However, this is not pathognomonic and the same abnormalities have been observed with fungal infections, fibromuscular dysplasia, infectious vasculitis, and primary CNS lymphoma. The absence of systemic symptoms and signs supports the eventual diagnosis. The biopsy discloses Langerhans-type giant cells, lymphocytes, histiocytes, and plasma cells.

Diagnosis Primary angiitis of the central nervous system [40].

Comment Severe headaches, stroke-like evolution and confusion are the usual initial manifestations. Although angiography and CSF evaluation have the best chance of revealing diagnostic information, the results are commonly not pathognomonic. The differential diagnosis is noted above and biopsies are usually required.

Case 25 A 42-year-old woman is referred by her PCP because of persistent dizziness one month after an ocean cruise. The patient reports that the morning after an Alaskan cruise of 10 days the dizziness occurred. She denies vertigo, headache, nausea, hearing loss or tinnitus. She describes the dizziness as a rocking sensation that is a bit worse when sitting such that she prefers to be physically active. Nevertheless, driving seems to relieve her symptoms. She believes there may be slight improvement over the last week. She has no illnesses and takes no medicines. She has no history of migraine.

Neurologic examination is completely normal including the Dix-Hallpike maneuver, head thrust and dynamic visual acuity tests.

Case 25 Questions

1. What workup is indicated? What are the likely results?
2. What is the differential diagnosis?

Case 25 Analysis

1. Electronystagmography should be performed to evaluate for peripheral vestibular disease since evidence for vestibular neuritis or Ménière's disease may be discovered. A diagnostic audiogram is performed because of the possibility of Ménière's disease. Low frequency hearing loss supports the diagnosis. Consider MRI if the symptoms persist or worsen. Both electronystagmography and the diagnostic audiogram are likely to be normal.
2. Vestibular migraine, Ménière's disease, residual from vestibular neuritis, chronic anxiety, withdrawal syndrome from SSRI medications. A perilymph fistula or superior canal dehiscence are considerations if the syndrome follows air travel.

Diagnosis Mal de debarquement syndrome [2, 42].

Comment This frequently overlooked syndrome has been well-documented. It occurs most often after a cruise of more than one week, less frequently after air travel. About 90% of patients are women between the ages of 40 and 60. Similar symptoms may arise after withdrawal from or initiation of SSRI medicines, usually the former. The duration of symptoms varies from weeks to even years. These facts suggest both a hormonal factor and serotonin-related disorder. Another hypothesis is a genetic predisposition.

Case 26 A 53-year-old woman is brought to her internist under duress by her family because of a 5-month history of behavioral changes, loss of memory, and poor balance. She has become withdrawn, depressed, and paranoid. She accuses her husband of having a mistress and cannot be dissuaded from this fixed belief (Othello syndrome). Her only medical illness is asthma which is well-controlled with albuterol. The family history is significant as her father was bedridden from Parkinson's disease and died at age 62. One of four siblings has tremor and a gait disorder.

Neurologic Examination Blood pressure 110/70 and pulse 96, regular.

The patient appears sullen and hostile. Her Mini-Mental State Exam score is 24/30. Her speech is dysarthric. She has difficulty initiating saccades which are clearly slow and are accompanied by simultaneous head movements. Optokinetic nystagmus is difficult to elicit and quick phases of nystagmus are slow. She is unable to protrude her tongue for more than 1 s. When checking for arm drift, facial grimacing is prominent. She appears restless and fidgety. Her strength is normal but grasp is characterized by repetitive squeezing of the examiner's fingers. Her gait is ataxic and lurching.

Case 26 Questions

1. What are the three major elements of the patient's illness?
2. What is the name of this patient's eye movement disorder and does it have diagnostic significance?
3. What type of movement disorder does this patient have?
4. What is the significance of repetitive squeezing of the examiner's fingers when checking grasp?
5. What is the most likely diagnosis as well as other illnesses which may produce similar presentations?

Case 26 Analysis

1. Psychosis, memory loss, and movement disorder.
2. Ocular motor apraxia. It is an early manifestation of this disease but it is not pathognomonic.
3. Hyperkinetic and choreiform.
4. Repetitive squeezing of the examiner's fingers ("milkmaid's grip") as well as intermittent tongue protrusion ("trombone tongue") are both common with chorea.

5. *Diagnosis*: Huntington's chorea [22, 55].

Comment The major differential diagnoses are:

(a) Metabolic disorders: hyperthyroidism, hypoparathyroidism, hypernatremia, hyponatremia, hypomagnesemia, hyperglycemia, hypoglycemia, nutritional deficiencies, and acquired hepatocerebral degeneration.
(b) Infectious diseases: Sydenham's chorea, encephalitis, and Creutzfeldt–Jakob disease.
(c) Genetic diseases: Wilson's disease, benign hereditary chorea, adult onset neurodegenerative disease with brain iron accumulation, and neuroacanthocytosis (very rare).
(d) Drugs: phenytoin, amphetamines, neuroleptics, dopaminergic drugs, tricyclics, oral contraceptives.
(e) Degenerative diseases: multiple system atrophy (MSA), progressive supranuclear palsy (PSP), corticobasal degeneration (CBD).
(f) Senile chorea.
(g) Systemic lupus erythematosus.
(h) Paraneoplastic disease.
(i) Autoimmune disorders usually of acute or subacute onset.
(j) Celiac disease.

The genetic basis of Huntington's chorea is a mutation on chromosome 4 which contains an unstable expansion of CAG (cytosine, adenine, guanine) repeats. This causes an increase in the Huntingtin protein which has a predilection for damaging neurons in the caudate nucleus.

The family history must be scrutinized as the disease has an autosomal dominant inheritance pattern. Since parkinsonism is a well-known feature in some cases of Huntington's chorea her father probably suffered from this disease. MRI scans show cerebral and caudate nucleus atrophy. DNA testing is available.

Case 27 A 45-year-old woman is brought to the Emergency Room because of the abrupt onset of left-sided weakness and double vision. She has no previous history of neurologic disease other than migraine and a remote history of an optic neuritis with mild residual visual impairment. There is no family history of neurologic disease or stroke. She is a lawyer, married for 20 years, and has no children although she has wanted them. She has mild hypertension treated with atenolol and it has been under good control. She smokes a half a pack of cigarettes per day.

Neurologic Examination Blood pressure 140/105. Pulse 82, regular.

O.D.: Visual acuity 20/30, central scotoma to red matches, and a relative afferent pupillary defect.
O.D.: Remains midline and has full up and down gaze but there are no horizontal eye movements.
O.S.: Deviated to the left and also has full vertical eye movements but there are no horizontal eye movements.

She has a mild left arm pronator drift, impaired finger and foot tap on the left side and poor rapid alternating movements of the left arm.

She has a left hyperreflexia, Hoffmann's and Babinski sign.

Laboratory data: CBC is normal except for a platelet count of 86,000 /cu mm. Metabolic profile, liver functions, PT and ESR are normal. The PTT is elevated by 1 s.

Case 27 Questions

1. What structures are affected that produce these neurologic abnormalities?
2. What is the name of the eye movement syndrome?
3. What two disease categories are the primary considerations?

Neuroimaging MRA (head and neck) are normal. MRI (head) shows a few scattered T2 and FLAIR hyperintensities which are both subcortical and in the brainstem but not periventricular. Diffusion-weighted imaging (DWI) shows a hyperintense lesion in the right pontine tegmentum extending to the basis pontis. The finding supports a diagnosis of an acute infarction.

Cerebrospinal fluid is normal including IgG index and oligoclonal bands.

Case 27 Additional Questions

4. Since a vascular etiology is likely because of an elevated PTT, thrombocytopenia multifocal signs and abnormal DWI on MRI, what additional information should be obtained from the patient?
5. What additional laboratory tests should be drawn?
6. What diagnosis is suspected and proven?

Case 27 Analysis

1. The previous optic neuritis could be either on an ischemic or demyelinating basis. If it was ischemic, the diagnosis was likely to be anterior ischemic optic neuropathy. The lesion which explains the horizontal paresis of the right eye would be a right MLF lesion causing a right adduction paresis and a right PPRF lesion which causes a right gaze paresis. Hence, the right eye has no horizontal movement. The left eye deviates to the left because of the right PPRF lesion.
2. One-and-a-half syndrome. Horizontal nystagmus to left, O.S., may also occur.
3. Vascular and demyelinating disease.
4. The patient should be questioned about whether she had spontaneous abortions. She responds that she had three.
5. Lupus anticoagulant, anticardiolipin antibodies, ANA, RPR, FTA-ABS.

   Results are elevated anticardiolipin antibodies, positive test for lupus anticoagulant, ANA positive 1:320, RPR positive, FTA-ABS negative. The patient has already had a platelet count which was low at 86,000 /cu mm and a PTT elevated by 1 s. An abnormal PTT is a major clue for this diagnosis even if minimally elevated.

6. *Diagnosis*: Antiphospholipid antibody syndrome [31].

Comment Common manifestations of this syndrome include migraine, visual disturbances, a history of spontaneous abortion, thrombophlebitis, pulmonary

embolism, and recurrent ischemic stroke. Acute encephalopathy, seizures, and disseminated intravascular coagulation have been reported.

The primary treatment is anticoagulation without which the majority of patients would probably have recurrent complications including ischemic stroke. Prednisone is generally not effective nor is it used unless anticoagulation is unsatisfactory.

Case 28 A 31-year-old woman is brought to the Emergency Room because of the sudden onset of severe headache, mild confusion, paranoid ideation and rapid, jerky, uncontrollable movements of both hands. Four months ago she had the abrupt loss of consciousness, facial grimacing, and lip smacking lasting 2 min. An MRI (head) with and without contrast was normal. An EEG disclosed a right temporal sharp wave focus. The patient had four similar focal unaware nonmotor seizures (complex partial seizures) until a satisfactory lamotrigine level was achieved 2 months ago. She has had no seizures since then. Three months ago, she noted burning and tingling sensations in the feet associated with slowly progressive weakness of both legs, and poor balance. One month ago she became severely depressed.

Neurologic Examination Blood pressure 160/90. Pulse 84, regular. The patient is agitated, disoriented to month and year and recalls 1/3 words after 3 min have elapsed. She has rapid, jerky movements of both hands. There is mild proximal and moderate distal leg weakness. She has an unsteady gait with bilateral footdrop. Reflexes are absent in the legs. Position sense is impaired at the toes and there is loss of vibratory perception at toes and ankles. There is distal sensory loss to pin in both legs and both hands.

Case 28 Questions

1. Where is or are the lesions? Could this patient have a myelopathy?
2. What is the name of the movement disorder?

Laboratory Data CBC, electrolytes, and glucose are normal. Creatinine is 2 mg/dl and BUN 39 mg/dl. Liver functions are normal.

The patient is treated with haloperidol and is no longer paranoid or agitated. On the third hospital day she is still confused. The neurologic examination reveals an alert patient oriented × 1 only, who follows just simple commands. She is unable to add 14 + 7 and reverse the word "hand." Her short-term recall is 0 after 3 min have elapsed.

Case 28 Additional Questions

3. What other neurologic studies are indicated? What might they show?
4. Could this patient have multiple sclerosis?
5. This patient has a unique cluster of symptoms and signs that point to a specific illness. Your thoughts?
6. Are the CSF findings compatible with this disease?
7. What additional laboratory tests can be diagnostic?

Case 28 Analysis

1. There is both diffuse and focal cerebral hemisphere involvement. The focal involvement is manifested by the history of seizures due to a right temporal lobe epileptic focus. Diffuse involvement is manifested by the confusional state. The abnormal involuntary movements indicate an extrapyramidal disorder. Neuropathy is evident because of absent reflexes, distal greater than proximal weakness, and distal sensory loss. There are no signs of myelopathy such as spasticity, asymmetric, increased or pathologic reflexes, or a sensory level.
2. Chorea. The rapid, jerky movements with predilection for distal musculature are characteristic findings.
3. Electroencephalography and lumbar puncture.

   The EEG shows a diffusely slow pattern with a few right temporal sharp waves, an epileptiform finding. Cerebrospinal fluid shows six wbc/cu mm (lymphocytes), protein of 77 mg/dl, increased IgG index, and oligoclonal bands.
4. No. Multiple sclerosis does not cause neuropathy and rarely, if ever, an acute confusional state. Although abnormal involuntary movements may occur, they are rare.
5. The acute confusional state in a young woman who has seizures, depression with psychotic features, choreiform movements and neuropathy point to neuropsychiatric systemic lupus erythematosus (NPSLE). Additionally, renal insufficiency supports the diagnosis of a systemic illness.
6. Yes.

Diagnosis Systemic lupus erythematosus, specifically NPSLE [25].

7. ANA is positive in 98% of patients with neuropsychiatric manifestations of SLE (NPSLE). Anti-double-stranded DNA is positive in 60% of patients with NPSLE. SSA, SSB, anti-Smith, anticardiolipin, and lupus anticoagulant studies are frequently positive.

Comment The acute confusional state may be due to antineuronal antibodies, but this is a diagnosis of exclusion in view of other possible etiologies such as venous thrombosis, multiple strokes, seizures, metabolic encephalopathy, and opportunistic infections, particularly fungal diseases. Chorea may be due to small vessel ischemic disease or antineuronal antibodies. Seizures are thought to be related to antiphospholipid antibodies as well as antineuronal antibodies.

Case 29 A 30-year-old woman complains of difficulty using her right hand for delicate movements required for making jewelry. This began just 1 week ago simultaneous with numbness of the left leg. She has been healthy otherwise except for a transient episode of visual impairment when on a 2-week backpacking trip on the Appalachian Trail 2 years before. She had blurred vision with the left eye lasting for about 1 week. When she saw her ophthalmologist 1 week later, she felt well, had normal vision, and the examination was normal.

Neurologic Examination Blood pressure is 120/70 and pulse 80, regular. Funduscopic examination shows optic disk pallor O.D., decreased color perception O.D. as red matches look maroon. She has 20/20 vision O.U. and a relative afferent pupillary defect O.D. She has mild weakness of right interossei, opponens pollicis, abductor pollicis brevis, extensor pollicis longus, and wrist extensors. There is mild spasticity of the right arm and the right leg as well as decreased finger and foot tap on the right side. She has a right Hoffmann's and right Babinski sign. There is a T10 sensory level on the left side to pin and temperature.

Case 29 Questions

1. Where is the pathology?
2. Can a lesion in one location explain all of the findings except for the ophthalmologic manifestations? What pathways are involved?
3. An MRI (head) with and without contrast is normal. A lumbar puncture discloses 60 wbc/cu mm, 80% of which are neutrophils. A CSF protein is 80 mg/dl. Oligoclonal bands are not present.
   (a) Can an MRI (head) be normal in patients with multiple sclerosis?
   (b) Are these CSF findings compatible with a diagnosis of multiple sclerosis?
4. What other test is indicated?

Case 29 Analysis

1. Optic nerve and spinal cord. Impaired color perception is an early sign of optic nerve disease and may be a residual finding after symptomatic recovery from an optic neuritis or retrobulbar neuritis. Visual acuity is often normal.
2. Yes. The patient has a partial Brown-Séquard syndrome involving the lateral column of the cervical spinal cord. There are signs of corticospinal tract disease on the right side because of ipsilateral spasticity, right arm weakness, right Hoffmann's, and right Babinski signs. The lateral spinothalamic tract is also affected because of impaired pain and temperature perception on the left side up to T10. The sensory level is not always up to the lesion level and therefore does not necessarily indicate an additional thoracic cord lesion. Weakness of specific muscles does not require a diagnosis of a brachial plexopathy.
3. (a) Yes.
   (b) No. The CSF protein is usually normal in multiple sclerosis patients. The CSF white count seldom exceeds 40 wbc/cu mm and are all mononuclear.
4. MRI of cervical and thoracic spine. When a diagnosis of myelopathy of unknown origin is made, the entire spinal cord should be imaged. This patient has a three-segment lesion in the cervical cord from C3–C6 on the right side. An NMO-IgG test is ordered.

Diagnosis Neuromyelitis optica (Devic's disease) [21, 58].

Comment Neuromyelitis optica is caused by an antibody which targets the blood-brain barrier water channel, aquaporin 4. Neuromyelitis optica has different CSF findings than multiple sclerosis. There is usually a high CSF protein level, no oligoclonal

bands, and frequently a marked pleocytosis with sometimes a predominance of neutrophils. The MRI seldom shows any cerebral, brainstem or cerebellar abnormalities but MRI of the spinal cord reveals abnormal T2-weighted images extending over three or more vertebral segments. This is called longitudinally extensive transverse myelitis (LETM). Optic neuritis must also be present as in this patient. The CSF findings support the diagnosis of neuromyelitis optica and the NMO-IgG test is positive confirming the diagnosis. This blood test has about a 70% positivity rate.

Case 30 A 62-year-old man is seen because of an episode of impaired speech 1 week ago. He was struggling to find the correct word and his perceptive wife detected that either the syllables were incorrect or the chosen word spoken correctly did not fit the context of the sentence. The event lasted just 5 min.

Past medical history is remarkable for hypertension, gout, and mild renal insufficiency. Medications are allopurinol and losartan.

Neurologic Examination Blood pressure is 115/60 and pulse 80, regular.

The patient has normal speech and there is weakness of abduction O.S. The pupils measure 2 mm O.S. and 3 mm O.D. They both react well to light. The palpebral fissures are asymmetric, right greater than left.

Case 30 Questions

1. The patient's wife reported abnormal speech. What did she describe? What is the diagnosis of this event?
2. Explain the pupillary findings. What bedside test might help to localize the lesion which causes the pupillary asymmetry?
3. Is there any connection between the pupillary findings and the lateral rectus weakness and can a single lesion cause both findings?
4. How can these disparate findings by history and examination be related to each other?

Case 30 Analysis

1. The incorrect syllables were phonemic paraphasias. The incorrect word was a semantic paraphasia. The patient had a transient ischemic attack in the left carotid-middle cerebral artery distribution.
2. The patient has a significant pupillary asymmetry because the difference is greater than 0.5 mm. The good reaction to light nullifies a right third nerve palsy. The smaller pupil and palpebral fissure on the left, ptosis and miosis, supports the presence of a partial left Horner's syndrome. Anhidrosis is detected by placing the dorsum of the examiner's fingers on both cheeks and forehead just above the eyes. Warmth indicates the side of the anhidrosis. It was not present in this patient which suggests a lesion of the sympathetic system distal to the bifurcation of the common carotid artery as the sudomotor fibers which regulate sweating and cool the cheek follow the external carotid artery. Otherwise, the sympathetic fibers travel in the sheath of the internal carotid artery.

3. Yes. The sixth nerve is located in the cavernous sinus just lateral to the internal carotid artery. The sheath of the internal carotid artery contains the sympathetic fibers to the eye but not the face. The sympathetic fibers to the face run along the external carotid artery. Thus, a lesion in the cavernous sinus is likely to explain the findings. This should be a vascular lesion in view of the transient ischemic attack. Carotid angiography reveals an aneurysm.

Diagnosis Left cavernous carotid aneurysm with cranial neuropathy and transient ischemic attack [50].

Comment

4. The mechanism of the dual pathologies can be best explained by a thrombus within the aneurysm, and embolism from the thrombus to the left middle cerebral artery. The aneurysm compresses the 6th nerve and disrupts the sympathetic fibers which travel through the sheath of the internal carotid artery.

Case 31 A 78-year-old widow complains of burning feet and unsteadiness of 3 weeks duration. She has fallen twice in the past week without suffering an injury. She is having progressive difficulty climbing stairs over the last 6 months.

Past medical history is remarkable for an idiopathic cardiomyopathy and she has been treated with digoxin. She is a nonsmoker, has a glass of wine with dinner, and eats well. Current medicines are digoxin, furosemide and aspirin.

Neurologic Examination Blood pressure 88/60. Heart rate 66, regular.

She has bilateral weakness of anterior tibialis 4/5, iliopsoas 4 + / 5, deltoids 4 + / 5, infraspinatus and supraspinatus 4 + / 5. There is moderate heel-to-shin and mild finger-to-nose ataxia. She has a wide-based ataxic gait. Reflexes are absent except for 1 + triceps bilaterally. Vibration perception is absent at the toes. Position sense is normal. There is distal sensory loss to pin and temperature in all extremities and the patient does not perceive light touch on the toes.

Case 31 Questions

1. Where is the pathology?
2. In view of the location of the pathology what should the patient be questioned about in more detail?
3. What are the diagnoses?

Case 31 Analysis

1. (a) The patient has a neuropathy because of absent reflexes, distal weakness in the feet, and distal sensory loss as described.
   (b) The patient has a myopathy because of proximal weakness of arms and legs.
   (c) The patient has cerebellar disease because of heel-to-shin and finger-to-nose ataxia as well as a wide-based ataxic gait.

2. Alcohol consumption history must be carefully questioned. This is frequently underestimated especially by elderly patients. Sometimes the only clue may be macrocytic blood indices.
3. *Diagnoses*:

   (a) Myopathy secondary to alcoholism [38].
   (b) Neuropathy secondary to alcoholism.
   (c) Cerebellar ataxia secondary to alcoholism.

Comment The combination of myopathy, neuropathy and cerebellar system dysfunction strongly suggests the presence of alcoholism. The "idiopathic" cardiomyopathy should also be a clue to the diagnosis.

Case 32 A 72-year-old man had the acute onset of paresthesias of the left face and body 1 week ago. He was on a European vacation and was unable to return until just yesterday. The paresthesias have gradually evolved into a burning sensation which is becoming more intense and now is nearly unbearable.

Past medical history is remarkable for hypertension and he is being treated with ramipril and amlodipine.

Neurologic Examination Blood pressure 140/100 and pulse 90, regular.

The patient has hypesthesia to pin on the left face and body with normal perception perceived on the body 2 cm to the left of the midline and on the face 0.5 cm to the left of the midline.

Case 32 Questions

1. Are the sensory findings unusual?
2. Where could the lesion be and what is the syndrome called?
3. What is the most likely etiology?

Case 32 Analysis

1. No. The sensory findings are expected. Most patients display sensory loss off the midline and towards the side of the defect because of overlapping sensory fibers. This is more apparent on the body than the face.
2. The most common lesion location for this syndrome is in the thalamus, but parietal lobe and brainstem lesions involving the lateral spinothalamic tract can produce similar symptoms. This patient has a thalamic syndrome.

3. *Diagnosis*: Right thalamic infarction manifested by a thalamic syndrome secondary to vascular disease in the right posterior cerebral artery distribution [6, 56].

Comment The posterior cerebral artery irrigates the thalamus and an occlusion, due to embolism or intracranial vascular disease, of a branch of this artery is the most likely cause. It may be a manifestation of "top of the basilar syndrome" [9]. Prognosis for successful treatment is fair but current options may give good relief. These include gabapentin, pregabalin, duloxetine and tricyclic compounds.

Case 33 A 16-year-old boy fell off his bike and struck his head on a concrete embankment. He was unconscious for 2 h. The day after the injury he complained of double vision with the images "on top of one another."

Neurologic Examination Blood pressure 110/80 and pulse 86, regular. On right lateral and direct forward gaze, the left eye is hypertropic.

Case 33 Questions

1. What structure was affected to cause the loss of consciousness?
2. What causes the hypertropia?
3. What bedside test confirms the localization?
4. Is this type of diplopia rare or common with head injury?
5. What is the diagnosis?

Case 33 Analysis

1. The dorsal midbrain was shifted against the tentorium cerebelli and the midbrain reticular formation was injured resulting in loss of consciousness.
2. Paresis of the left superior oblique muscle due to a left fourth nerve lesion.
3. Bielschowsky test. The head is tilted to the left which increases the hypertropia and diplopia. Head tilt to the right corrects the diplopia since it eliminates the need for intorsion. This may result in a persistent unconscious head tilt, a major clue for the diagnosis.
4. Common.
5. *Diagnosis*: Craniocerebral trauma with concussion and residual left trochlear neuropathy [8].

Case 34 A 73-year-old man is referred because of loss of balance. Over the past 3–4 months, he has noted a tendency to fall backwards. His wife adds that his movements have slowed considerably. He prefers to sit in a chair with armrests so he can push himself up to stand. Over the last week he has required assistance to stand. Despite the decline in motor function he has been violently "acting out his dreams," sometimes attempting to punch his wife who struggles to restrain him. Noticeably prominent is a poor attention span. Neurologic abnormalities were slow movements, cogwheel rigidity and retropulsion.

Case 34 Questions

1. What four findings should be searched for on the examination?
2. Is the sleep disorder relevant?
3. What medicine is likely to have been prescribed?

The patient returns 4 months later. For three-and-a-half months he had modest improvement in motor function as he had been able to get out of a chair independently. During the past 2 weeks, however, he has had vivid frightening hallucinations, on one occasion seeing a group of foxes scampering across the front lawn. He has complained of a foul odor in the house on several occasions, each lasting 1–2 h. He has been accusing his wife of infidelity (Othello syndrome).

Neurologic Examination A Mini-Mental State Exam score has dropped from 28/30 to 22/30. His short-term recall is zero. His attention waxes and wanes. He exhibits hypomimia (masked facies), bradykinesia, cogwheel rigidity, and retropulsion as he needs support on his back to sit on the examining table.

Case 34 Additional Questions

4. What is the diagnosis?

Case 34 Analysis

1. The history suggests an extrapyramidal disorder, possibly Parkinson's disease. The four key features include a resting tremor, cogwheel rigidity, bradykinesia and postural instability. The patient exhibited bradykinesia, retropulsion and cogwheel rigidity on his first visit. Thus, he had three of the four cardinal manifestations of Parkinson's disease. Resting tremor is not required for the diagnosis.
2. Yes. He has REM sleep behavior disorder which is a common early symptom of Parkinson's disease or other allied disorder such as corticobasal degeneration, multiple system atrophy, Lewy body disease and progressive supranuclear palsy. All of these illnesses may be preceded by REM sleep behavior disorder.
3. He was begun on carbidopa/levodopa.
4. *Diagnosis*: Lewy body disease [35].

   The clinical features of this disease are psychosis, hallucinations, fluctuating attention, impaired executive function, dementia, and parkinsonism with a suboptimal response to levodopa. This disorder may begin with signs of Parkinson's disease, dementia, or behavioral abnormalities. When the initial feature is the extrapyramidal disorder, dementia or behavioral abnormalities develop within 1 year of the onset of the disease. The dementia is more severe than Parkinson's disease dementia and is associated with a greater degree of cortical atrophy. The Lewy body, which is present in patients with Parkinson's, Lewy body and Alzheimer's diseases, is an eosinophilic cytoplasmic inclusion which contains a pathogenic protein, alpha-synuclein.

Case 35 A 66-year-old retired banker complains of a 6-month history of poor memory and nocturnal headaches which force him out of bed. These are occasionally associated with nausea but no vomiting. He has had insulin-dependent diabetes mellitus since age 18 and has been meticulous about his care. Past medical history otherwise includes asthma and glaucoma. Medications are insulin, albuterol and latanoprost eye drops.

Neurologic Examination Blood pressure is 160/80 and pulse 62, regular. Abnormal findings include bradyphrenia, bradykinesia, a stooped posture, and poverty of associated movements. Normal laboratory studies include a cbc, thyroid functions, metabolic panel, liver functions, calcium, phosphorus, RPR, and vitamin B_{12} level. An MRI (head) noncontrast is normal.

Case 35 Questions

1. What blood test was omitted?
2. What additional examination would be helpful?
3. Treatment was initiated and the patient returns for follow-up in 6 weeks feeling well. What treatment was given?

Case 35 Analysis

1. ESR. Any patient over age 50 who complains of headaches requires this examination to rule out temporal arteritis. The ESR is 16 mm/h.
2. Neuropsychological testing. This patient showed no evidence of impaired cognition, but rather indications of depression.
3. The patient was treated with sertraline and returned to normal in 6 weeks.

Diagnosis Pseudodementia of depression [12].

Comment One of the most common causes of nocturnal pain of any type associated with a sleep disorder is depression. In the context of this patient's clinical course, bradyphrenia and bradykinesia would be better termed psychomotor retardation. This treatable condition should never be overlooked.

Case 36 A 48-year-old man is referred because of a 10-day history of bilateral leg weakness, tingling of the entire left leg and loss of balance. For one month he has had daily occipital throbbing headaches and involuntary yawning. His wife reports a disturbing change in his personality over recent months. He has always been prim and proper but now he jokes inappropriately. When her parents visited for dinner 3 weeks ago he commented about how he missed visiting prostitutes and then laughed uproariously. Furthermore, he yawns very often and loudly in company. His past medical history is negative and he takes no medicines. He does have a history of occasional sores on his lips as well as periodic arthritis affecting ankles and elbows.

General medical examination reveals a temperature of 100.1 °F. Blood pressure is 140/90 and pulse 98, regular. Abnormal findings are a sore on the inner surface of the left lower lip which looks like an aphthous ulcer and a swollen mildly tender left ankle.

Neurologic abnormalities include concrete proverb interpretation of "people in glass houses should not throw stones"; he responds, "The glass will shatter." Short-term recall is 1/3 words after 1 min has elapsed. He has normal pursuit eye movements but slow adduction saccades of both eyes. Strength of anterior tibialis muscles is 4 + / 5 bilaterally. He has spasticity of both legs and cannot perform tandem gait. There is unsustained right ankle clonus of 4 beats. Plantar responses are withdrawal bilaterally. He has a sensory level to pin and temperature on the left side at L1.

Case 36 Questions

1. Using only the history of the present illness what parts of the central and/or peripheral nervous system are involved?
2. What word describes the patient's inappropriate joking?
3. What explains the abnormal eye movements?
4. Does poor tandem gait have localizing value?
5. Is there localizing significance of the unsustained right ankle clonus?
6. Could the sensory findings occur with peripheral nervous system involvement?
7. What part of the neurologic examination must be commented on in view of the history and vital signs?

An MRI (brain) and an MRI (cervical and thoracic) are obtained. There are bilateral frontal lobe infarctions, a midline pontine and a medullary infarction. There is a right-sided intramedullary T11 nonenhancing spinal cord lesion. An MRA reveals moderate-to-severe, bilateral middle cerebral artery, midbasilar and left vertebral artery stenoses.

Case 36 Additional Questions

8. Why was a lumbar MRI not performed?
9. What tests should be performed immediately?
10. Does the MRI provide a precise diagnosis?
11. What part of the general physical examination, often not performed, may be diagnostic?
12. Is there a specific test that may be diagnostic?
13. What is the diagnosis?

Case 36 Analysis

1. Personality changes indicate cerebral pathology. Bilateral leg weakness suggests myelopathy or neuropathy. The tingling of the entire left leg supports myelopathy rather than neuropathy as the latter ordinarily produces tingling of both legs. Involuntary yawning or hiccupping suggests pathology affecting the medulla.
2. Witzelsucht (see Chap. 13 for a definition), characteristic of frontal lobe lesions.
3. Slow adducting saccades indicate bilateral lesions of the medial longitudinal fasciculus. The saccadic system is affected first with lesions of this pathway.
4. No. It may be abnormal with leg weakness, position sense impairment, spasticity, cerebellar system or vestibular system dysfunction.
5. Yes, because it is asymmetric. It indicates corticospinal tract involvement and, in this context, due to a myelopathy.
6. No. The sensory level is diagnostic of a myelopathy.
7. Since this patient has fever and headache a comment about nuchal rigidity must be made. End nuchal rigidity was found.
8. The spinal cord usually ends at about L1 and is covered by a thoracic MRI. The neurologic signs are not compatible with a diagnosis of lumbar radiculopathy.
9. Lumbar puncture. This reveals 28 white cells 90% of which are lymphocytes, negative cultures and stains, a protein of 86 mg%, and glucose of 91 mg%.

10. No.
11. Examination of the genitalia. The clue to this examination is the patient's lip ulcer. Examination of the genitalia discloses an ulcer on the scrotum.
12. The pathergy test. A small sterile needle is inserted into the skin of the forearm. A red nodule or pustule at that site 1 or 2 days afterward is a positive test.
13. *Diagnosis*: Neuro-Behçet's disease with aseptic meningitis, multiple frontal lobe, pons and medullary infarctions as well as a myelopathy [26].

Comment Neuro-Behçet's disease is a large vessel vasculitis which often affects both central and peripheral nervous systems, causes large joint arthritis and oral-genital ulcerations. In the mouth they appear as aphthous ulcers. Skin lesions and gastrointestinal dysfunction are common. The etiology is unknown but it may be an autoimmune disorder.

Case 37 A 66-year-old woman requests an evaluation because of a drooping left shoulder which has been progressive over 5 years. A complete review of systems elicits a history of hoarse voice and occasional sharp left ear pain which lasts 5–10 s, rarely longer, and then may be accompanied by dizziness and pallor for several seconds.

Past Medical History Crohn's disease and inactive rheumatoid arthritis.

Current Medications Prednisone 5 mg. q.d., p.r.n. zolpidem and alprazolam, the latter for rare panic attacks.

Neurologic Examination by a First-Year Neurology Resident Blood pressure 110/70. Pulse 50, regular. There is mild weakness of head turn to the right and left shoulder shrug.

Case 37 Questions

1. What additional questions are relevant to both the history and examination?
2. What part of the examination should be reassessed?
3. What nerves are involved?
4. Where is the lesion?
5. What is the most likely etiology? Is the past medical history important?

Case 37 Analysis

1. (a) Please describe the dizziness. Response: Lightheadedness but no vertigo and "I turn pale."

   Lightheadedness and pallor suggest hypotension. The carotid sinus mediates blood pressure control and is innervated by the 9th cranial nerve (glossopharyngeal). The glossopharyngeal nerve has a branch, Jacobson's nerve, which innervates the tympanic membrane and, therefore, ear pain is often present with glossopharyngeal neuralgia.

   (b) Do you have throat pain? Response: Yes.

The glossopharyngeal nerve supplies the pharynx and its involvement is supported by this additional history.

(c) Do you have any impairment of taste? Response: Yes, my taste is a little less sensitive. The posterior third of the tongue is supplied by taste fibers mediated by the 9th cranial nerve. Her hoarse voice indicates vagus nerve involvement.

(d) Do you have any trouble swallowing? Response: Very little but occasionally I cough when drinking water. This symptom suggests weakness of pharyngeal muscles, not expected with pure glossopharyngeal neuralgia.

2. The soft palate and tongue should be reassessed carefully. There is a decreased gag reflex (9th cranial nerve) when stimulating the left soft palate. Stimulating the right soft palate causes the uvula to elevate on the right but not the left side (10th cranial nerve). The tongue is midline and moves well.
3. Ninth, tenth and eleventh cranial nerves on the left side.
4. Jugular foramen. An MRI scan confirms the presence of a mass lesion at the left jugular foramen.
5. The slow progression of symptoms over several years indicates a benign process. The past medical history is not relevant. The differential diagnosis of a jugular foramen syndrome includes benign neoplasm such as paraganglioma, schwannoma and meningioma as well as sarcoidosis, metastatic neoplasm, jugular vein thrombosis, abscess, trauma with fractures at the skull base and carotid aneurysm at the skull base.

Diagnosis Jugular foramen syndrome (left), due to a glomus jugulare neoplasm (paraganglioma).

Comment The initial history obtained from the patient is perplexing. How can one connect ear pain to shoulder weakness? Only a meticulous analysis of symptoms and signs with accurate neuroanatomic localization can make sense of this clinical presentation and add pertinent information for the neuroradiologist who interprets the MRI scan and who may add additional views of this region.

Case 38 A 37-year-old woman is brought to the hospital because of the acute onset of auditory command hallucinations. She has been told to murder her husband. She believes she has been taken to prison, not the Emergency Room. She appears suspicious and seldom speaks but occasionally repeats a phrase she has just heard. After admission to the hospital she immediately asks to attend daily church services although she has not attended church for over 10 years.

Two weeks before admission she had a bout of diarrhea and a low grade fever for 2 days. This was immediately followed by acute anxiety and insomnia which persisted for 3 days.

Past medical history is negative. Her parents, 2 siblings and 2 children are well. She is a nonsmoker and has an occasional glass of wine.

Neurologic Examination Blood pressure varies from 80/60 to 145/62 and the heart rate is 120 beats per min.

Mini-Mental Status Exam 28/30. Her 2 errors are in short-term recall. She makes occasional phonemic paraphasic errors, e.g. fen for pen.

The patient has prominent saccadic ocular pursuit in vertical and horizontal planes. She has buccal and lingual dyskinesias.

Lab Results CBC, complete metabolic panel and TSH are normal.

Neuroimaging MRI (brain) is normal.

Case 38 Questions

1. What three parts of the central nervous system are affected by this illness?
2. What language disorders are present? Do they have localizing significance? What are the extrapyramidal signs?
3. Other than her auditory hallucinations what other behavior or psychological traits does she exhibit?
4. What is the fourth abnormal element?
5. What tests would be most likely to yield findings which prove a central nervous system lesion rather than a psychotic disorder?
6. What additional studies should be performed on blood and spinal fluid?

Case 38 Analysis

1. Cerebral (psychiatric), extrapyramidal, speech abnormalities.
2. She demonstrates echolalia, repeating a phrase just spoken to her. Although echolalia is commonly associated with aphasia, this sign, in isolation, does not have localizing value. The paraphasias, however, do indicate dominant hemisphere dyfuction. Extrapyramidal signs are the dyskinesias.
3. Delusions, religiosity and paranoia.
4. Autonomic nervous system dysfunction because of the fluctuating blood pressure and tachycardia.
5. Electroencephalography and lumbar puncture. The EEG shows moderate generalized slowing and a few sharp wave discharges over the right frontal region. The CSF studies disclose 22 lymphocytes, abnormal IgG index and the presence of oligoclonal bands. Additionally, 4 cc of cerebrospinal fluid were saved.
6. Acute serum for encephalitis screening. Check the CSF and blood for anti-NMDAR antibodies (N-methyl-D-aspartate receptor antibodies). The tests were positive and a CT (pelvis) with and without contrast revealed an ovarian mass. Gynecology consultation was obtained and surgery performed.

Diagnosis Encephalitis due to anti-NMDAR antibodies associated with an ovarian teratoma [13].

Comment This patient had removal of an ovary which contained a teratoma. Of note is that 80% of all patients are female. It must be recognized that recovery may not be complete and recrudescences are not unusual.

There are protean manifestations of this autoimmune encephalitis which include Klein-Levin syndrome (hypersomnia, hyperphagia, hypersexuality and apathy) and

Kluver-Bucy syndrome (bulimia, hypersexuality, memory loss and flat affect). This usually implies bilateral involvement of amygdaloid nuclei. Relapses occur in 20–25% of patients. About 75% recover well after treatment with IVIg, steroids or plasma exchange.

NMDAR antibodies are found in higher concentrations in blood than CSF; this suggests that antibody production is systemic. The antibodies attack the NR1 subunit of the NMDAR receptor.

Case 39 A 52-year-old man complains of left shoulder pain, severe nonradiating low back pain, dizziness and restless sleep. The shoulder pain is moderately severe, unremitting and began one year ago. It has reduced left arm mobility. His low back pain began 3 months ago and interferes with rising from a chair. His dizziness occurs only when walking and he first noticed this one month ago. He has a 5-year history of restless sleep. His wife reports that he has lost interest in going out to dinner or to the movies. She adds that he is exhausted when he returns home from work which is information technology.

Past Medical History Type II diabetes and hypothyroidism.

Medications Metformin and levothyroxine.

Neurologic Examination Neurologic examination reveals an alert, obese man with a height of 5′7″ and weight of 244 lbs. His BMI is 38. Blood pressure is 140/90 and pulse 64 and regular. Abnormalities include a flat affect, soft voice and he rises slowly from a chair with obvious pain. His gait is slow with a normal base and a slightly short stride.

Case 39 Questions

1. What additional history should be obtained from his wife?
2. What additional history should be obtained from the patient? Will this history lead to a more detailed evaluation?
3. Are there additional specific useful tests of cranial nerve function?
4. What should be observed about his motor system, gait and reflexes?

Case 39 Analysis

1. Is her husband restless at night? She replies that 2 or 3 times per week he flings his arms violently, shouts and upon awakening says he is fighting off attackers, i.e., REM sleep behavior disorder.
2. The patient is questioned about symptoms of hypotension such as nausea, sweating, blurred vision and shortness of breath, all of which he denies but he says he just feels unsteady. Nevertheless he is checked for orthostatic hypotension in supine, sitting and standing positions, the latter up to 3 min. The results are normal.
3. Olfaction and eye movements. Hyposmia is a major clue for neurodegenerative disease. Lewy bodies may be first seen in olfactory bulb neurons. Abnormal eye

movements which may be found include hypometric (small) and inaccurate saccades which thus require one or more adjustments to reach the target, saccadic pursuit which is easily seen when the patient follows a slowly moving target and poor convergence.
4. Look for cogwheel rigidity, reassess for bradykinesia, observe arm swing which is usually reduced, and turning. Abnormal findings may include extra steps when turning associated with a rigid posture (en bloc) as the head remains aligned with the body rather than leading a turn. A positive glabellar response is nearly always present. This patient has all of these abnormalities.

Diagnosis Parkinson's disease [22].

Comment This patient only complains of the nonmotor manifestations of Parkinson's disease. These include shoulder and low back pain, sleep disorder (RBD), fatigue, apathy and dizziness.

The non-motor symptoms of Parkinson's disease, which may precede the motor signs by as much as 10 years, can be divided into 4 categories.

1. Neuropsychiatric: Depression, anxiety, impaired cognition and psychosis.
2. Sleep: RBD, restless legs syndrome, excessive daytime somnolence.
3. Dysautonomia: Orthostatic hypotension, urinary tract symptoms, erectile dysfunction, and gastrointestinal disorders such as gastroparesis and constipation.
4. Hyposmia.

A diagnostic algorithm has been proposed [39].

1. Bradykinesia associated with either or both cogwheel rigidity and resting tremor.
2. Supportive criteria include a clear response to dopaminergic therapy (most important), rest tremor or one ancillary test such as MIBG scintigraphy[1] or DaTscan.[2] These latter two tests are not required.
3. Absence of drug-induced parkinsonism.
4. Exclusionary criteria.

   (a) Early autonomic failure.
   (b) Early bulbar dysfunction.
   (c) Rapid progression.
   (d) Early dementia or psychosis (less than 1 year). Timing is controversial.
   (e) Early falls.
   (f) Absence of nonmotor signs.
   (g) Symmetrical parkinsonism or lower half Parkinson's disease.

[1] MIBG scintigraphy: ^{123}I-metaiodobenzylguanidine. This test measures postganglionic sympathetic cardiac innervation. It shows damage to the postganglionic part of the autonomic nervous system in all patients with Parkinson's disease.

[2] DaTscan: Dopamine transporter single photon emission computerized tomography imaging technique. It provides visual evidence of nigrostriatal degeneration because of reduced density of dopamine transporters.

(h) Supranuclear ophthalmoplegia.
(i) Neurologic signs indicating pathology outside of the nigrostriatal pathway such as aphasia, apraxia or visual loss.
(j) Movement disorders such as dystonia and myoclonus.

Case 40 A 46-year-old woman requests an evaluation and diagnosis of her tremor which has developed gradually over 6 months. It affects both arms, right greater than left, and the chin. The tremor is quite troublesome when she writes or uses a soup spoon. She finds that alcohol reduces the tremor and before attending a social function always has a glass of wine. She has no illnesses and takes no medication. A maternal aunt has a 30-year history of nonprogressive tremor responsive to propranolol. Her mother died at age 39 of breast cancer.

Neurologic examination confirms the patient's observations. She has a tremor of her chin and both arms when reaching and raising a glass. At rest a tremor of her right thumb and index finger is seen.

Case 40 Questions

1. Might there be a quick way of finding an abnormality supporting a diagnosis of Parkinson's disease?
2. What features of the history and examination support a diagnosis of essential tremor?
3. What features of the history and examination support a diagnosis of Parkinson's disease?
4. What features occur with both forms of tremor?

Case 40 Analysis

1. Check sense of smell which is usually deficient in patients with Parkinson's disease.
2. Tremor occurring when writing or using a soup spoon, lessening with alcohol and a positive family history.
3. Tremor of the chin, asymmetry of tremor, rest tremor of the fingers and recent development.
4. Cogwheel rigidity is commonly present in both essential tremor and Parkinson's disease. Action and postural tremor may occur with Parkinson's disease and a rest tremor rarely occurs with essential tremor.

Diagnoses

1. Probable Parkinson's disease.
2. Essential tremor [22].

Comment A trial of carbidopa/L-dopa will be the next step in the process of establishing a diagnosis.

Feature	PD[a]	ET[a]
Duration of tremor before consultation request	Usually several months	Usually several years

Feature	PD[a]	ET[a]
Family history	5–15% with affected first degree relative	Autosomal dominant + history (>60%)
Position of maximal activation	Rest	Maintenance of posture or movement
Frequency	3–6 Hz	6–12 Hz
Character	Pill-rolling	Flexion-extension
Body parts affected	Arm, leg, chin, lips, tongue	Arm, head, voice
Handwriting	Micrographia (tested by writing a long sentence on 1 line)	Tremulous (tested by copying an Archimedes spiral)
Associated signs	Bradykinesia, hypomimia, hypophonia, gait disorder	Failure of check, occasionally
Walking	Abnormal	Normal
Response to medicines or substance	Carbidopa/L-dopa	Alcohol

[a]*PD* Parkinson's Disease, *ET* Essential Tremor

Case 41 A 45-year-old man is referred by his gastroenterologist because of blurred vision and horizontal oscillations of the environment. These symptoms began 2 months ago and simultaneously his jaw began to jerk uncontrollably. He believes that there is a decline in his memory and he is depressed.

He sought a G-I consultation 4 months ago because of a 6-month history of frequent loose yellow stools associated with abdominal pain and a 15-lb weight loss. Additionally, he has had intermittent low grade fever and migrating joint pain.

Past medical history and social history is remarkable for type II diabetes and arthralgia. He does not smoke or drink. He is a soybean farmer.

General medical examination reveals a blood pressure of 110/70, pulse 65 and axillary adenopathy.

Neurologic Examination Normal mental status other than errors reversing 5-letter words and impaired short-term recall as he remembers 1 of 3 words after 2 min have elapsed. He has paresis of upgaze, pendular convergence nystagmus synchronous with jaw contractions.

MRI (brain) is normal.

Case 41 Questions

1. Where is the lesion that causes upgaze paresis?
2. What term is used to describe the eye and jaw movement?
3. What medical symptom is the major clue for the diagnosis?
4. What should be the most useful test for the diagnosis?
5. If negative, what is the next examination?
6. Can these neurologic signs occur in isolation as the first sign of this disease?

Case 41 Analysis

1. Posterior commissure.

2. Oculomasticatory myorhythmia.
3. Diarrhea with steatorrhea.
4. Lumbar puncture. This reveals a CSF wbc of 71/cumm with 80% neutrophils, 20% lymphocytes and a protein of 81 mg%. The centrifuged pellet shows positive PAS (periodic acid-Schiff) macrophages.
5. Duodenal or jejunal biopsy and PCR test for Tropheryma whipplei.
6. Yes.

Diagnosis Whipple's disease with cerebral and brainstem involvement [45].

Prognosis This disease is fatal without treatment. Several antibiotics have been used successfully.

Comment This patient exhibits the diagnostic triad of ocular paresis with oculomasticatory myorhythmia, gastrointestinal symptoms and cognitive decline. It is most common among Caucasian males who work with soil or animals. In about 5% of patients the initial manifestations are neurologic. Eventually, up to about 40% of patients develop neurologic symptoms. An MRI (brain) can be normal as in this case but often shows T2 hyperintensities in midbrain, corticospinal tract, mesial temporal lobe and hypothalamus.

Case 42 An orthopedic surgeon requests an urgent neurologic consultation at 7 p.m. for a 61-year-old man who is acutely disoriented and agitated 3 days after a total left hip replacement. That morning he complained of diffuse muscle pain and tremor. He is now unable to provide a lucid history.

Past medical history is remarkable for insulin-dependent diabetes mellitus, diagnosed at age 15, hypertension, rheumatoid arthritis and a 5-year history of Parkinson's disease manifested by tremor, bradykinesia and an apraxic gait. His Parkinson's disease treatment has eliminated his bradykinesia, reduced his tremor and improved his gait.

Current medications are insulin, amlodipine, enoxaparin and celecoxib.

Neurologic Examination Blood pressure is 150/118. Pulse 108. Temperature 101 °F. The nurse has recorded an 8 a.m. blood pressure of 107/70, pulse 72 and temperature 99 °F. At noon a blood pressure of 155/108, pulse 122 and temperature 102 °F were reported.

Pertinent findings include a lethargic patient who is easily roused and oriented to city and state, not month or year. He appears frightened and is intermittently agitated. He follows just 2-step commands and immediate recall is 0/2 words after 1 min has elapsed. He is unable to count fingers but responds to visual threat in both fields. Ocular pursuit and saccades cannot elicit a full range of eye movements but the oculocephalic maneuver elicits full horizontal and vertical eye movements. Pupils are 2 mm, equal and with a 3 + / 4 reaction to

light. He exhibits a mild postural/action tremor and paratonic rigidity. Reflexes are barely elicited.

Case 42 Questions

1. What are the key abnormal features of the patient's history and neurologic examination and what term should describe his mental status?
2. What eye finding is abnormal?
3. What complication must be prevented? What blood and urine test will shed light on the diagnosis?
4. What is the diagnosis and the differential diagnosis?

Case 42 Analysis

1. The key features are agitation and disorientation, decreased level of consciousness, fever, paratonic rigidity, tremor and autonomic instability. The patient manifests delirium.
2. Oculocephalic maneuver. In a normal individual the oculocephalic maneuver performed without instruction or visual fixation does not elicit consistent smooth eye movements. The incomplete range of eye movements may be due to the patient's poor attention span.
3. Acute renal failure due to rhabdomyolysis. The triad of rhabdomyolysis is muscle pain, muscle weakness and dark red or brown urine due to myoglobin which can damage the kidney. Test results which show distinctive abnormalities include a cbc, urinalysis and CK. The results in this patient are a white blood cell count of 14,000 with 82% neutrophils, platelet count of 520,000, a CK of 990 U/L and the urine is a reddish-brown due to myoglobin.
4. *Diagnosis*: Neuroleptic malignant syndrome [3].

Comment The patient has Parkinson's disease and treatment was beneficial. There is a high likelihood, if not certainty, that he was taking carbidopa/L-dopa or a dopamine agonist such as pramipexole or ropinirole. Sudden cessation may cause this syndrome. He had the typical findings of fever, rigidity, altered mental status with agitation and autonomic dysfunction. The hallmark laboratory results are leukocytosis and an elevated CK. The differential diagnosis is use of neuroleptics, serotonin syndrome, toxicity with cocaine, lithium and amphetamine and Lewy body disease. The major differential diagnosis is the serotonin syndrome. Hyperreflexia and clonus occurs with the latter, absent in this patient, and the typical laboratory abnormalities of neuroleptic malignant syndrome are present.

Case 43 A 58-year-old man is referred for neurologic evaluation because of short-term memory loss, irritability and anger outbursts which include verbally abusing his wife. This has been progressing in severity over the past year. His marriage of 25 years is now threatened. Prior to one year ago he was calm, rational and thoughtful. An additional development beginning about 8 years ago was loss of taste, anorexia and he lost 15 lb over the last year.

His past medical history is remarkable only for hypothyroidism. His parents are in their 80s and healthy. He drinks 2 glasses of red wine nightly and this is confirmed by his wife. He smoked one pack of cigarettes per day while a war correspondent in Iraq and Afghanistan about 6 years ago.

Neurologic Examination Blood pressure 134/68, pulse 68 and regular. His Mini-Mental Status Exam score is 26/30. He forgot 2 of 3 words after 1 min elapsed, did not successfully draw intersecting pentagons and followed just 2 of a 3-step command. His responses were rapid and impulsive. He made errors with double simultaneous stimulation using the face-hand test. A brief touch of the right face and left hand simultaneously was perceived only on the face and vice versa with the test repeated 4 times. Normal individuals, especially when anxious, usually make only 1 or 2 errors when prompted to report all touches perceived.

MRI (brain) is normal. An electroencephalogram reveals mild diffuse slow activity. A cbc, complete metabolic panel and thyroid functions are normal.

Case 43 Questions

1. What part of his history requires further questioning?
2. What part of the cranial nerve examination, commonly omitted, can be useful?
3. Is the abnormal face-hand test result of clinical significance?
4. What is the most likely diagnosis?

Case 43 Analysis

1. The patient is queried about his experiences in Afghanistan. He reports three concussions while accompanying patrols in Iraq and Afghanistan. On the third occasion he felt irritable and had mild memory impairment for 4 months. He also had a short retrograde and longer anterograde amnesia. Thus, he had a postconcussive syndrome, persistent neurologic symptoms for over 3 months.
2. Olfaction. When patients complain of loss of taste their sense of smell is likely to be impaired. A common cause is head trauma. An olfactory groove neoplasm such as a meningioma is a theoretical consideration only.
3. Yes. Normal individuals, especially when anxious, will occasionally be unaware of the hand touch once or twice but rarely more. Bilateral unawareness (extinction) gives supportive evidence of bilateral cerebral dysfunction. Unilateral extinction suggests a contralateral focal lesion.

4. *Diagnosis*: Chronic traumatic encephalopathy (CTE) [49].

Comment Traumatic brain injury (TBI) may be manifested by a concussion, postconcussive syndrome (neurologic symptoms for more than 3 months) and CTE, a delayed progressive dementia. The delay is ordinarily 8–10 years. Usually the patient has a few TBIs that precipitate this delayed dementia which often simulates Alzheimer's disease. Contact sports such as boxing, football, soccer (heading the ball), hockey and war-related TBIs are probably the most common etiologies. Of interest is a recently developed evaluation, the King-Devick test, that assesses real-

time concussion and asymptomatic concussion in athletes using rapid number naming. Pre- and post-season testing has been recommended [14].

CTE is a tauopathy, a pathological accumulation of tau protein in neurofibrillary tangles which interferes with axonal transport of nutrients and synaptic vessels leading to cell death. It is more prevalent in patients with an APOE-4 allele which certainly suggests that there is a predisposition for this disease. There are several other tauopathies which include progressive supranuclear palsy, corticobasal degeneration and frontotemporal dementia. The mean duration of CTE is 17.5 years, much slower than Alzheimer's disease.

Case 44 A 31-year-old biologist, who has just returned from a research trip to Brazil, requests an evaluation because of bilateral footdrop. He booked an urgent flight home because of a 7-day illness manifested by progressive shortness of breath, fever, a severe, generalized maculopapular rash and a nonpurulent conjunctivitis. The rash was the most worrisome symptom until his feet became weak. He has a completely negative past medical history and takes no medications.

Neurologic Examination Vital Signs. These are normal other than a temperature of 100 °F.

Medical examination reveals a mildly dyspneic patient who has a normal chest examination. The rash and conjunctivitis are no longer present. Abnormal neurologic findings are bilateral 3/5 strength of anterior tibialis, bilateral 4/5 strength of gastrocnemius muscles and absent reflexes in the legs. He has no sensory symptoms or signs.

Case 44 Questions

1. What practical decision must be made? Why?
2. What specific examination is most urgent?
3. If abnormal what order should be given?
4. What changes in the neurologic examination should one expect?
5. What specific tests should be ordered?
6. What is the suspected diagnosis?

Case 44 Analysis

1. Admit the patient to the hospital because he is short of breath.
2. Vital capacity. Arterial blood gases should also be obtained but are most often initially normal when the etiology is a neuromuscular disorder. Although clearly important, they cannot be depended on to evaluate pulmonary function in a patient with neurologic disease.
3. Transfer to the Intensive Care Unit. Consider intubation if there is a precipitous drop in the vital capacity.
4. Progressive ascending weakness and loss of reflexes.

5. Blood, urine and CSF test to check for Zika virus infection. This is an RT (reverse transcription)-PCR which can be positive in any body fluid. Positive CSF and urine studies were found in this patient.

6. *Diagnosis*: Acute inflammatory demyelinating polyneuropathy (Guillain-Barré syndrome), acute motor axonal neuropathy variant associated with the Zika virus [47].

   The prognosis in cases so far evaluated is very good for complete recovery.

Comment In addition to a maculopapular rash, fever, nonpurulent conjunctivitis, myalgia and headache are common. Other rare neurologic complications include meningoencephalitis, encephalopathy, seizures, myelitis and Fisher syndrome. The better-known complications are seen in neonates of women infected with the Zika virus. They may have microcephaly, retardation, retinal and optic nerve disease.

Zika virus (ZIKV) is an RNA virus first discovered in Uganda and transmitted by the Aedes africanus mosquitoes. The first human outbreak occurred in Micronesia in 2007 and most recently in South America in 2014. The virus may be transmitted by sexual intercourse. Blood transfusions are a suspected additional means of acquiring the disease. It should be noted that probably 80% of human infections are asymptomatic.

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Chapter 13
Neurologic Terminology

This chapter provides clarification of acronyms, brief definitions of signs, and short descriptions of syndromes. The names given to these signs and syndromes are those of the distinguished neurologists who first described them and therefore are of historic interest. Detailed elaboration of some of these will be found in the text. Short outlines of rare syndromes will be added as full discussions cannot be included in an introductory text. By necessity this will only be a selection from the myriad numbers of syndromes and signs to choose from.

Glossary

Acronyms

ACA	Anterior cerebral artery
ACoA	Anterior communicating artery
ADEM	Acute demyelinating encephalomyelitis
ADHD	Attention deficit hyperactivity disorder
AHI	Apnea–hypopnea index
AICA	Anterior inferior cerebellar artery
AIDP	Acute inflammatory demyelinating polyneuropathy (Guillain-Barré syndrome)
AIDS	Acquired immune deficiency syndrome
AION	Anterior ischemic optic neuropathy
ALS	Amyotrophic lateral sclerosis
AMS	Altered mental status
AVM	Arteriovenous malformation
BPPV	Benign paroxysmal positional vertigo

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CADASIL	Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy
CGRP	Calcitonin gene-related peptide
CIDP	Chronic inflammatory demyelinating polyneuropathy
CNS	Central nervous system
CPEO	Chronic progressive external ophthalmoplegia
CPS	Cycles per second
CSA	Central sleep apnea
CSD	Cortical spreading depression
CSF	Cerebrospinal fluid
CST	Corticospinal tract
CTS	Carpal tunnel syndrome
DHE	Dihydroergotamine
GABA	Gamma-aminobutyric acid
GAD	Glutamic acid decarboxylase
HIV	Human immunodeficiency virus
Hz	Hertz
INO	Internuclear ophthalmoplegia
IO	Inferior oblique muscle
IR	Inferior rectus muscle
JME	Juvenile myoclonic epilepsy
LPS	Levator palpebrae superioris
LR	Lateral rectus muscle
MCA	Middle cerebral artery
MELAS	Mitochondrial encephalopathy with lactic acidosis and stroke
MLF	Medial longitudinal fasciculus
MR	Medial rectus muscle
MSA	Multiple system atrophy
MSLT	Multiple sleep latency test
NMO	Neuromyelitis optica (Devic's disease)
NPH	Normal pressure hydrocephalus
NSAIDS	Nonsteroidal anti-inflammatory drug
OCD	Obsessive compulsive disorder
OKN	Optokinetic nystagmus
OSA	Obstructive sleep apnea
PCA	Posterior cerebral artery
PCR	Polymerase chain reaction
PICA	Posterior inferior cerebellar artery
PION	Posterior ischemic optic neuropathy
PLMS	Periodic limb movements of sleep
PML	Progressive multifocal leukoencephalopathy
PNS	Peripheral nervous system
PPRF	Paramedian pontine reticular formation
PRES	Posterior reversible encephalopathy syndrome
PSP	Progressive supranuclear palsy

RAPD	Relative afferent pupillary defect
RBD	REM sleep behavior disorder
REM	Rapid eye movement
riMLF	Rostral interstitial nucleus of the medial longitudinal fasciculus
RSD	Reflex sympathetic dystrophy
SAH	Subarachnoid hemorrhage
SCA	Superior cerebellar artery
SR	Superior rectus muscle
SNRI	Selective norepinephrine reuptake inhibitor
SSEP	Somatosensory-evoked potential
SSRI	Selective serotonin reuptake inhibitor
SUNA	Short-lasting unilateral neuralgiform headaches with cranial autonomic symptoms
SUNCT	Short-lasting unilateral neuralgiform headaches with conjunctival injection and tearing
VEP	Visual-evoked potential
VPL	Ventral posterolateral nucleus of thalamus
VPM	Ventral posteromedial nucleus of thalamus
WEBINO	Wall-eyed bilateral internuclear ophthalmoplegia
WEMINO	Wall-eyed monocular internuclear ophthalmoplegia

Signs

Aberrant reinnervation	After a nerve is injured there is regrowth of axons but some are redirected to the wrong muscle. This commonly results in a synkinesia. A good example is after recovery from a Bell's palsy when an eye blink provokes movement of the mouth (orbicularis oris).
Abulia	Patients with abulia are passive, apathetic, and have little interest in their surroundings.
Adie's pupil (tonic pupil)	This is a large, usually unilateral pupil which is nonreactive to light and slowly constricts to a prolonged near stimulus.
Adson's maneuver	Examination method for detecting a thoracic outlet syndrome.
Aftersensation	This is continued perception of a stimulus, typically a pin, after it is removed.
Agrammatism	Defective syntax.
Agnosia	Normal reception of a specific sensory stimulus with the inability to recognize the object using the same sensory system. There is retained ability to recognize it using a different sensory pathway. For example, a patient may not be able

	to identify a key visually but is able to identify it when placed in his hand.
Agraphia	Inability to write.
Akathisia	Voluntary movements to relieve an inner restlessness typically manifested by walking or rocking. Ordinarily, this is due to use of dopamine receptor blockers.
Akinetic mutism	Patients in an akinetic mute state are immobile, do not speak and appear vigilant as the eyes are open. They may visually track a moving target.
Alexander's law	Nystagmus is more rapid when the eyes are deviated in the direction of the quick phase.
Alexia	Inability to read.
Alexia without agraphia	Patients are unable to read what they have just written due to a lesion of the dominant occipital lobe and splenium of the corpus callosum.
Alien hand sign	Unilateral, wandering involuntary hand movements, a sign often observed with corticobasal degeneration, but not pathognomonic of this disorder.
Allesthesia	Sensation of a stimulus on one side is perceived as arising from the contralateral side in the same location.
Allodynia	A nonpainful stimulus perceived as painful.
Anarthria	See aphemia.
Anesthesia dolorosa	Pain in a region of hypesthesia, typical of postherpetic neuralgia.
Anosodiaphoria	Lack of concern about a neurologic deficit, typically a hemiparesis.
Anosognosia	Absolute denial of a neurologic deficit, typically a hemiparesis.
Aphasia	Impaired language function.
Aphemia	The patient is mute but is able to write. Lesions are usually in Broca's area or in adjacent subcortical white matter.
Apneustic	This refers to a breathing pattern of 2–3 s of apnea after a deep inspiration.
Apraxia	Impaired performance of a learned movement despite preserved strength.
Argyll-Robertson pupil	Small irregular pupils, poorly or nonreactive to light with a normal reaction to a near stimulus.
Asomatognosia	Loss of awareness of one-half of the body.
Astasia-abasia	A lurching gait with irregular steps associated with a conversion reaction.

Asterixis	Flapping downward movements typically seen in the hands when the arms are extended in the pronated position with the wrists dorsiflexed. This is considered a negative myoclonus and is associated with any type of metabolic encephalopathy.
Asymboly for pain	The patient is indifferent to threats of pain and sometimes to a painful stimulus itself.
Athetosis	Slow, writhing, involuntary, large amplitude movements involving distal upper extremities, and less often face and trunk musculature.
Autotopagnosia	Failure of a patient to recognize or name his own limb or body part.
Ballism	Abrupt swinging movements of an arm or leg involving proximal muscles due to a lesion at various sites within the contralateral basal ganglia although previously thought to be only the subthalamic nucleus.
Beevor's sign	Movement of the umbilicus upward with head flexion when there is paresis of lower abdominal muscles due to a spinal cord lesion between T10 and T12.
Bell's phenomenon	A normal eye movement up and out with eye closure.
Bielschowsky head tilt test	Increased diplopia due to a 4th nerve lesion when the head is tilted toward the side of the lesion.
Bradykinesia	Slow movements.
Bradyphrenia	Slow thinking.
Broca's aphasia	Nonfluent aphasia with good comprehension and poor repetition.
Brudzinski's sign	Sign of meningeal irritation.
Camptocormia	Condition in which the thoraco-lumbar spine is flexed when walking but not in bed. This sign is common in Parkinson's disease, Parkinson-plus syndromes, and dystonia.
Cataplexy	Sudden decrease in muscular tone most often in the legs occasionally resulting in falls and commonly provoked by a surprise event. This is a cardinal feature of narcolepsy.
Catathrenia	Nocturnal groaning.
Causalgia	See complex regional pain syndrome.
Chaddock's sign	Extensor plantar response when the lateral side of the foot is scraped beginning at the heel and extending up to the base of the fifth toe.

Cheyne-Stokes	Refers to abnormal respiration manifested by short periods of hyperpnea alternating with apnea in a crescendo-decrescendo pattern.
Chorea	Rapid jerky movements of the extremities, most prominent in distal musculature.
Chvostek's sign	Tapping over the parotid gland produces spasmodic contraction of ipsilateral facial muscles. This is a sign of hypocalcemia.
Cogan's lid twitch sign	When patients with ocular myasthenia gravis look from a down to a neutral position, the upper eyelid may twitch upward transiently uncovering the sclera.
Collier's sign	Eyelid retraction associated with the pretectal syndrome (Parinaud's, Sylvian aqueduct, dorsal midbrain syndromes).
Conduction aphasia	Fluent aphasia with good comprehension and poor repetition.
Coprolalia	Use of obscene language.
Copropraxia	Use of obscene gestures.
Cruciate paresis	Paresis of one arm and the contralateral leg.
Crural paresis	This refers to a hemiparesis, leg greater than arm.
Cushing's response	Signs of increased intracranial pressure which are hypertension, bradycardia, and slow respiratory rate.
Dazzle	Light is perceived as irritating, excessively bright and even painful.
Déjà vu	Sense of reliving an experience.
Delusion	A false belief.
Depersonalization	Sense of detachment from the body.
Derealization	Feeling of being disconnected from the environment.
Dix–Hallpike test	Specific test for benign paroxysmal positional vertigo.
Double elevator palsy	Monocular elevation paresis due to a contralateral supranuclear pretectal lesion or an ipsilateral lesion of efferent fibers from the riMLF to SR and IO subnuclei.
Dysarthria	Slurred speech.
Dysdiadochokinesis	Impairment of rapid alternating movements, a nonlocalizing neurologic sign caused by lesions involving the corticospinal tract, extrapyramidal system or cerebellar pathways.
Dysesthesia	Unpleasant sensations provoked by an ordinary stimulus.

Dyskinesia	Abnormal involuntary repetitive movements.
Dysphagia	Difficulty swallowing.
Dysprosody	This term is usually applied to loss of inflection in speech producing a monotone quality. It also refers to changes in the emphasis or timing of words and pauses between words in a phrase.
Dystonia	Slow involuntary movements or sustained postures usually involving truncal and proximal-greater-than-distal movements of the extremities.
Echolalia	The repetition of words or phrases just spoken to the patient.
Epiphora	Excessive tearing.
Erb's palsy	This term refers to an upper brachial plexus lesion affecting C5–C6 roots. The name is usually applied to a birth injury but may be used with any traumatic lesion or idiopathic plexitis.
Extra-axial	This term refers to a lesion adjacent to brain.
Festination	Uncontrollable acceleration of gait most often observed in patients with Parkinson's disease.
Gegenhalten	See paratonia.
Gelastic	Term used to describe sudden, uncontrollable laughter associated with a seizure disorder.
Glabellar reflex	Abnormal response to repetitive tapping over the bridge of the nose manifested by continuous involuntary blinking.
Glasgow Coma Scale	Scale which provides an objective recording of the conscious state of a person after an acute medical illness or head trauma.
Graefe's sign	Lid lag on looking down due to thyroid disease.
Hallucination	Sensory experience without an external stimulus.
Hippus	Pupillary instability with rhythmic alternating constriction and dilation which is usually a normal variant but may occur in patients with altered mental status, Cheyne-Stokes respiration, severe liver and renal disease, and traumatic encephalopathies.
Hoffmann's sign	Flexion of the distal phalanx of the thumb when the middle finger is hyperextended and the nail is flicked downward.
Hoover's sign	Sign associated with feigned weakness of a leg as the patient does not apply the downward

	pressure on the contralateral leg when requested to raise the weak leg.
Hunt–Hess Scale	Scale to assess severity of subarachnoid hemorrhage.
Hutchinson pupil	Widely dilated, poorly or nonreactive pupil which is an early sign of uncal herniation due to compression of the peripherally located pupillary fibers of the third nerve.
Hyperekplexia	Exaggerated startle response to unexpected tactile or auditory stimuli commonly associated with hypertonia which is mainly truncal. This is classically a genetic disorder but can be acquired and associated with abnormal glycine neurotransmission.
Hyperesthesia	Acute sensitivity to a sensory stimulus.
Hyperpathia	Exaggerated response to a painful stimulus.
Hypesthesia	Decreased perception of a stimulus.
Hypomimia	Refers to a patient with little spontaneous expression and is also known as masked facies.
Hypophonia	Decreased voice volume.
Illusion	Distortion of a sensory perception.
Incubus	Night terrors in adults manifested by screaming during N_3 (stage 3) sleep.
Internuclear ophthalmoplegia	Ipsilateral medial rectus paresis with or without nystagmus in the contralateral abducting eye, with or without preservation of convergence. The lesion is in the medial longitudinal fasciculus. It preferentially affects the saccadic system.
Intra-axial	This term refers to a lesion within brain.
Jamais vu	Feeling that one's surroundings are unfamiliar.
Kakopsia	Objects appear ugly or sinister.
Kalopsia	Objects appear beautiful and friendly.
Kernig's sign	Sign of meningeal irritation.
Kernohan's notch	Compression of the opposite cerebral peduncle against the incisura of the tentorium cerebelli during uncal herniation. This causes a hemiparesis ipsilateral to the involved cerebral hemisphere.
Klumpke paresis	Lower brachial plexopathy involving C8–T1 roots usually due to trauma or infrequently an invasive neoplasm and rarely a stretch injury in neonates.
La belle indifference	Demeanor inconsistent with the presumed illness.
Lasegue's sign	Induced pain along the course of the sciatic nerve when the extended leg is lifted from the bed.

Lhermitte's sign	Electricity-like sensations which radiate down the arms, occasionally the back and legs, provoked by head flexion. This may be due to increased sensitivity of the posterior columns and is a sign most often associated with multiple sclerosis but may occur with other pathologies such as cervical spinal stenosis.
Logorrhea	Pathologic verbosity.
Macropsia	Objects appear larger than normal. When briefly perceived, seconds to a few minutes, a focal aware seizure (simple partial seizure) may be the etiology.
Main en griffe	Claw hand deformity due to an ulnar nerve lesion above the elbow. There is hyperextension of the 4th, 5th and occasionally third fingers at the metacarpal phalangeal joints and flexion at the interphalangeal joints.
Magnetic gait	Patients have difficulty initiating steps and their feet appear stuck to the floor. If able to walk the gait is shuffling and turning requires several steps.
Marche à petit pas	See magnetic gait.
Marcus Gunn phenomenon	Unilateral lid retraction with jaw movement or swallowing.
Marcus Gunn pupil	See relative afferent pupillary defect.
Meralgia paresthetica	Compression of the lateral femoral cutaneous nerve of the thigh (L2–L3) under the inguinal ligament causing numbness, pain, and paresthesias in the nerve's distribution over the anterolateral thigh.
Metamorphopsia	Distortion of form such as a straight line becoming crooked.
Micropsia	Objects appear smaller than normal. When briefly perceived, seconds to a few minutes, a focal aware seizure (simple partial seizure) may be the etiology.
Milkmaid's grip	This is a common sign in patients with Huntington's chorea manifested by repeatedly gripping and releasing the doctor's fingers.
Myerson's sign	See glabellar reflex.
Myoclonus	Brief shock-like movement due to either muscle contraction (positive) or muscle inhibition (negative).
Myokymia	Continuous slow muscle twitching producing an undulation of the muscle surface.

Myotonia	Impaired muscle relaxation after it is tapped, usually at the thenar eminence.
Neglect	Term refers to a patient who pays no attention to a weak limb but, when specifically requested, can use it normally. This sign is usually associated with contralateral parietal lobe lesions, ordinarily the nondominant side.
Neologism	Paraphasia manifested by a new word manufactured by the patient.
Notalgia paresthetica	Burning, itching, and paresthesias at the medial margin of the scapula in a well-circumscribed region a few inches in diameter. The etiology is unknown.
Nylen-Barany test	See Dix–Hallpike test.
Oculomotor apraxia	Absence of volitional saccades and pursuit.
Ondine's curse	Loss of automatic breathing during sleep. This can be caused by lesions of the tegmentum of the medulla or high cervical cord at C1–C2.
Onion skin pattern	This term refers to the type of facial sensory loss with intramedullary lesions involving the trigeminal sensory system.
Oppenheim's sign	Extensor plantar sign evoked by firmly scraping down the shin from the knee to the foot using the knuckles.
Optic ataxia	Inability to reach a target which is clearly seen.
Oscillopsia	Illusory perception of movement of the environment.
Otolithic crisis	Drop attack associated with Ménière's disease and described by patients as a sensation of being pushed or thrown to the ground.
Palilalia	Compulsive repetition of phrases or words at increasing speed and diminishing volume.
Palinacusis	Patient perceives an auditory stimulus after the auditory stimulus has been removed.
Palinopsia	Persistence or recurrence of visual images after the stimulus object has been removed. This is nearly always due to a right parietooccipital lesion.
Paraphasia	Term refers to abnormal formation of words, inappropriate use of words, or manufactured new words. This is a diagnostic feature of aphasia.
Paratonia	Patients with paratonia actively resist passive motion at a joint despite an admonition to relax. This is also known by the term Gegenhalten.

Pavor-nocturnus	Night terrors in children manifested by screaming during N (stage 3) sleep.
Pelopsia	A sense that objects are looming up in front of the patient. When briefly perceived, seconds to a few minutes, a focal aware seizure (simple partial seizure) may be the etiology.
Perseveration	Repetition of the same response to a new question.
Phalen's sign	Flexion of the wrist to 90 ° for up to 60 s may produce paresthesias in the hand due to irritation of the median nerve, a common finding in CTS.
Phosphenes	Flashes of light which may occur with pressure on the globe, rapid saccades, traction on the vitreous, and accommodation. They can be an early sign of retinal detachment.
Photopsia	Spontaneous perceived flashes of light most often associated with posterior vitreous detachment, migraine with aura, migraine aura without headache, retinal detachment, and occipital lobe lesions.
Pisa sign	Sustained involuntary lateral flexion of head and body to one side commonly associated with Parkinson's disease and occasionally with use of narcoleptics and cholinesterase inhibitors.
Polyopia	Optic illusion of seeing many images. This may occur in patients with occipital lobe lesions who have homonymous scotomas.
Prosopagnosia	Selective inability to recognize faces.
Pseudobulbar palsy	Involuntary laughing or crying associated with bilateral lesions of corticobulbar pathways. Impairment of speech, swallowing, chewing, and breathing may also be present.
Pseudo-von Graefe phenomenon	A type of aberrant third nerve regeneration with elevation of the lid on downgaze.
Punding	Purposeless motor activity such as fiddling with the bed sheets.
Rapid adaptation	Perception of a stimulus for only a few seconds despite its continued application.
Reflex sympathetic dystrophy	See complex regional pain syndrome.
Relative afferent pupillary defect (Marcus-Gunn pupil)	Normal consensual pupillary response to light but pupil dilation when the light is rapidly switched back from the normal to the involved eye. The

	involved pupil may react normally or sluggishly to a direct light stimulus. This response indicates optic nerve pathology.
Riddoch's phenomenon	Visual perception of movement in a hemianopic field.
Romberg's sign	Unsteadiness when standing with eyes closed and feet together. This is nearly always due to impaired proprioception or vestibular dysfunction.
Scintillating scotoma	Spot of flickering light, often with a zig-zag pattern, which expands and obscures vision within boundaries of the light.
Simultanagnosia	Ability to see individual elements of a picture or scene but inability to comprehend or synthesize its meaning or how to interrelate the parts.
Singultus	Hiccup.
Skew deviation	Vertical separation of the globes due to a supranuclear lesion.
Somnambulism	Sleep walking.
Somniloquy	Sleep talking.
Spetzler–Martin Grading Scale	Grading of an arteriovenous malformation by its size, location, and venous drainage.
Stellwag's sign	Infrequent blinking in Grave's disease.
Synesthesia	Condition in which one sensory stimulus evokes a sensation of another sensory modality such as when a whiff of smoke produces a reddish coloration of the environment.
Synkinesia	Involuntary movement of a muscle which should not ordinarily contract when a voluntary movement is initiated elsewhere. Common after Bell's palsy.
Tardive	Term applied to delayed development of dyskinesias or dystonia after initiating treatment with a dopamine-blocking agent.
Teichopsia (fortification spectra)	Dazzling zig-zag lines resembling the walls of a medieval fort.
Teleopsia	Objects appear at a distance. Brief episodes of teleopsia may indicate focal aware seizures (simple partial seizures).
Tic	Brief sudden movements or sounds which are often repetitive and stereotyped.
Tinel's sign	Tingling provoked by percussion over an injured nerve.
Todd's phenomenon	Focal neurologic deficit temporarily present after a seizure.

Torticollis	Cervical dystonia manifested by spasm of neck musculature with the head drawn to one side and the chin pointing to the other side.
Torsional	Refers to nystagmus which has a predominant rotatory component.
Trombone tongue	Inability to keep the tongue protruded on command.
Tullio phenomenon	Paroxysmal vertigo and nystagmus provoked by a sound at a specific frequency. Etiologies include superior canal dehiscence, perilymph fistula, vestibular fibrosis and rarely Ménière's disease.
Tumarkin's otolithic crisis	See otolithic crisis.
Uhthoff's sign	Exacerbation or provocation of a neurologic deficit due to exercise or elevation of body temperature.
Utilization behavior	When a patient picks up and uses irrelevant objects placed in front of him. This is often due to anterior frontal lobe lesions.
Vegetative state	Condition in which the patient is awake but unaware.
Vestibular triad	Vertigo, vomiting, and diaphoresis.
Visual synesthesia	Optic phenomena induced by another sensory stimulus. For example, seeing numbers, colors or forms when hearing a particular sound.
Von Graefe's sign	Lid lag.
Wernicke's aphasia	Fluent aphasia with poor comprehension and repetition.
Witzelsucht	Inappropriate affect manifested by joking which may be present in patients with frontal lobe lesions.
Xanthochromia	Yellow color of centrifuged CSF supernatant after CNS hemorrhage. The yellow color is due to bilirubin.

Syndromes

Alice-in-Wonderland	Self-experienced paroxysmal illusions of body image manifested by distortions of mass, size, shape and position in space of patient's own body commonly accompanied by depersonalization and derealization.

Angelman syndrome	Genetic disorder, new mutation on chromosome 15, manifested by severe intellectual disability, delayed development, microcephaly, impaired balance, seizures, impaired speech and a movement disorder.
Anterior interosseous syndrome (Kiloh-Nevins)	The anterior interosseous nerve is a pure motor branch of the median nerve. An injury causes pain in the forearm and weakness of pincer movement between thumb and index finger.
Anterior spinal artery syndrome	Occlusion that causes infarction of the anterior two-thirds of the spinal cord which results in a complete motor paralysis below the level of the lesion (corticospinal tract), loss of pain and temperature sensation below the level of the lesion (spinothalamic tract) and frequent autonomic dysfunction variably manifested by hypotension, sexual dysfunction, bowel and bladder dysfunction.
Antiphospholipid antibody syndrome	Autoimmune hypercoagulable state which promotes arterial and venous thrombosis and pregnancy-related complications such as miscarriages and preeclampsia.
Anton's syndrome	Denial of blindness which is usually a sign of bilateral occipital lobe infarctions.
Balint's syndrome	Simultanagnosia, optic ataxia and oculomotor apraxia.
Bassen–Kornzweig syndrome	Autosomal recessive disorder associated with external ophthalmoplegia and clinical signs indicating posterior column, spinocerebellar, and corticospinal tract involvement. Laboratory abnormalities include abetalipoproteinemia, acanthocytosis, and hypocholesterolemia.
Benedikt syndrome	Ipsilateral 3rd nerve palsy and contralateral choreiform movements due to a lesion involving nerve fibers in the red nucleus/substantia nigra region.
Breughel's syndrome	Oromandibular dystonia, blepharospasm, hemifacial spasm, tongue protrusion, platysma spasm, and forceful jaw opening or closing.
Brown-Séquard syndrome	Hemisection or damage to one-half of the spinal cord which results in an ipsilateral spastic paresis, ipsilateral loss of vibration and position sense

	below the level of the lesion, and contralateral pain and temperature loss one or two levels below the lesion.
Brown superior oblique tendon sheath syndrome	Mechanical restriction of the superior oblique tendon at the pulley suggesting an inferior oblique paresis by preventing upward and inward movement of the globe.
Call-Fleming syndrome	See reversible cerebral vasoconstriction syndrome.
CANVAS syndrome	Cerebellar ataxia, neuropathy and arreflexia.
Capgras syndrome	Irrational belief that a familiar person has been replaced by an imposter. This occurs with Lewy body disease and other neurodegenerative disorders.
Carpal tunnel syndrome	Paresthesias and/or weakness in the distribution of the median nerve due to its compression between the carpal bones and the transverse carpal ligament.
Cauda equina syndrome	Lesion of lower lumbar (L4–L5) and sacral roots (S1–S5) which may cause a paraparesis, sphincter disturbances, and severe pain with sensory loss in the buttocks, perianal, genital, and perineal regions.
Cavernous sinus syndrome	Lesions within the cavernous sinus which variably affect the 3rd, 4th, and 6th cranial nerves, the first two divisions of the 5th cranial nerve and sympathetic fibers within the carotid sheath.
Central cord syndrome	Quadriparesis with greater involvement of arms than legs, bladder dysfunction and variable sensory loss below the level of the lesion. The most common etiology is a severe hyperextension injury in patients with cervical spondylosis.
Cerebellopontine angle syndrome	Lesions in this angle affect primarily the 5th, 7th, and 8th cranial nerves and adjacent cerebellum. Schwannomas of the 8th cranial nerve are the most common etiology.
Charles Bonnet syndrome	Syndrome characterized by vivid, visual, and nonthreatening hallucinations of people or objects in patients with severe visual loss, most often due to severe retinal disease. The patient is aware that they are unreal.
Claude syndrome	Ipsilateral 3rd nerve palsy with contralateral ataxia and tremor due to a lesion involving 3rd

	nerve fibers, red nucleus and superior cerebellar peduncle.
Claude Bernard syndrome	Oculosympathetic irritation causing periodic pupillary dilatation, lid retraction, facial hyperhidrosis, and headache.
Cogan's syndrome	Chronic inflammatory autoimmune disease causing an arteritis of large and medium sized vessels. Manifestations include interstitial keratitis, uveitis, sensorineural hearing loss and vestibular symptoms.
Collett-Sicard syndrome	Ipsilateral weakness of cranial nerves 9, 10, 11 and 12 due to lesions usually adjacent to the jugular foramen and outside the skull.
Complex regional pain syndrome	Type 1 (reflex sympathetic dystrophy) – A disorder usually affecting one limb manifested by pain, swelling, limited range of motion with skin and bone changes. It occurs after an injury such as a fracture but without a specific nerve involvement. Type 2 (causalgia) – The same symptoms and signs but due to a specific nerve injury.
Cubital tunnel syndrome	Ulnar neuropathy due to the nerve being compressed at the elbow by a fibrous band, bone fragment, or bulging of the medial collateral ligament.
Dandy–Walker syndrome	This disorder includes a cystic 4th ventricle, partial or complete absence of the cerebellum and an enlarged posterior fossa.
Dejerine medial medullary syndrome	Ipsilateral paresis, atrophy, and fasciculations of the tongue which protrudes toward the side of the lesion, contralateral hemiplegia sparing the face, contralateral loss of position and vibration sensation and occasionally upbeat nystagmus.
Dorsal midbrain syndrome	See pretectal syndrome.
Droopy shoulder syndrome	Thoracic outlet syndrome primarily in women secondary to intermittent compression of the brachial plexus caused by drooping shoulders associated with a long swan neck and downward slope of the clavicles.
Duane's syndrome	Type I is paresis of abduction of one eye associated with narrowing of the palpebral fissure with or without retraction of the globe on attempted adduction. Type II is impaired adduction.

	Type III is impaired abduction and adduction. The lesion is probably of congenital origin. The retraction syndrome may be due to anomalous innervation of the lateral rectus muscle by the inferior division of the oculomotor nerve.
Eagle's syndrome	Facial pain caused by an elongated styloid process.
Eight-and-one-half syndrome	Lesion in the dorsal tegmentum of caudal pons involving PPRF or abducens nucleus, medial longitudinal fasciculus plus the nucleus and fasciculus of the 7th cranial nerve. This is essentially a one-and-a-half syndrome with ipsilateral facial involvement.
Ekbom's syndrome	1. Fixed belief of being infested by parasites. 2. Restless legs syndrome.
Fisher syndrome	Ophthalmoplegia, ataxia, and areflexia associated with anti-GQ1b and GT1a antibodies.
Foix-Alajouanine syndrome	An arteriovenous malformation of the spinal cord primarily affecting lower thoracic and lumbosacral levels with necrosis of the affected cord region and with a predilection for gray matter involvement.
Foster Kennedy syndrome	Ipsilateral anosmia, optic atrophy, and contralateral papilledema. This is usually due to an olfactory groove meningioma. A pseudo-Foster Kennedy syndrome may be due to sequential AION.
Foville midbrain syndrome	Ipsilateral gaze deviation and contralateral hemiparesis.
Foville syndrome	Pontine lesion which causes an ipsilateral 7th nerve paresis with ipsilateral gaze paresis and contralateral hemiparesis. The eyes look at the hemiparesis.
Fragile X syndrome	The typical age of onset is 2 years and it is manifested by intellectual disability, delayed speech, seizures, autism, attention deficit hyperactivity disorder due to breakage of the X chromosome.
Fragile X-associated tremor/ataxia syndrome (FXTAS)	This is manifested by a variable combination of cerebellar ataxia, intention tremor, executive dysfunction, parkinsonism, dementia, neuropathy and global brain atrophy. The age of onset is over 50 years primarily in males.

Froehlich's syndrome	An acquired disorder, typically in males, manifested by obesity, hypogonadism, mental retardation due to lesions (often neoplasm) affecting the pituitary gland and hypothalamus.
Froin's syndrome	Combination of xanthochromia, markedly elevated protein and hypercoagulation of cerebrospinal fluid (CSF). Etiologies include mass lesion (tumor or abscess) which block CSF flow and meningitis.
Gerstmann's syndrome	Acalculia, finger agnosia, agraphia, and right–left confusion due to a lesion of the dominant angular gyrus.
Gilles de la Tourette syndrome	See Tourette's syndrome.
Gradenigo's syndrome	Lesion which affects the ophthalmic division of the trigeminal nerve and the 6th cranial nerve associated with either an infection (petrositis) or neoplasm of the apex of the temporal bone.
Guillain–Barré syndrome	Acute inflammatory demyelinating polyneuropathy.
Harlequin syndrome	Unilateral flushing and sweating of the face and neck with a contralateral Horner's syndrome.
Horner's syndrome	Ptosis, miosis, and anhidrosis.
Isaac's syndrome (neuromyotonia)	The prominent feature of neuromyotonia is continuous myokymia especially of distal musculature which persists in sleep. Symptoms include muscle stiffness, cramps, and occasionally hyperhidrosis.
Jugular foramen syndrome (Vernet's syndrome)	Ninth, 10th, and 11th cranial nerve deficits usually due to a mass at the jugular foramen or a basilar skull fracture.
Kearns–Sayre syndrome	Chronic progressive external ophthalmoplegia (CPEO) beginning in childhood associated with heart block, retinal pigment degeneration, short stature, abnormal muscle mitochondria, spongiform encephalopathy, and occasionally cerebellar ataxia.
Klein – Levin syndrome	Episodes of hypersomnia, hyperphagia, and hypersexual behavior.
Klippel-Feil syndrome	Congenital fusion of 2 or more (usually upper) cervical vertebra which may be associated with a short neck, low hairline and restricted mobility of the cervical spine.
Klüver–Bucy syndrome	Hyperorality, hypersexuality and lack of capacity for anger or fear secondary to bilateral

	lesions in the frontotemporal parts of the limbic system (amygdala, piriform cortex and adjacent hippocampus).
Korsakoff's syndrome	Loss of short-term memory plus confabulation. Although it is a well-known complication of chronic alcoholism, it is not a pathognomonic sign and is not infrequent in patients with Alzheimer's disease. Lesions are located primarily in the dorsomedial nucleus of the thalamus and the mammillary bodies.
Lacunar syndromes	Characteristic syndromes associated with small ischemic infarctions in subcortical or brainstem locations. These lacunar infarctions are due to disease of small vessel penetrating arteries.
Lateral medullary syndrome	See Wallenberg's syndrome.
Lambert–Eaton syndrome	Autoimmune disorder in which antibodies are formed against presynaptic voltage-gated calcium channels in the neuromuscular junction causing a decreased release of acetylcholine packets from the presynaptic terminal. The primary clinical features are proximal leg weakness and autonomic dysfunction.
Lance-Adams syndrome	Action myoclonus caused by an hypoxic brain injury.
Landau–Kleffner syndrome	Acquired epileptic aphasia in children.
Laurence-Moon syndrome	Autosomal recessive disease manifested by retinitis pigmentosa, mental disabilities and spastic paraplegia.
Leigh syndrome (subacute necrotizing encephalomyelopathy)	Inherited neurometabolic disorder especially affecting infants but occasionally adolescents and adults. Manifold manifestations include gastrointestinal disturbances, ataxia, seizures, dystonia, eye movement disorders, hypertrophic cardiomyopathy, neuropathy, and respiratory failure. There is excessive lactic acid in urine, blood, and cerebrospinal fluid.
Lennox–Gastaut syndrome	Childhood onset of multiple seizure types associated with mental retardation which is cryptogenic or symptomatic and often refractory to treatment.
Locked-in syndrome	Quadriplegia, horizontal gaze palsy, preservation of vertical eye movements with normal alertness, and cognition.

Lutz syndrome	Posterior internuclear ophthalmoplegia (reverse internuclear ophthalmoplegia) manifested by abduction restriction and contralateral slow adduction nystagmus thought to be secondary to a partial lesion of the abducens nucleus.
Man-in-a-barrel syndrome	Bilateral arm paresis with good preservation of leg function.
Marie–Foix syndrome	Ipsilateral cerebellar ataxia, contralateral hemiparesis, and variable contralateral hemihypesthesia due to a lateral pontine lesion involving the middle cerebellar peduncle and adjacent corticospinal tract.
Martin-Gruber anastomosis	Forearm nerve anomaly where there is a communicating nerve branch between the median and ulnar nerve which carries motor fibers with variable patterns of connections and manifestations.
Medial medullary syndrome of Dejerine	Combination of ipsilateral paresis, atrophy and fasciculations of the tongue which protrudes toward the lesion side, contralateral hemiplegia with sparing of the face, contralateral loss of position and vibratory sensation and occasionally upbeat nystagmus.
Meige syndrome	Oral mandibular dystonia and blepharospasm.
Melkersson–Rosenthal syndrome	Recurrent unilateral or bilateral facial palsies with fissured (scrotal) tongue and facial swelling.
Millard-Gubler syndrome	Ipsilateral peripheral 7th nerve paresis and lateral rectus paresis with contralateral hemiparesis due to a ventral pontine lesion involving fascicles of the 6th and 7th cranial nerves and corticospinal tract.
Möbius syndrome	Facial diplegia with variable degrees of lateral gaze paralysis and esotropia.
Morvan's syndrome	Autoimmune disorder manifested by irregular contractions of long muscles, hyperhidrosis, hypertension, severe insomnia, pleuritis, and neuromyotonic discharges.
Moya-Moya syndrome	Extracranial and intracranial vascular occlusions typically affecting the distal intracranial internal carotid artery system surrounded by small collateral vessels (puff of smoke sign) which are prone to hemorrhage and aneurysm formation.

Munchausen syndrome	These patients simulate illness to obtain medical treatment without an obvious motive.
Munchausen by proxy	Inducing illness in another person, usually a child, to obtain medical treatment without obvious motive.
Neuroleptic malignant syndrome	Hyperthermia, extrapyramidal signs, altered mental status, and elevated CK due to an idiosyncratic reaction to neuroleptics or an abrupt withdrawal from levodopa treatment.
Neuromyotonia	See Isaac's syndrome.
Numb-chin syndrome	Neuropathy of the mental nerve causing numbness of the chin, occasionally lower lip, and mucus membrane of the inside of the lower lip. It can be a sign of metastatic neoplasm.
One-and-a-half syndrome	This occurs from a unilateral PPRF and adjacent MLF lesion. It causes an ipsilateral gaze palsy and ipsilateral adduction paresis with consequent retention of only abduction of the contralateral eye. Vertical eye movements are usually preserved.
Opalski's syndrome	Variant of lateral medullary syndrome which includes an ipsilateral hemiparesis probably due to involvement of the corticospinal tract after the decussation of the pyramids.
Othello syndrome	Delusion of infidelity by a spouse or partner.
Parinaud's syndrome	See pretectal syndrome.
Parry-Romberg syndrome	*A* slowly progressive atrophy of one-half of the face involving skin and soft tissues often associated with alopecia, hyperpigmentation, vitiligo, seizures, and trigeminal neuralgia.
Parsonage – Turner syndrome	This is a painful brachial plexitis usually of viral or immune origin.
Piriformis syndrome	Tingling, pain, and numbness in the sciatic nerve distribution due to entrapment of the nerve as it passes through the greater sciatic notch. It may be aggravated by internal rotation of the flexed leg. Causes include mass lesions, buttock trauma, fibrous bands and piriformis muscle anomalies.
POEMS syndrome	Polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes.
Post-polio syndrome	Recurrent weakness, atrophy, fatigue, and pain occurring 15 years or more after acute poliomyelitis.

Posterior reversible encephalopathy syndrome (PRES)	Presenting acute manifestations are headache, confusion, seizures and visual impairment most often associated with malignant hypertension, eclampsia, drug toxicity with a predilection for involvement of parieto-occipital regions. Treatment produces a rapid reversal of clinical symptomatology.
Posterior spinal artery syndrome	Loss of proprioception, vibration sense, and absent myotatic and cutaneous reflexes below the involved level. There are no motor deficits.
Postural orthostatic tachycardia syndrome	Tachycardia, 30 beats higher than the resting rate, with minimal exertion, and associated with chronic fatigue.
Prader-Willi syndrome	Age of onset is 1–3 years of hypogonadism, mental retardation, obesity, hyperphagia and small stature. This is an autosomal recessive trait in males associated with deletion of chromosome 15.
Pretectal syndrome (dorsal midbrain, Sylvian aqueduct and Parinaud's syndrome)	Paresis of upward gaze and, variably, convergence-retractory nystagmus, lid retraction, lid lag, and large round pupils poorly or nonreactive to light. Light-near dissociation may be present.
Pronator syndrome	Compression of the median nerve at the elbow which can cause pain and numbness in the median nerve distribution as well as weakness of the muscles innervated by the anterior interosseous nerve. These are the flexor pollicis longus, flexor digitorum profundus of the index finger, and the pronator quadratus.
Raeder's paratrigeminal syndrome	Persistent pain in the ophthalmic division of the trigeminal nerve associated with a partial Horner's syndrome (miosis and ptosis).
Rabbit Syndrome	Involuntary fine rhythmic vertical movements of mouth, but not tongue, a side effect of high potency antipsychotic drugs after many years of treatment.

Ramsay Hunt syndrome Herpes zoster affecting the geniculate ganglion causing a facial palsy of Bell's type often with a vesicular eruption on the eardrum and in the external auditory meatus.

Raymond's syndrome Ipsilateral lateral rectus paresis and contralateral hemiparesis sparing the face due to a unilateral lesion of the ventral medial pons affecting 6th nerve fascicles and corticospinal tract.

Raymond-Cestan syndrome Cerebellar ataxia with "rubral" tremor, contralateral hypesthesia including the face involving all sensory modalities with variable contralateral hemiparesis and ipsilateral gaze palsy due to a lesion of the rostral dorsal pons.

Reflex sympathetic dystrophy See complex regional pain syndrome.

Rett's syndrome X-linked disorder in girls who develop stereotypical behaviors, cognitive impairment, and extrapyramidal manifestations. It is considered an autism spectrum disorder.

Reversible cerebral vasoconstriction syndrome Primary hallmarks are thunderclap headaches, focal neurologic signs and occasional seizures associated with segmental vasoconstriction of cerebral arteries that resolve by 3 months. Etiologies include childbirth, pregnancy complications and illicit drug use, especially vasoactive substances.

Reye's syndrome Acute encephalopathy with altered mental status and liver dysfunction manifested by elevated liver enzymes and/or hyperammonemia probably secondary to a virus (influenza A, B and varicella virus) with a concomitant exposure to an exogenous substance, especially aspirin.

Riley-Day syndrome (familial dysautonomia) Autosomal recessive disorder associated with orthostatic hypotension, excessive sweating, emotional instability, stunted growth, lack of tears, defective temperature control, fixed pupils, loss of pain and temperature perception affecting Jewish children.

Schwartz–Jampel syndrome Autosomal recessive myotonic disorder in children manifested by continuous motor activity in muscles, especially in the face and thighs, blepharospasm, and constant motor activity of chin and lips.

Serotonin syndrome	Hyperthermia, myoclonus, extrapyramidal signs, hyperreflexia, and altered mental status usually secondary to SSRIs or monoamine oxidase inhibitors (MAOIs) or amphetamine interacting with other antidepressants.
Shy–Drager syndrome	Parkinsonism plus autonomic dysfunction. This is now encompassed by the term multiple system atrophy (MSA).
Sneddon's syndrome	Combination of transient ischemic attack or stroke, livedo reticularis (bluish-purple net-like skin mottling) often associated with antiphospholipid antibodies, acrocyanosis, and Raynaud's phenomenon.
Spasmus Nutans	Benign triad of head nodding, nystagmus, and abnormal head posture in children which may mimic neoplasm around the chiasm and 3rd ventricle.
Steele–Richardson–Olszewski syndrome	Progressive supranuclear palsy. This combines parkinsonism, vertical gaze paresis (primarily downgaze), dementia, and nuchal rigidity.
Stiff-person syndrome (stiff-man's)	This motor system disease, occasionally paraneoplastic, is manifested by painful fluctuating rigidity and spasms of axial and limb musculature commonly exacerbated by external stimuli. There are usually markedly increased antibodies to glutamic acid decarboxylase (GAD), an enzyme which breaks down glutamic acid to GABA, an inhibitory neurotransmitter.
Subclavian steal syndrome	Retrograde blood flow in a vertebral artery due to a proximal stenosis or occlusion of the ipsilateral subclavian artery. This retrograde circulation supplies blood to the arm of the involved side which results in transient ischemic attacks but not stroke in the vertebrobasilar distribution.
Superior orbital fissure syndrome	Findings are similar to the cavernous sinus syndrome since the third, fourth, ophthalmic division of 5th and 6th cranial nerves pass through this fissure. Pain, paresthesias and sensory loss in the ophthalmic division of the 5th nerve, Horner's syndrome, and exophthalmos may be present.

Susac's syndrome	Hearing loss with tinnitus, multiple branch retinal artery occlusions and encephalopathy.
Sylvian aqueduct syndrome	See pretectal syndrome.
Tarsal tunnel syndrome	Entrapment of the posterior tibial nerve as it passes through the tarsal tunnel on the medial portion of the ankle.
Terson's syndrome	Vitreous hemorrhage associated with intracranial hemorrhage.
Tethered cord syndrome	This is typically a cauda equina syndrome arising from an abnormal taut filum terminale, lipoma or other lesion causing tension on the inferior aspect of the spinal cord.
Thalamic syndrome	Severely disagreeable or painful cutaneous symptoms contralateral to a thalamic lesion.
Thoracic outlet syndrome	Symptoms and signs due to compression of the brachial plexus and arteries in that region. The C8 and T1 roots are especially susceptible to damage from fibrous bands over a cervical rib.
Tolosa–Hunt syndrome	Granulomatous inflammation in the cavernous sinus causing a painful ophthalmoplegia with variable involvement of the 3rd, 4th, first division of the 5th and 6th cranial nerves. There is occasional optic nerve involvement and Horner's syndrome.
Top-of-the-basilar syndrome	Vascular occlusive disease of the rostral portion of the basilar artery, commonly cardioembolic, resulting in midbrain, thalamic, temporal lobe and occipital lobe infarctions, often bilateral.
Tourette's syndrome	Repetitive stereotyped tics, motor and vocal (phonic) and rarely coprolalia, often associated with an obsessive compulsive disorder and attention deficit hyperactivity disorder beginning in childhood.
Vernet's syndrome	See jugular foramen syndrome.
Vertical one-and-a-half syndrome	Vertical upgaze palsy and monocular paresis of downgaze associated with thalamo-mesencephalic infarctions.
Vogt-Koyanagi-Harada syndrome	Uveomeningoencephalitic syndrome of probable autoimmune origin with variable combinations of diffuse uveitis, meningitis with pleocytosis, tinnitus, vertigo, hearing loss, cranial nerve palsies, transverse myelitis and, especially, cutaneous findings of vitiligo, alopecia, and poliosis.

Wallenberg's syndrome (lateral medullary syndrome)	Unilateral infarction of the dorsolateral medulla due to ischemia in the distribution of the posterior inferior cerebellar artery. Characteristic findings are horizontal gaze-evoked nystagmus, ipsilateral Horner's syndrome, ipsilateral facial hypesthesia, contralateral hemihypesthesia, ipsilateral palate and vocal cord paresis, ipsilateral cerebellar ataxia and, occasionally, singultus (hiccups).
Wartenberg's syndrome	Injury to the superficial cutaneous branch of the radial nerve resulting in numbness and paresthesias of the dorsal aspect of the first three fingers and dorsum of the hand, radial portion. This is also known as cheiralgia paresthetica.
Weber's syndrome	Third nerve palsy and contralateral hemiparesis including the lower face due to a midbrain lesion affecting fascicles of the 3rd cranial nerve and pyramidal fibers in the cerebral peduncle.
Wernicke's syndrome	Altered sensorium, ataxia, and oculomotor abnormalities due to thiamin deficiency, usually a complication of alcoholism. Hemorrhagic lesions are found in midbrain periaqueductal gray matter and medial thalamic regions.
West syndrome (infantile spasms, Salaam attacks)	Seizures in infancy manifested by flexor or extensor spasms, mental retardation, and a typical EEG pattern called hypsarrhythmia.

Case Report Index by Disease

(X/Y where X = chapter number and Y = case number in that chapter.)

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