

FIGURE 11.12 At the decussation of the pyramids in the lower medulla, the arm fibers lie medial to the leg fibers. Arm fibers decussate first and come to lie in the medial portion of the lateral corticospinal tract in the upper cervical spinal cord. Leg fibers decussate more caudally and come to lie in the lateral portion of the lateral corticospinal tract. The syndrome of the pyramidal decussation (cruciate or crossed paralysis) is spastic weakness of one arm and the contralateral leg because of a lesion at the decussation.

The lateral medulla contains the spinal tract and nucleus of CN V; nearby run ascending spinothalamic (anterolateral system) fibers. The nucleus ambiguus, because of its branchial arch origin, lies deep in the tegmentum anterolaterally, in a position analogous to that of the CN VII nucleus in the pons. It extends from the level of entry of CN VIII at the upper border of the medulla to the level of the decussation of the ML or even to the beginning of the corticospinal decussation. From the nucleus ambiguus, motor fibers exit laterally to enter both the ninth and tenth nerves. The dorsal motor nucleus of the vagus, the autonomic component of CN X, sends fibers laterally to join the exiting ambiguus fibers. The solitary tract lies lateral to the dorsal motor nucleus of the vagus, and it receives entering taste fibers from CNs VII and IX. Descending in the reticular core are sympathetic fibers destined for the intermediolateral gray column of the thoracic and lumbar cord.

OVERVIEW OF CRANIAL NERVES III–XII

This section provides a brief overview of the CNs that arise or terminate in the brainstem. The nerves are covered in more detail in succeeding chapters.

Oculomotor (CN III)

CN III arises from the oculomotor complex in the midbrain and conveys motor fibers to extraocular muscles, plus parasympathetic fibers to the pupil and ciliary body. It exits the midbrain in the interpeduncular fossa, travels between the posterior cerebral and superior cerebellar artery, and runs alongside the posterior communicating artery. The nerve travels through the cavernous sinus where it has important relationships with the carotid artery, ascending pericarotid sympathetics, and CNs IV, V, and VI. After exiting the cavernous sinus and passing through the superior orbital fissure, the third nerve innervates the medial rectus, inferior oblique and superior and inferior recti, and the levator palpebrae.

Long ciliary nerves swerve off to the ciliary ganglion, from which short ciliary nerves arise to innervate the iris and ciliary body.

Trochlear (CN IV)

CN IV arises from the trochlear nucleus at the level of the inferior colliculus and travels backward and around to decussate and exit through the tectum. The nerve winds around the brainstem, then runs forward, passes through the cavernous sinus in proximity to CN III, traverses the superior orbital fissure, and enters the orbit to supply the superior oblique.

Trigeminal (CN V)

Motor fibers of CN V arise from the motor nucleus in the midpons, exit laterally, pass through the gasserian ganglion, and travel with the mandibular sensory branch to exit the skull through the foramen ovale. Trigeminal motor fibers innervate the masseter, temporalis, and pterygoids.

Sensory trigeminal fibers arise from the ophthalmic, maxillary, and mandibular divisions supplying the face. Ophthalmic division fibers enter the skull via the superior orbital fissure, and maxillary fibers enter through the foramen rotundum; both pass through the cavernous sinus before joining the ganglion. The mandibular fibers enter through the foramen ovale. Sensory fibers terminate in the principal sensory nucleus in the pons and in the nucleus of the spinal tract, which extends from the pons to the upper cervical spinal cord.

Abducens (CN VI)

The cells of origin of the CN VI lie in the pons near the pontine lateral gaze center. Axons pass forward through the substance of the pons, weaving among descending corticospinal fibers, and exit anteriorly. CN VI ascends the clivus, traverses the cavernous sinus in company with the CNs III, IV, and V, and then passes through the superior orbital fissure and enters the orbit to innervate the lateral rectus.

Facial (CN VII)

Axons of CN VII arise from the facial nucleus in the pontine tegmentum, travel backward, up and around the nucleus of CN VI, and then cross the pons to exit laterally. In the company of CN VIII, CN VII crosses the CPA, enters the internal auditory meatus, and travels along the internal auditory canal. It curves down and away from CN VIII at the external genu in the vicinity of the geniculate ganglion. After traversing the remainder of the petrous bone, CN VII exits through the stylomastoid foramen, turns forward, passes under the parotid gland, and ramifies into upper and lower divisions to supply the muscles of facial expression. Running in company with the facial nerve is the nervus intermedius; its primary component is the chorda tympani, which provides taste sensation to the anterior two-thirds of the tongue.

Vestibulocochlear (CN VIII)

Auditory stimuli activate hair cells in the organ of Corti. Nerve fibers supplying the hair cells are the peripheral processes of the bipolar neurons that make up the spiral ganglion lying in the center of the cochlea. The central processes of these neurons form the auditory nerve, which follows a direct course through the internal auditory canal and across the CPA, enters the brainstem at the pontomedullary junction, and synapses in the cochlear nuclei.

The vestibular nerve arises from the vestibular (Scarpa's) ganglion. The peripheral processes of its bipolar neurons receive impulses from the utricle, saccule, and three semicircular canals; the central processes convey these impulses through the vestibular portion of CN VIII.

Glossopharyngeal (CN IX)

The nucleus ambiguus sends axons via CN IX to innervate the pharyngeal plexus. The functions of CNs IX and X are virtually inseparable in this regard. The only muscle innervated solely by CN IX is the stylopharyngeus. In company with CNs X and XI, the nerve exits the skull through the jugular foramen. CN IX also conveys taste fibers from the posterior third of the tongue and supplies parasympathetics to the parotid gland.

Vagus (CN X)

CN X carries motor fibers from the nucleus ambiguus to the palate, pharynx, and

larynx. In addition, a heavy input arises from the dorsal motor nucleus of the vagus, which conveys parasympathetic fibers to innervate viscera of the thorax and abdomen. The vagus also carries visceral afferents and taste fibers.

Accessory (CN XI)

The accessory nerve has two parts. The spinal portion arises from lower motor neurons in the upper cervical cord. Because of its branchial arch origin, it exits laterally, runs upward to enter the skull through the foramen magnum, and ascends to the jugular foramen. These fibers ultimately innervate the sternomastoid and trapezius muscles. The cranial portion of CN XI arises from the nucleus ambiguus, exits laterally, joins the spinal root briefly, and then quickly turns off to join IX and X. Its functions are not separable from those of the vagus.

Hypoglossal (CN XII)

CN XII arises from motor neurons in the hypoglossal nucleus, exits the medulla anteriorly in the groove between the pyramid and the olive, leaves the skull through the hypoglossal foramen, and runs forward to innervate the tongue.

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CHAPTER 12

The Olfactory Nerve

ANATOMY AND PHYSIOLOGY

The first-order neurons of the olfactory system are bipolar sensory cells that lie in the olfactory epithelium, which occupies a small area on the superior nasal concha, upper nasal septum, and roof of the nose. Their peripheral ramifications are ciliated processes that penetrate the mucous membrane of the upper nasal cavity. Tiny knobs on the cilia are the sites of chemosensory signal transduction. Odorant binding to receptors causes ion fluxes, excitation, and the activation of messenger systems. Specific odorants stimulate specific receptor cells, and specific cells respond to particular odorants.

Most nasally inspired air fails to reach the olfactory epithelium because of its location in the nasal attic. Sniffing creates a better airflow pattern for reaching the olfactory endings. The central processes of the olfactory neurons are unmyelinated axons that form approximately 20 branches on each side. These are the olfactory nerves. They penetrate the cribriform plate of the ethmoid bone, acquire a sheath of meninges, and synapse in the olfactory bulbs ([Figure 12.1](#)). Basal cells in the olfactory epithelium can regenerate, an unusual neuronal property. Olfactory receptor cells are continuously replaced by newly formed cells. The olfactory apparatus is sensitive to processes such as chemotherapy that affect rapidly replicating cell systems. Receptor regeneration with recovery of olfactory function can occur after some insults.

Within the olfactory bulbs, axons of incoming fibers synapse on dendrites of mitral and tufted cells in the olfactory glomeruli. The mitral and tufted cells are the output cells of the olfactory bulb. The axons of the second-order neurons, mainly the mitral cells, course posteriorly through the olfactory tracts, which lie in the olfactory grooves, or sulci, beneath the frontal lobes in the floor of the anterior cranial fossa.

The olfactory bulbs and tracts are sometimes mistakenly called the olfactory nerves. The olfactory nerves are the unmyelinated filaments, wrapped by a special type of glia called olfactory ensheathing glia, that pass through the cribriform plate. The olfactory tracts are mainly formed by axons myelinated by oligodendrocytes and are thus part of the central nervous system (CNS). The bulbs and tracts are part of the rhinencephalon. The proximity of the olfactory tracts to the inferior surface of the frontal lobes is an important anatomic relationship (see [Figure 11.3](#)).

Olfactory information is processed in primitive areas of the brain. Olfaction is the only sensation not directly processed in the thalamus. The olfactory tracts divide into medial and lateral olfactory striae that run on either side of the anterior perforated substance. The triangular area thus formed is called the olfactory trigone. Some olfactory stria fibers decussate in the anterior commissure to join the fibers from the opposite side; some go to the olfactory trigone and tuberculum olfactorium within the anterior perforated substance. Fibers of the medial olfactory stria terminate on the medial surface of the cerebral hemisphere in the parolfactory area, subcallosal gyrus, and inferior part of the cingulate gyrus. The lateral olfactory stria courses obliquely along the anterior perforated space and beneath the temporal lobe to terminate in the uncus, anterior hippocampal gyrus, piriform cortex, entorhinal cortex, and amygdaloid nucleus ([Figures 12.2](#) and [12.3](#)). Structures collectively referred to as the primary olfactory cortex include the anterior olfactory nucleus, the piriform cortex, the anterior cortical nucleus of the amygdala, the periamygdaloid complex, and the rostral entorhinal cortex.

The parahippocampal gyrus sends impulses to the hippocampus. The hippocampi and amygdaloid nuclei on the two sides are intimately related through the anterior commissure. These nuclei send projection fibers to the anterior hypothalamic nuclei, mammillary bodies, tuber cinereum, and habenular nucleus. These in turn project to the anterior nuclear group of the thalamus, interpeduncular nucleus, dorsal tegmental nucleus, striatum, cingulate gyrus, and mesencephalic reticular formation. Functional magnetic resonance imaging has shown that chemosensory signals cause activation of cortical areas not previously known to have olfactory functions. Communications with the superior and inferior salivatory nuclei are important in reflex salivation. Pheromones are also detected by neurons in the vomeronasal organ. These project via the olfactory tract to the accessory olfactory bulb, then to the piriform cortex and amygdala.

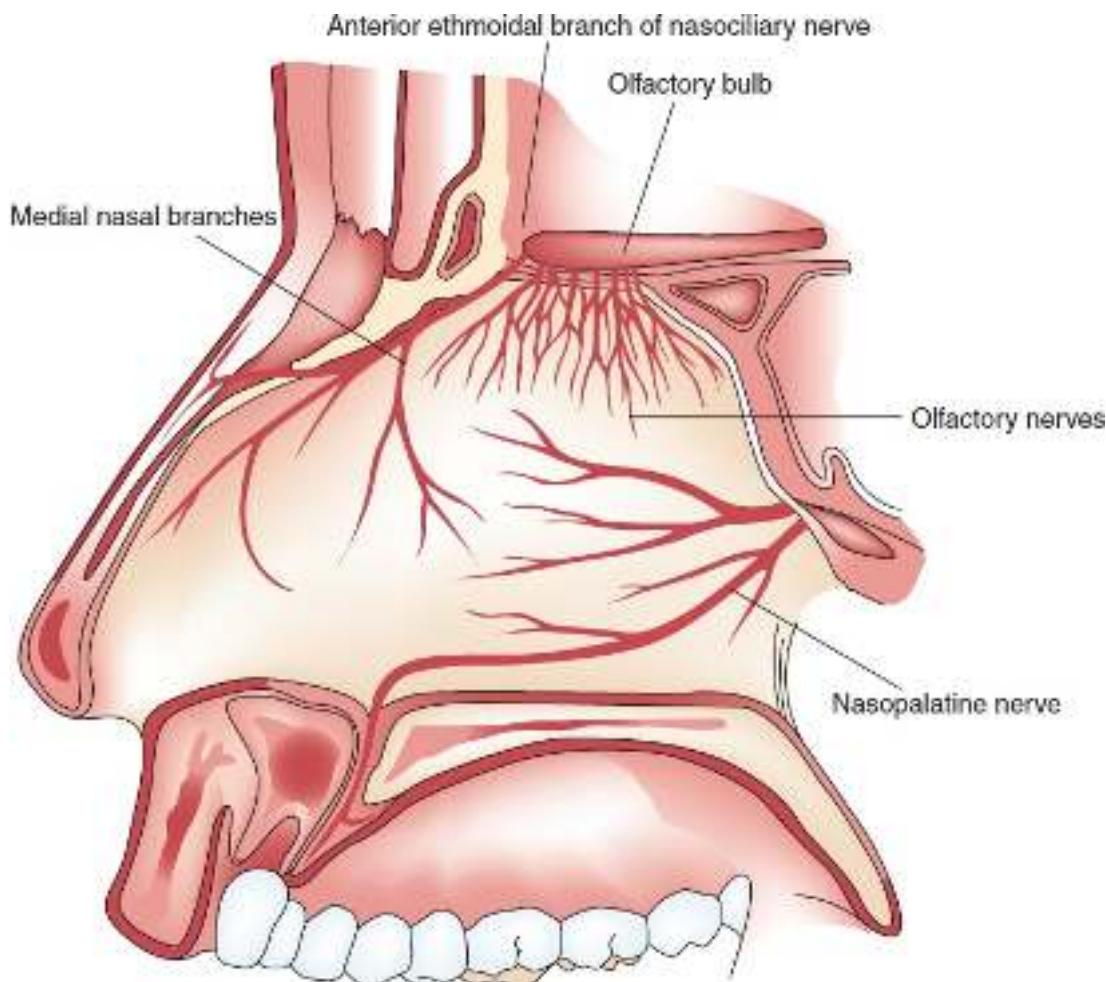


FIGURE 12.1 The distribution of the olfactory nerves within the nose.

Olfaction is a phylogenetically ancient sensation. In lower mammals in whom olfaction is extremely important, the olfactory cortex constitutes a large part of the cerebral hemispheres. The connections between the olfactory system, hypothalamus, certain brainstem nuclei, and autonomic centers are pertinent to the understanding of many visceral functions.

The olfactory nerve is a sensory nerve with but one function—smell. The ability to perceive and identify various odors differs from person to person. Only volatile substances soluble in lipids or water are perceived as odors. In true anosmia, there is loss of ability to perceive or recognize not only scents but also flavors, for much of what is interpreted as taste involves smell. Flavor is a synthesis of sensations derived from the olfactory nerves, taste buds, and other sensory end organs. A patient with olfactory impairment may complain of loss of taste rather than of smell. Patients with unilateral anosmia may be unaware of any impairment.

CLINICAL EXAMINATION

Impairments because of anosmia are not trivial. The problem is not merely that patients with disturbances of smell sensation miss out on some of life's pleasures; they may also miss olfactory danger signals, such as spoiled food, smoke, and leaking gas. As with hearing, olfactory deficits are sometimes divided into (a) conductive deficits, because of processes interfering with the ability of odorants to contact the olfactory epithelium, such as nasal polyps; and (b) sensorineural or neurogenic deficits, because of dysfunction of the receptors or their central connections.

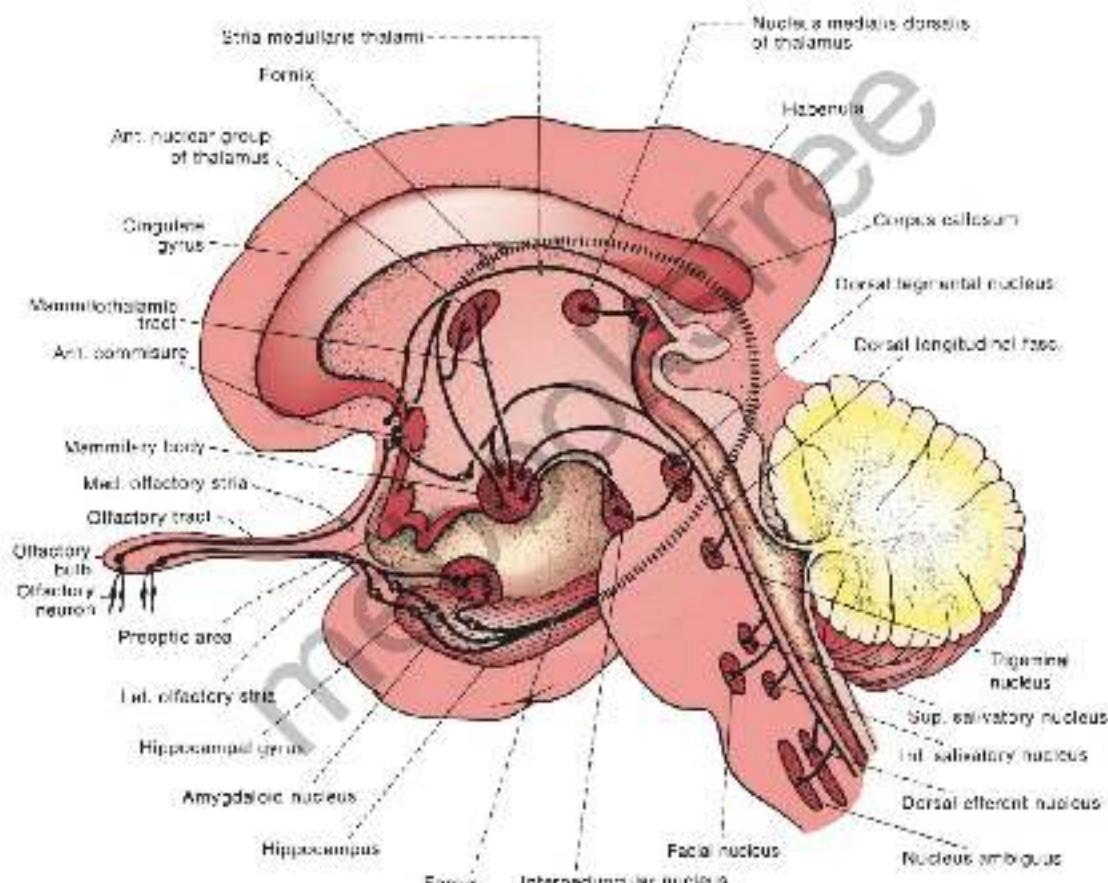


FIGURE 12.2 The olfactory pathway and its central connections.

Important historical points to address in a patient with a smell or taste disturbance include past head injury; smoking; recent upper respiratory tract infection (URI); systemic illness; nutrition; and exposure to toxins, medications, or illicit drugs. Feldman contends that changes in the flavor of coffee may be particularly informative. Unilateral loss of smell is more significant than

bilateral, which may be caused by many conditions, primarily conductive ([Table 12.1](#)).

Before evaluating smell, ensure that the nasal passages are open. Most cases of impaired smell are due to intranasal obstructions. Acute or chronic rhinitis and chronic sinusitis may seriously interfere with olfaction.

Smell is tested using nonirritating stimuli. Avoid substances such as ammonia that may stimulate the trigeminal nerve instead of the olfactory nerve, causing a response that can be confused with olfaction. The nasal passages are richly innervated by free nerve endings from the trigeminal system, which respond to many substances. Some patients with impaired taste and smell enjoy spicy food because of its stimulation of the trigeminal system.

Examine each nostril separately while occluding the other. With the patient's eyes closed and one nostril occluded, bring the test substance near the open one. Ask the patient to sniff and indicate whether she smells something and, if so, to identify it. Repeat for the other nostril and compare the two sides. The side that might be abnormal should be examined first. Many substances can be used to test smell (e.g., wintergreen, cloves, coffee, and cinnamon). At the bedside or in the clinic, one can use mouthwash, toothpaste, alcohol, soap, and similar substances. Commercial scratch-and-sniff strips are available. Commercially available quantitative smell and taste tests include the University of Pennsylvania smell identification test (UPSIT) and the Connecticut chemosensory test. The UPSIT requires no trained personnel and may be self-administered. Its forced-choice design helps identify malingering.

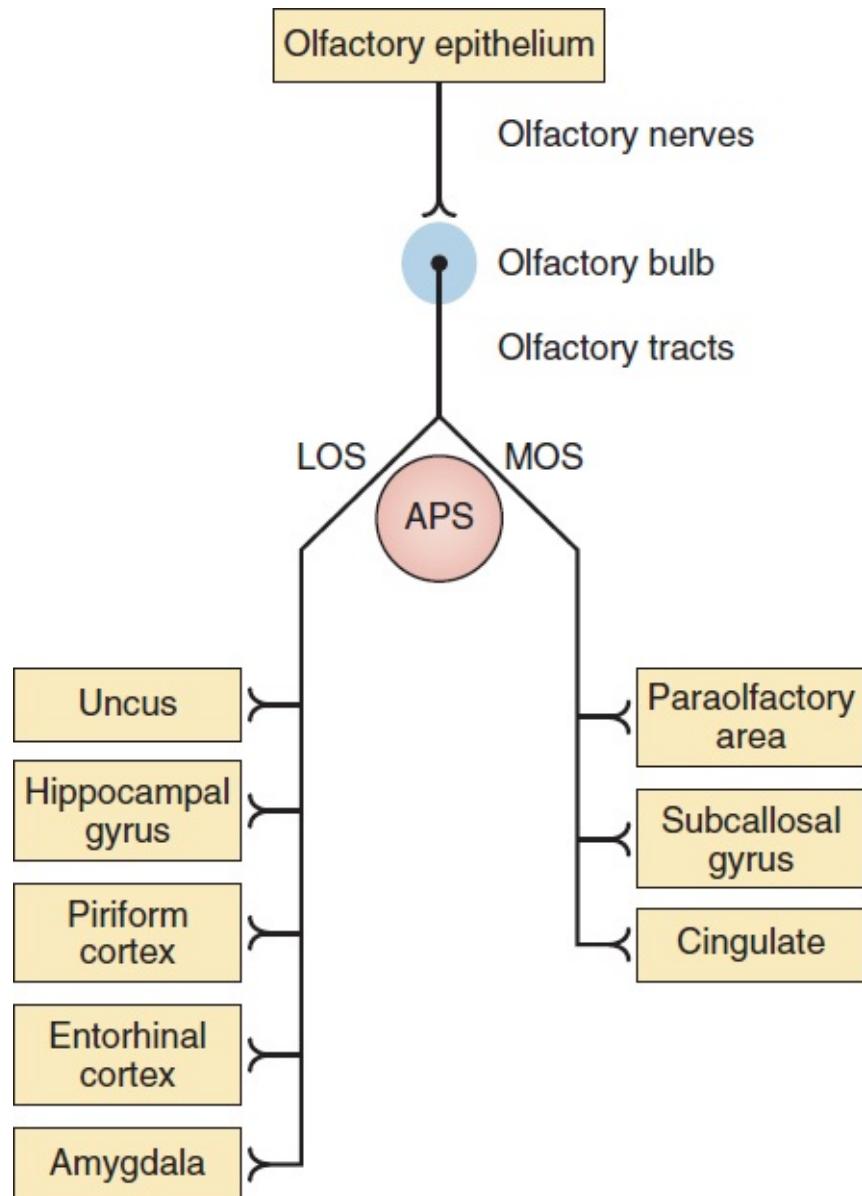


FIGURE 12.3 The olfactory pathways. APS, anterior perforated substance; LOS, lateral olfactory stria; MOS, Medial olfactory stria.

The perception of odor is more important than accurate identification. Perceiving the presence of an odor indicates continuity of the olfactory pathways; identification of the odor indicates intact cortical function as well. Because there is bilateral innervation, a lesion central to the decussation of the olfactory pathways never causes loss of smell, and a lesion of the olfactory cortex does not produce anosmia. The appreciation of the presence of a smell, even without recognition, excludes anosmia.

DISORDERS OF OLFACTORY FUNCTION

Some definitions regarding disorders of smell are reviewed in [Table 12.2](#). Loss of smell may occur in a variety of conditions ([Table 12.1](#)). Common causes of impaired smell are URI, trauma, nasal and sinus disease, and normal aging. Persistent olfactory loss following a URI is the most common etiology, accounting for 15% to 25% of cases.

TABLE 12.1

Some Causes of Persistent Loss of Smell

Olfactory groove meningioma	Smoking
Frontal lobe tumor, especially glioma	Chronic rhinitis
Sellar/parasellar tumor	Deviated nasal septum
Neuro-olfactory tumor (esthesioneuroblastoma)	Nasal polyps
Korsakoff's syndrome	Intranasal tumors (e.g., epidermoid carcinoma)
Vitamin deficiency (B ₆ , B ₁₂ , A)	Postviral
Zinc or copper deficiency	General anesthesia
Craniocerebral trauma, including surgery	Dental trauma
Alzheimer's disease	Chemical burns of the olfactory epithelium
Parkinson's disease	Normal aging
Multiple sclerosis	Pregnancy
Congenital anosmia	Meningitis
Arhinencephaly	Chemotherapeutic agents
Olfactory dysgenesis	Cadmium toxicity
Kallmann's syndrome (hereditary hypogonadism with anosmia)	Antihistamines
Familial dysautonomia	Propylthiouracil
Refsum's syndrome	Antibiotics
Psychiatric conditions (depression, conversion disorder, schizophrenia)	Levodopa
Chronic sinus disease	Cocaine
	Amphetamines
	Radiation therapy

**TABLE
12.2****Terms and Definitions Related to Olfactory Abnormalities**

Anosmia	No sense of smell
Hyposmia	A decrease in the sense of smell
Hyperosmia	An overly acute sense of smell
Dysosmia	Impairment or defect in the sense of smell
Parosmia	Perversion or distortion of smell
Phantosmia	Perception of an odor that is not real
Presbyosmia	Decrease in the sense of smell because of aging
Cacosmia	Inappropriately disagreeable odors
Coprosmia	Cacosmia with a fecal scent
Olfactory agnosia	Inability to identify or interpret detected odors

Age is the strongest correlate of olfactory decline, and decreased smell function occurs in the otherwise healthy elderly. Such decline often goes noticed and unreported. In those under the age of 65, about 2% of the population has impaired olfaction; the prevalence rises to about 50% between 65 and 80 and to nearly 75% in those over 80. This impaired olfaction may be related to ossification of the foramina in the cribriform plate, early neurodegenerative disease (see below), and degradation of receptor function related to repeated viral infections and other insults over the span of time.

Chronic intranasal cocaine use may cause anosmia. Toxins such as cadmium, chromium, or toluene may cause anosmia, usually accompanied by other neurologic abnormalities. Exposure, especially when chronic, to herbicides, pesticides, and solvents may lead to impaired smell. Disturbances of taste and smell may result from deficiency of vitamin B₁₂, B₆, or A and from the effects of some drugs. Decreased sense of smell has been often attributed to abnormalities in zinc metabolism.

Craniocerebral trauma may cause damage to the olfactory nerves at the

cribriform plate because of coup or contrecoup forces. The incidence of trauma-related olfactory dysfunction in the general population is 4% to 15%. The likelihood of smell impairment after head trauma is directly related to the severity. The incidence of anosmia may be as high as 80% in patients with cerebrospinal fluid (CSF) rhinorrhea. Head trauma accounted for about 20% of all chemosensory disorders in one referral center.

Neurologic causes of impaired smell are rare but important. Lesions involving the orbital surface of the brain may cause unilateral anosmia. Meningiomas of the sphenoidal ridge or olfactory groove and gliomas of the frontal lobe may damage the olfactory bulbs or tracts. A typical clinical picture with sphenoidal ridge meningioma consists of unilateral optic atrophy or papilledema and exophthalmos, and ipsilateral anosmia. In meningiomas of the olfactory groove or cribriform plate area, unilateral anosmia occurs early, progressing to bilateral anosmia, often accompanied by optic neuropathy. Anosmia may also occur with other frontal lobe tumors, with parasellar and pituitary lesions and with other mass lesions, such as giant anterior cerebral aneurysm.

The Foster Kennedy syndrome consists of anosmia accompanied by unilateral ipsilateral optic atrophy and contralateral papilledema, classically because of a large tumor involving the orbitofrontal region, such as an olfactory groove meningioma. It was first described by Sir William Gowers; later and more thoroughly by R. Foster Kennedy. The anosmia and optic atrophy are due to direct compression; the contralateral papilledema occurs late when intracranial pressure increases. The atrophic optic disk cannot swell and the unusual picture of optic atrophy in one eye and papilledema in the fellow eye develops. This ophthalmologic picture, without the anosmia, is more often due to anterior ischemic optic neuropathy, arteritic or nonarteritic, involving first one eye, leading to atrophy, then the other, leading to disk edema (the pseudo-Foster Kennedy syndrome). A mass causing asymmetric compression of both optic nerves may cause a similar picture.

Anosmia may accompany some degenerative dementias, especially Alzheimer's disease (AD). Dopamine is one of the neurotransmitters in the olfactory bulbs and Lewy bodies appear in the olfactory bulb early in Parkinson's disease (PD). Olfactory dysfunction has been recognized as a common finding in patients with PD and may help distinguish PD from atypical Parkinson syndromes. Deficits may involve odor detection, identification, and discrimination. In AD and PD, the deficit is present in 85% to 90% of patients even in the early stages of the disease. The sensitivity of olfactory testing in

detecting PD has been estimated as high as 0.91. In fact, Hawkes suggested that impaired smell identification is so common in PD that its absence should prompt reconsideration of the diagnosis. The prevalence of anosmia may be even higher in Lewy body dementia than in AD. Anosmia and visual hallucinations are both strong independent predictors of Lewy body pathology. Impaired smell may occur in other neurologic disorders ([Box 12.1](#)).

BOX 12.1

Other Neurologic Causes of Impaired Smell

Impaired smell has been found to occur in many other neurologic conditions, including Huntington's disease, Korsakoff's syndrome, hydrocephalus, disease of the anterior cerebral artery near its origin, basilar meningitis, frontal lobe abscess, Refsum's disease, Wilson's disease, corticobasal degeneration, spinocerebellar ataxias, narcolepsy, MS, pure autonomic failure, and following temporal lobectomy. Creutzfeldt-Jakob disease may cause anosmia, and prion protein immunoreactivity has been detected by olfactory biopsy to confirm the diagnosis. Kallmann's syndrome is a hereditary disorder that causes hypogonadism, anosmia, and mirror movements associated with developmental anomalies of the corticospinal tracts.

Anosmia sometimes occurs in conversion disorder; taste is usually not affected. In hysterical anosmia, irritating substances, such as ammonia, that stimulate the trigeminal endings are detected no better than subtle aromas.

Disorders of smell other than hyposmia or anosmia occasionally occur. Hyperosmia is usually functional, but it can occur with certain types of substance abuse and in migraine. Parosmia and cacosmia are often due to psychiatric disease but occasionally follow head trauma and may accompany conductive dysosmia. Olfactory hallucinations are most often due to psychosis, but they can result from a lesion of the central olfactory system, usually neoplastic or vascular, or as a manifestation of seizure. So-called uncinate fits are complex partial or temporal lobe seizures preceded by an olfactory or gustatory aura, usually disagreeable, and often accompanied, as the patient loses awareness, by smacking of the lips or chewing movements. Such attacks are typically because of a seizure focus involving medial temporal lobe structures.

There is never objective loss of smell interictally.

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CHAPTER 13

The Optic Nerve

ANATOMY AND PHYSIOLOGY

The optic nerve is a central nervous system (CNS) fiber pathway connecting the retina and the brain. The peripheral receptors, retinal rods and cones, are stimulated by light rays that pass through the cornea, lens, and vitreous. They send impulses to the inner nuclear or bipolar layer; cells there send axons to the ganglion cell layer ([Figure 13.1](#)). There are nearly 1.2 million ganglion cells and their axons that make up the optic nerve. The photoreceptor layer is the deepest layer of the retina; it lies adjacent to the choroid, and light must pass through the more superficial layers to reach it. The rods, more numerous than the cones, are scattered diffusely throughout the retina but are absent in the macula. They respond to low-intensity stimulation and mediate night vision, peripheral vision, and perception of movement. They cannot perceive color. Cones are also present throughout the retina but are concentrated in the macula lutea. The macula consists entirely of cones; it is the point of central fixation and the site of greatest visual acuity and color perception. The macular cones have a 2:1 ratio with ganglion cells, the highest in the eye. The macula (L. “spot”) is a small shallow depression in the retina that lies temporal to the disk ([Figure 13.2](#)). It has a slightly different color than the surrounding retina that can be seen with the ophthalmoscope. The fovea (L. “pit”) centralis is a tiny depression that lies in the center of the macula. The foveola is an even tinier depression in the center of the fovea. It is the point of most acute vision because the overlying retinal layers are pushed aside and light falls directly on the receptors; the foveola is the optical center of the eye. The macula is responsible for the central 15 degrees of vision and the discrimination of colors and fine visual details; its cones are stimulated by light of relatively high intensity and colors. The optic disk, or papilla, is the ophthalmoscopically visible tip of the intraocular portion of the

optic nerve. The nerve head is a 1.5×1.8 mm vertical ellipse, and it appears as a pink to yellowish-white disk. The disk normally inserts into the retina perpendicularly. When the angle is less than 90 degrees, a rim or crescent of choroid or sclera appears on the temporal side and the nasal side may appear elevated (tilted disk). It contains no receptor cells, does not respond to visual stimuli, and is responsible for the physiologic blind spot. The macula, not the disk, forms the center of the retina, and the macular fixation point is the center of the clinical visual field (VF).

The retinal ganglion cell axons form the retinal nerve fiber layer (NFL) as they stream toward the disk to exit through the lamina cribrosa (L. “sieve”), the collagenous support of the optic disk. Loss of axons and other abnormalities involving the NFL can sometimes be appreciated ophthalmoscopically. Using the red-free light of the ophthalmoscope helps visualize the NFL. Myelin in the optic nerve is CNS myelin, formed by oligodendroglia. The axons are unmyelinated in the retina and on the papillary surface but become myelinated at the posterior end of the optic nerve head as they pass through one of 200 to 300 holes in the lamina cribrosa. In about 1% of individuals, myelin extends into the peripapillary retinal NFL (myelinated nerve fibers). Optic nerve axons primarily carry visual impulses, but they also transmit the impulses that mediate accommodation and reflex responses to light and other stimuli. Optic nerve signals are coded spatially because of the location of cells in the retina, and they are also coded temporally because the frequency and pattern of firing relays information.

Macular vision is a critical function, and the projection of the macula to the optic nerve is massive. There are approximately 1.2 million fibers in each optic nerve; about 90% arise from the macula. Because of this preponderance of macular fibers, early signs of optic nerve disease reflect macular function: impaired color vision, impaired acuity, and central scotoma. A dense collection of axons, the papillomacular bundle (PMB), travels from the nasal hemimacula to enter the temporal aspect of the disk ([Figure 13.3](#)). Fibers from the temporal hemiretina and hemimacula arch around the macula and enter the disk as the superior and inferior retinal arcades. Lesions involving these arcades may create arcuate VF defects that have an arching shape. The horizontal temporal raphe demarcates superiorly from inferiorly sweeping axons traveling from the temporal hemimacula to the disk. All of the axons from the macula gather into the PMB as it enters the optic nerve. The fibers of the PMB are very vulnerable to toxins, ischemia, and pressure.

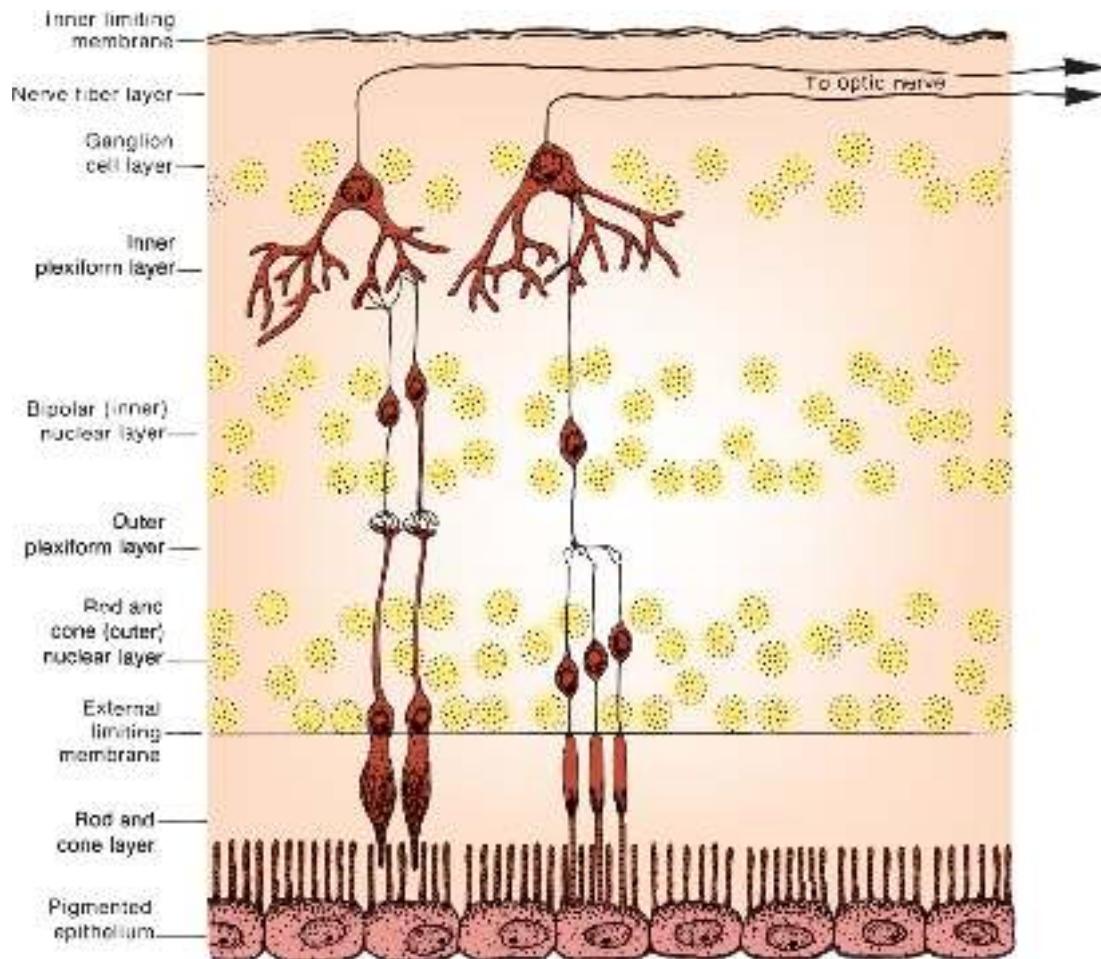


FIGURE 13.1 The layers of the retina and their relationship to the optic nerve. The inner limiting membrane is the most superficial structure; light must pass through the other layers to reach the rod and cone layer. (Modified from Ramon y Cajal S. *Histologie du Système Nerveux de l'Homme et Des Vertébrés*, vol 2. Paris: A. Maloine, 1909, 1911.)

The organization of the visual afferent system is not random. Tight retinotopic correlation prevails throughout the system; each point on the retina has a specific representation in the optic nerve, the chiasm, the tract, the radiations, and the cortex. The PMB, which forms the bulk of optic nerve axons, runs as a discrete bundle inside the optic nerve. The VF maintains its basic shape and structure throughout the system, although its orientation within the visual pathways changes (Figure 13.4). Fibers from the temporal hemiretina are located in the temporal half of the optic nerve, whereas fibers from the nasal hemiretina are located medially. Upper retinal fibers are located superiorly and lower retinal fibers inferiorly in the optic nerve; this relationship is retained except in the optic tract and lateral geniculate body (LGB).

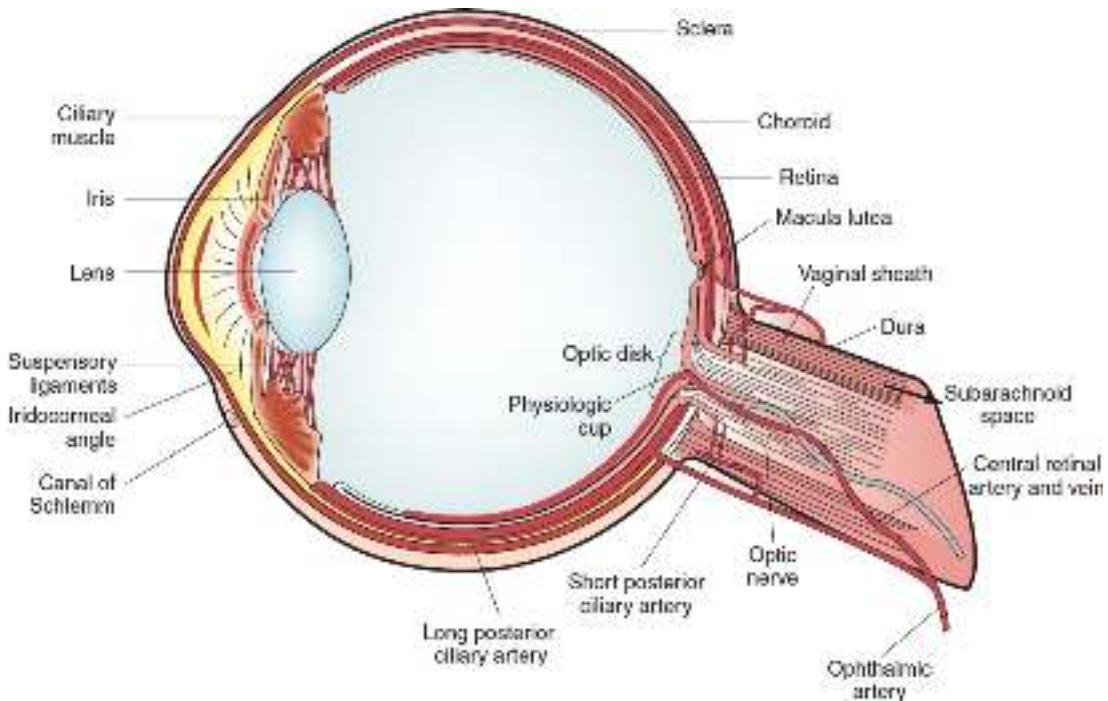


FIGURE 13.2 Structure of the eyeball.

The optic nerve extends from the retina to the optic chiasm; it is approximately 5 cm long. It is conventionally divided into four portions: intraocular (1 mm; the disk), intraorbital (about 25 mm), intracanalicular (about 9 mm), and intracranial (12 to 16 mm). The nerve is organized into 400 to 600 fascicles separated by connective tissue septa. The intraorbital portion is surrounded by fat ([Figure 13.5](#)).

The intracranial dura is continuous with the investments of the optic nerve; at the posterior globe, the dura fuses with Tenon's capsule, and at the optic foramen, it is adherent to the periosteum. The pia and arachnoid also continue from the brain and envelop the optic nerve. They fuse with the sclera where the nerve terminates. The intracranial meninges extend forward along the optic nerves for a variable distance, forming the vaginal sheaths ([Figure 13.2](#)). Through these sheaths, the intracranial subarachnoid space continues along the nerves and may transmit increased intracranial pressure, causing papilledema. Variations in vaginal sheath anatomy may explain the occasional asymmetry of papilledema. Decompression of the optic nerves by opening the sheaths is sometimes done to treat papilledema that threatens vision. The intervaginal space lies between the dura and the pia, divided by the arachnoid into a small subdural and a larger subarachnoid space. The ophthalmic artery, the ciliary ganglion and nerves, and the nerves to the extraocular muscles lie close to the

optic nerve in the orbital apex. The intraorbital optic nerve is sinuous, with about 8 mm of redundant length to accommodate eye movement. This excess of length allows about 9 mm of proptosis before the nerve begins to tether.

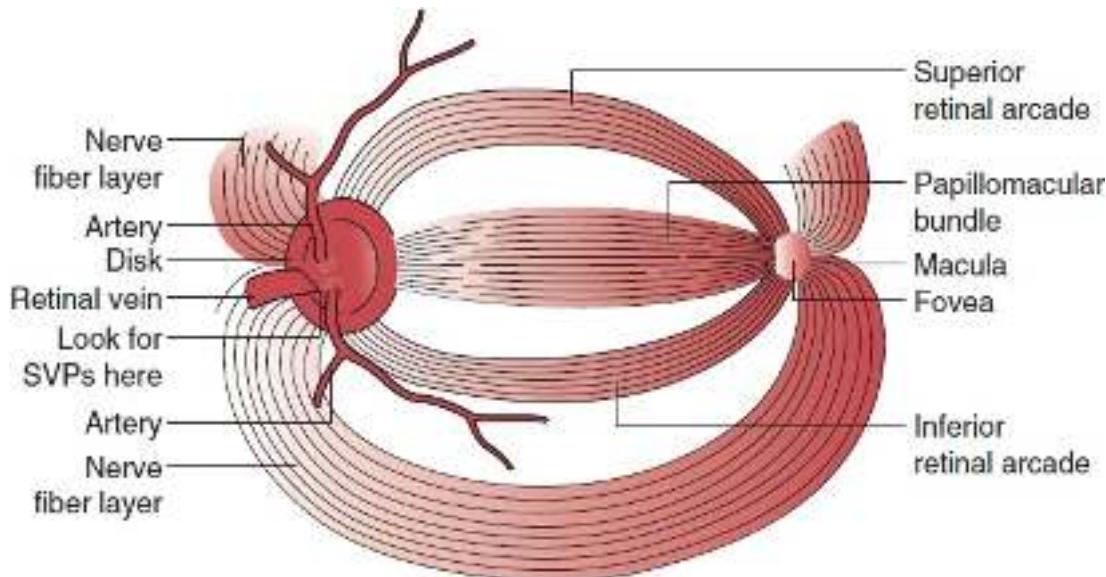


FIGURE 13.3 The optic disk and associated structures. Axons destined to form the bulk of the fibers in the optic nerve arise from the macula, those from the nasal side form the papillomacular bundle, and those from the temporal hemimacula enter the disk as superior and inferior arcades. Spontaneous venous pulsations are best seen by looking at the tip of the column of one of the large veins on the disk surface.

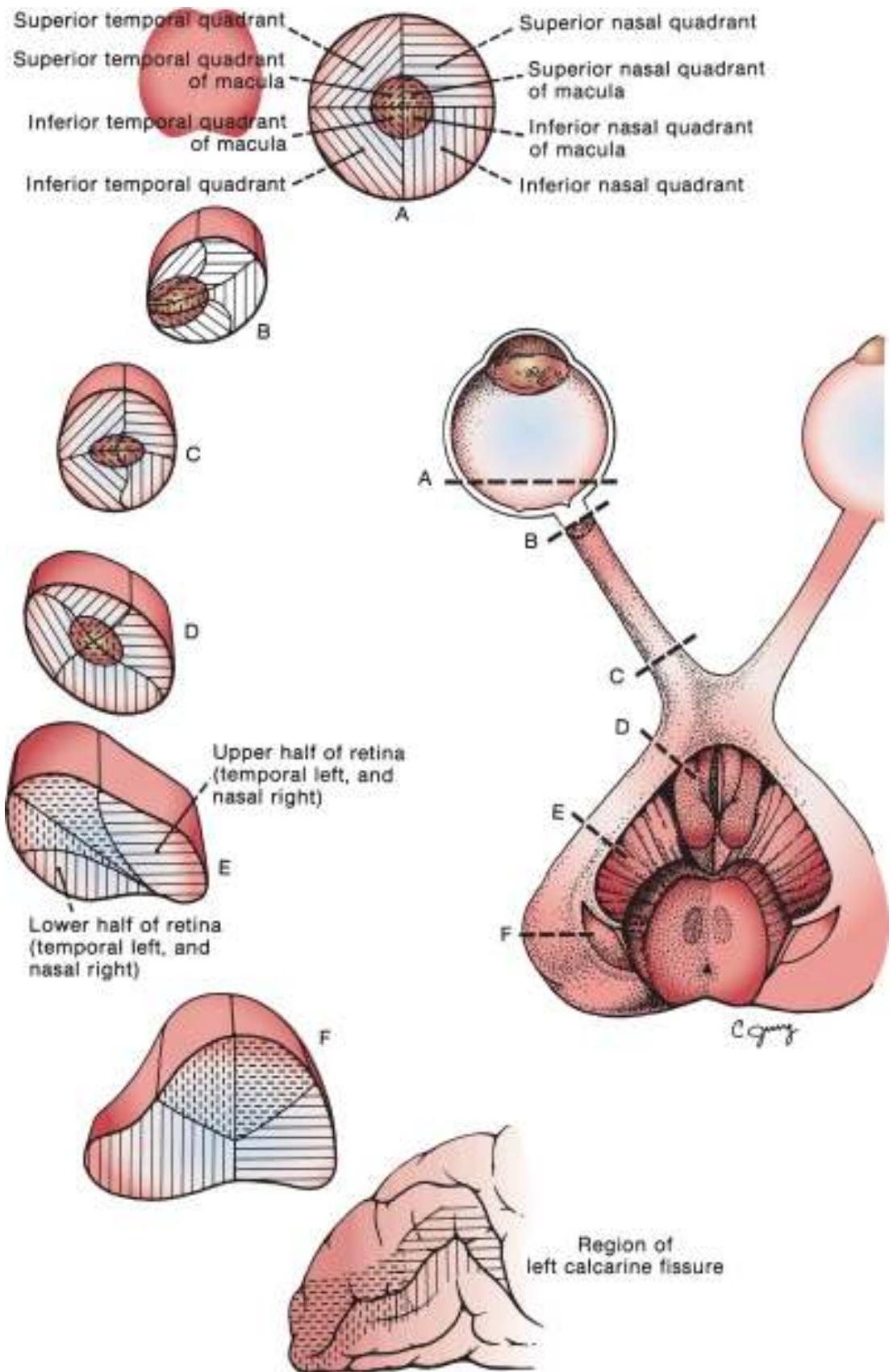


FIGURE 13.4 The grouping of visual fibers from the retinal quadrants and macular area in the optic nerve, optic tract, lateral geniculate body (LGB), and occipital cortex.

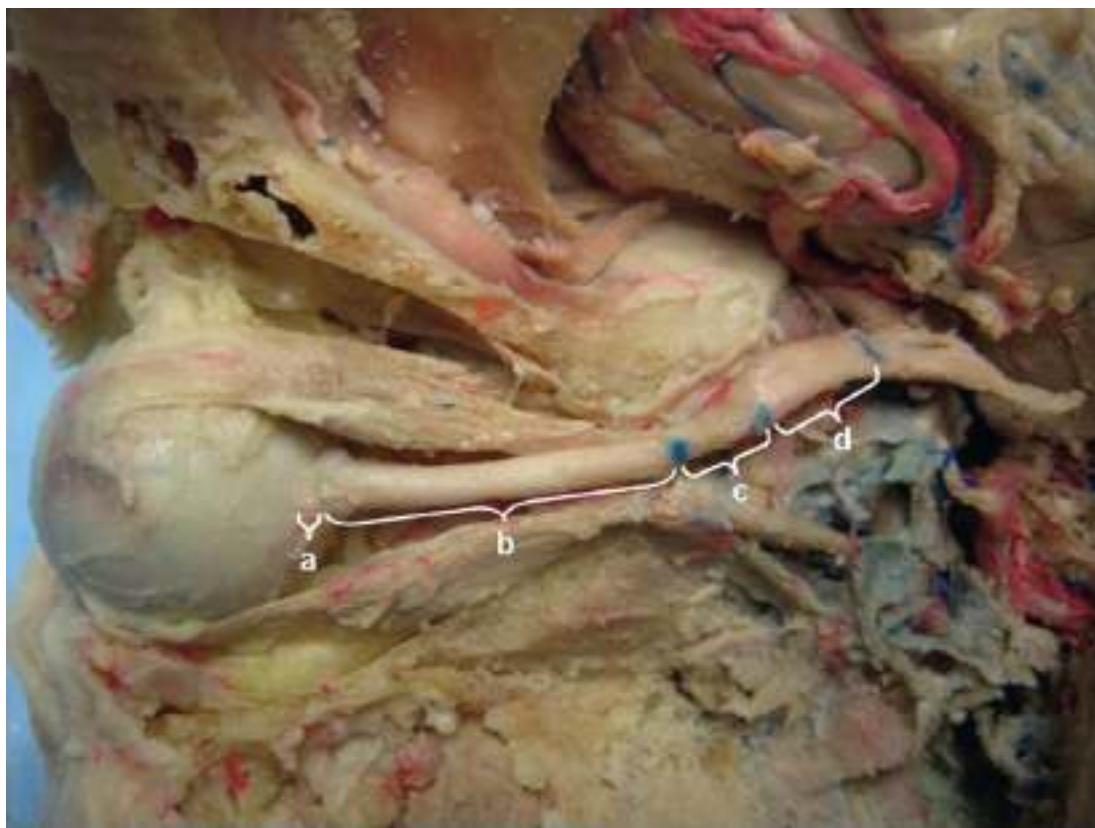


FIGURE 13.5 Optic nerve exposed from above with fat and the roof and lateral wall removed. The intraocular segment (a) is within the globe. The intraorbital segment (b) runs through the orbit to the entrance of the optic canal depicted by the left-most blue dot. The short intracanalicular segment (c) courses between the two blue dots. The intracranial segment (d) continues to its junction with the optic chiasm (blue bar). (Courtesy Dr. John B. Selhorst.)

In the peripheral portion of the nerve, near the eye, the PMB is positioned laterally and slightly inferiorly; this separates the temporal fibers into dorsal and ventral quadrants. These in turn crowd and somewhat displace the nasal quadrants (Figure 13.4). As the nerve approaches the chiasm, the PMB moves toward its center.

The intracanalicular portion of the optic nerve begins as it traverses the optic foramen at the orbital apex. The orbital opening of the canal is a vertical ellipse; the intracranial end is a horizontal ellipse. The intracanalicular portion is fixed tightly inside the optic canal with little room to move; intracanalicular lesions can compress the optic nerve while they are still small and difficult to visualize on imaging studies (the “impossible meningioma”). The ophthalmic artery and

some filaments of the sympathetic carotid plexus accompany the nerve through the canal.

After traversing the orbit and optic canal, the two optic nerves exit from the optic canals and rise at an angle of about 45 degrees to unite at the optic chiasm, so named because of its resemblance to the Greek letter chi (χ) (Figure 13.6). The orbital surface of the frontal lobes lies just above the intracranial optic nerves. The chiasm typically lies about 10 mm above the pituitary gland, separated by the suprasellar cistern. Fibers from the temporal retina continue directly back to enter the ipsilateral optic tract. Fibers from the nasal retina decussate to enter the opposite optic tract.

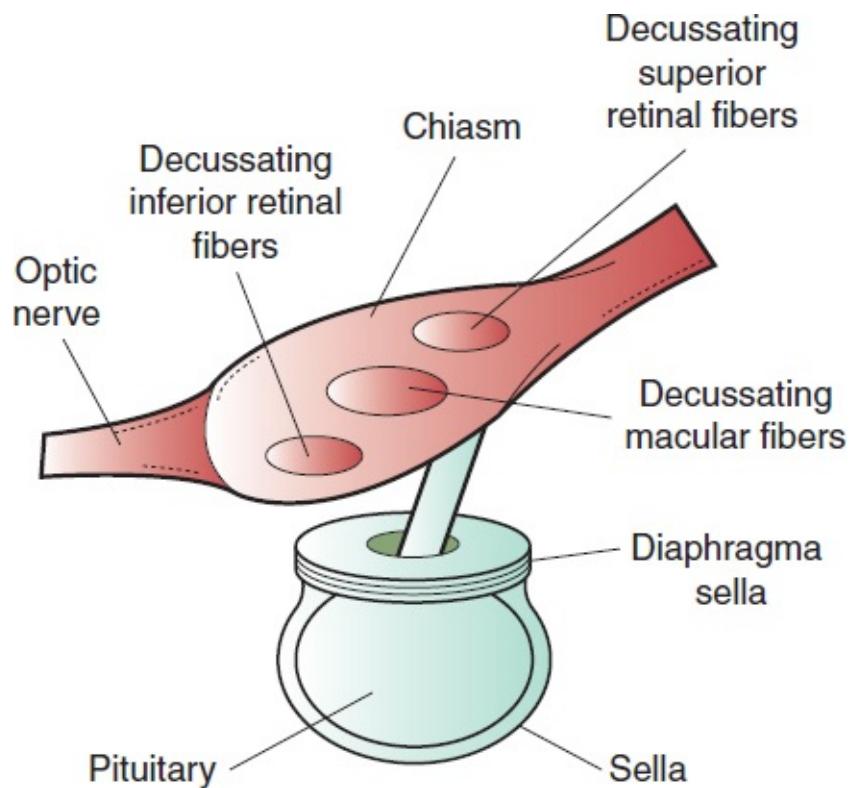


FIGURE 13.6 The macular fibers decussate as a separate compact bundle, inferior retinal (superior visual field [VF]) fibers cross inferiorly, and superior retinal (inferior VF) fibers cross superiorly. Masses impinging from below (e.g., pituitary adenoma) tend to cause early defects in the superior temporal fields; masses impinging from above (e.g., craniopharyngioma) tend to cause early defects in the inferior temporal fields.

In 80% of the population, the chiasm rests directly above the sella. In 10%, the chiasm sits forward over the tuberculum sellae with short optic nerves and long optic tracts (prefixed); in the other 10%, the chiasm sits posteriorly over the

dorsum sellae with long optic nerves and short optic tracts (postfixed) ([Figure 13.7](#)). The position of the chiasm in relation to the sella and the neoplasia-prone pituitary gland influences the clinical presentation of masses in the region.

The basic scheme of the chiasm with temporal hemiretinal fibers continuing ipsilaterally and nasal hemiretinal fibers decussating is straightforward ([Figure 13.8](#)). But there are intricacies in the chiasmal crossing. In the process of decussating, fibers from the inferior nasal quadrant loop forward into the opposite optic nerve for a short distance before turning back again, forming Wilbrand's knee ([Figure 13.9](#), see junctional scotoma in "Scotomas" section). In addition, some of the upper nasal fibers loop back briefly into the ipsilateral optic tract before decussation. In the chiasm, the fibers from the upper retinal quadrants lie superior and those from the lower quadrants inferior ([Figure 13.6](#)). Inferior nasal fibers decussate anteriorly and inferiorly in the chiasm, whereas superior nasal fibers cross posteriorly and superiorly, accounting for the difference in the pattern of evolution of the field defect in infrachiasmatic versus suprachiasmatic lesions ([Figure 13.9](#)). Macular fibers more or less decussate as a group, forming a miniature chiasm within the chiasm, primarily in the posterior superior portion.

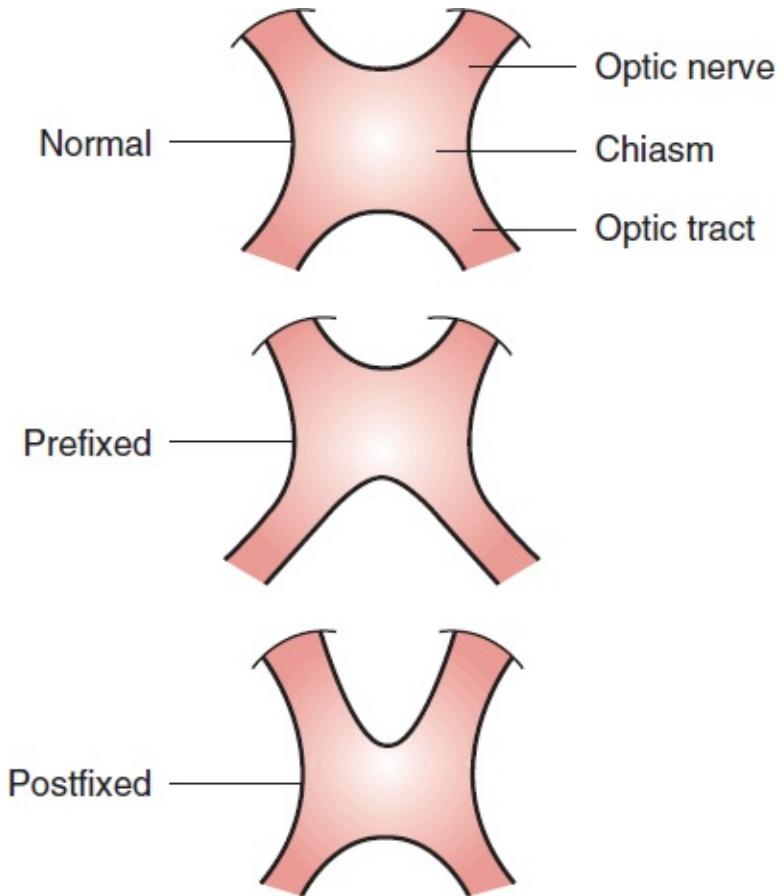


FIGURE 13.7 The normal position of the chiasm is shown in the top drawing. When the chiasm is prefixed, the optic nerves are short, the chiasm sits forward over the sella, and the optic tracts are long. When the chiasm is postfixed, the optic nerves are long, the chiasm sits posteriorly over the sella, and the optic tracts are short.

The cavernous sinuses and carotid siphons lie just lateral to the chiasm on either side. The anterior cerebral and anterior communicating arteries are in front and above, and the third ventricle and hypothalamus are behind and above. The sella turcica and sphenoid sinus lie below. The circle of Willis lies above, sending numerous small perforators to supply the chiasm. The ophthalmic artery runs alongside the optic nerve within the same dural sheath through the canal and orbit. About 8 to 12 mm posterior to the globe, the artery enters the nerve and runs along its center to the optic disk, where it becomes the central retinal artery, which pierces the nerve and runs forward onto the disk. The central retinal artery divides at the disk head into superior and inferior branches, which supply the retina. Other terminal branches of the ophthalmic, the short posterior ciliary arteries and choroidal vessels, form an arterial network, the circle of Zinn-Haller, which supplies the disk; the central retinal artery makes only a

minimal contribution to the vascular supply of the optic disk.

Posterior to the optic chiasm, the uncrossed fibers from the ipsilateral temporal hemiretina and the crossed fibers from the contralateral nasal hemiretina form the optic tract. About 55% of the axons of the optic tract arise from the contralateral nasal retina and 45% from the ipsilateral temporal retina, which roughly corresponds to the ratio of the area of the temporal field to the nasal field. The tracts contain approximately 80% visual afferents and 20% pupillary afferents. The tracts extend from the chiasm to the LGB, where the majority of fibers terminate. Retinotopic organization is maintained in the optic tract, but the orientation changes. There is a gradual inward rotation, so fibers from the upper retina assume a medial position, whereas those from the inferior retina lie lateral. Fibers of the PMB gradually assume a dorsal and lateral position, wedged between the upper and lower retinal fibers ([Figure 13.4](#)). The retinotopic organization in optic tracts is not as precise as elsewhere, which may contribute to the incongruity of VF defects that are characteristic of optic tract lesions.

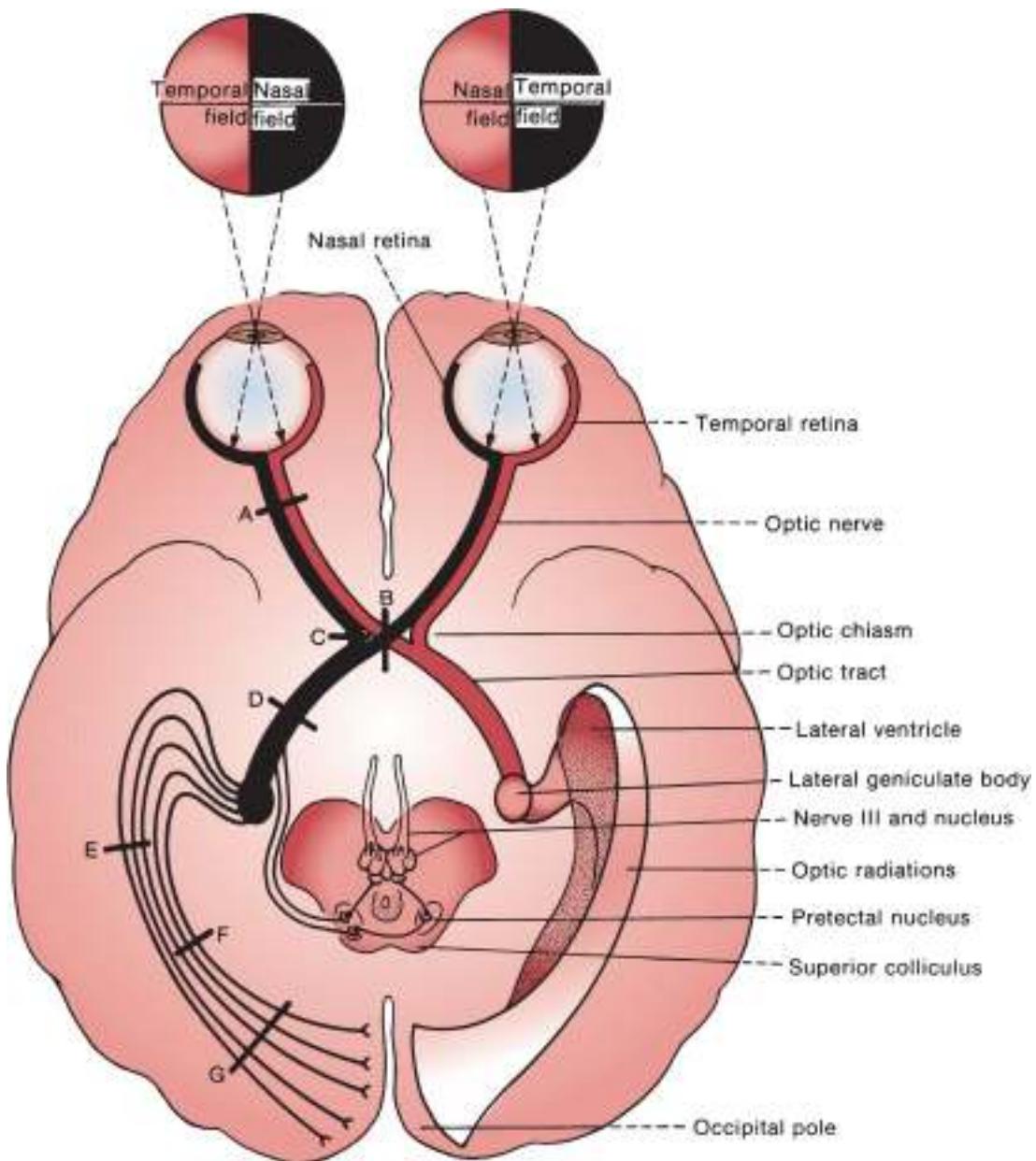


FIGURE 13.8 The course of the visual fibers from the retina to the occipital cortex. A to G show the sites of various lesions that may affect the fields of vision.

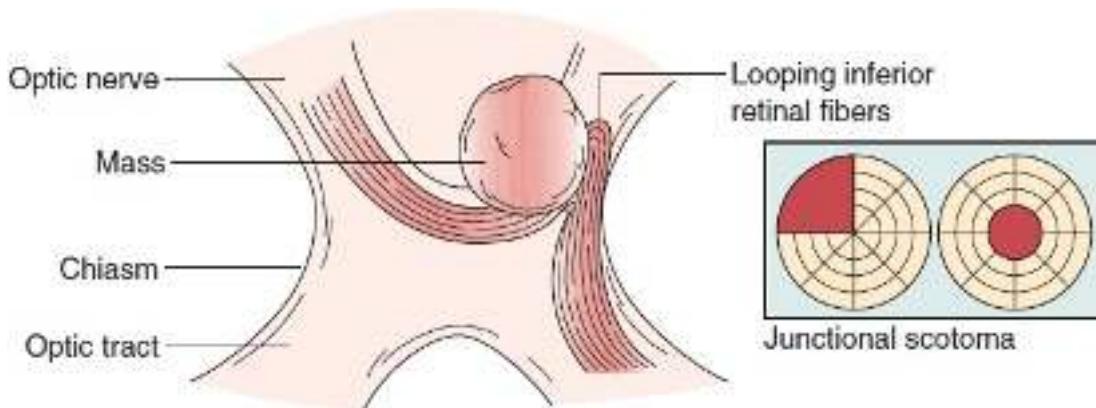


FIGURE 13.9 A mass impinging on the optic nerve at its junction with the chiasm, producing a junctional scotoma.

Afferent fibers from the pupil leave the tract just anterior to the geniculate to enter the pretectal area of the midbrain (Figure 13.10). The visual afferents synapse in the geniculate on second-order neurons, which give rise to the geniculocalcarine pathway (optic radiations).

There are six neuronal layers in the LGB, separated by myelinated nerve fibers. Uncrossed fibers from the ipsilateral temporal hemiretina synapse in layers 2, 3, and 5; those from the contralateral nasal hemiretina synapse in layers 1, 4, and 6. Upper retinal fibers remain medial and lower ones lateral (Figure 13.4). Macular fibers occupy an intermediate position in the dorsal, middle, and somewhat caudal portion. The LGB has large magnocellular and small parvocellular neurons. Some of the visual fibers pass over or through the LGB to terminate in the pulvinar of the thalamus, but the significance of this connection has yet to be determined for vision or visual reflexes. The magnocellular projections seem to process movement and depth, whereas the parvocellular projections mediate shape, pattern, and color.

The axons of LGB neurons pass posteriorly to form the geniculocalcarine tract, or optic radiations, and terminate in the calcarine cortex of the occipital lobe (Figure 13.11). Leaving the LGB, the optic radiations pass through the retro-lenticular portion of the internal capsule and then fan out. Retinotopically, upper retinal fibers resume an upper, and lower retinal fibers a lower, position in the radiations, with fibers subserving central vision intermediate between the two other bundles. Inferior retinal fibers arch anteriorly into the temporal lobe, sweeping forward and laterally above the inferior horn of the ventricle to run within 5 to 7 cm of the temporal tip, then laterally, down, and backward around the inferior horn. This creates a great arching shape referred to as Meyer's loop

(loop of Meyer and Archambault). The inferior retinal fibers then course through the temporal and occipital lobes. Peripheral retinal fibers loop further forward than macular fibers. Fibers from the superior retina run directly back in the deep parietal lobe in the external sagittal stratum, lateral to the posterior horn of the lateral ventricle. The inferior, or ventral, radiations may mediate recognition of visual objects, whereas the dorsal pathway processes spatial information and recognition of movement.

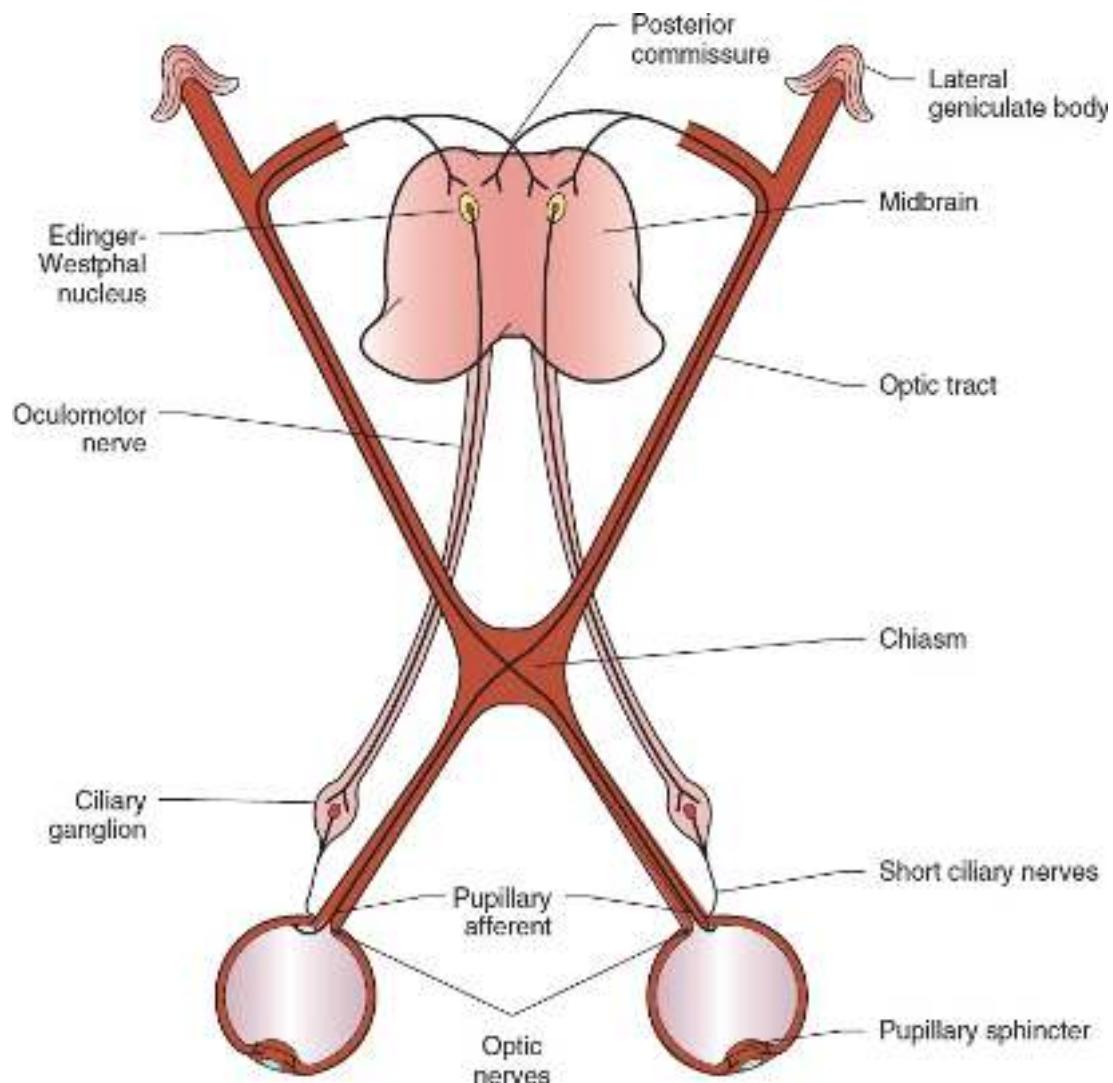


FIGURE 13.10 Pupillary afferent fibers from the right eye are crossed and uncrossed and run in both optic tracts. They leave the tract before the LGB and send projections to the pretectal region bilaterally. The Edinger-Westphal nucleus sends pupillomotor fibers through the third cranial nerve to the ciliary ganglion, and postganglionic fibers innervate the pupil sphincter. Because of the bilaterality of the pathways, a light stimulus in the right eye causes pupillary constriction in both eyes.

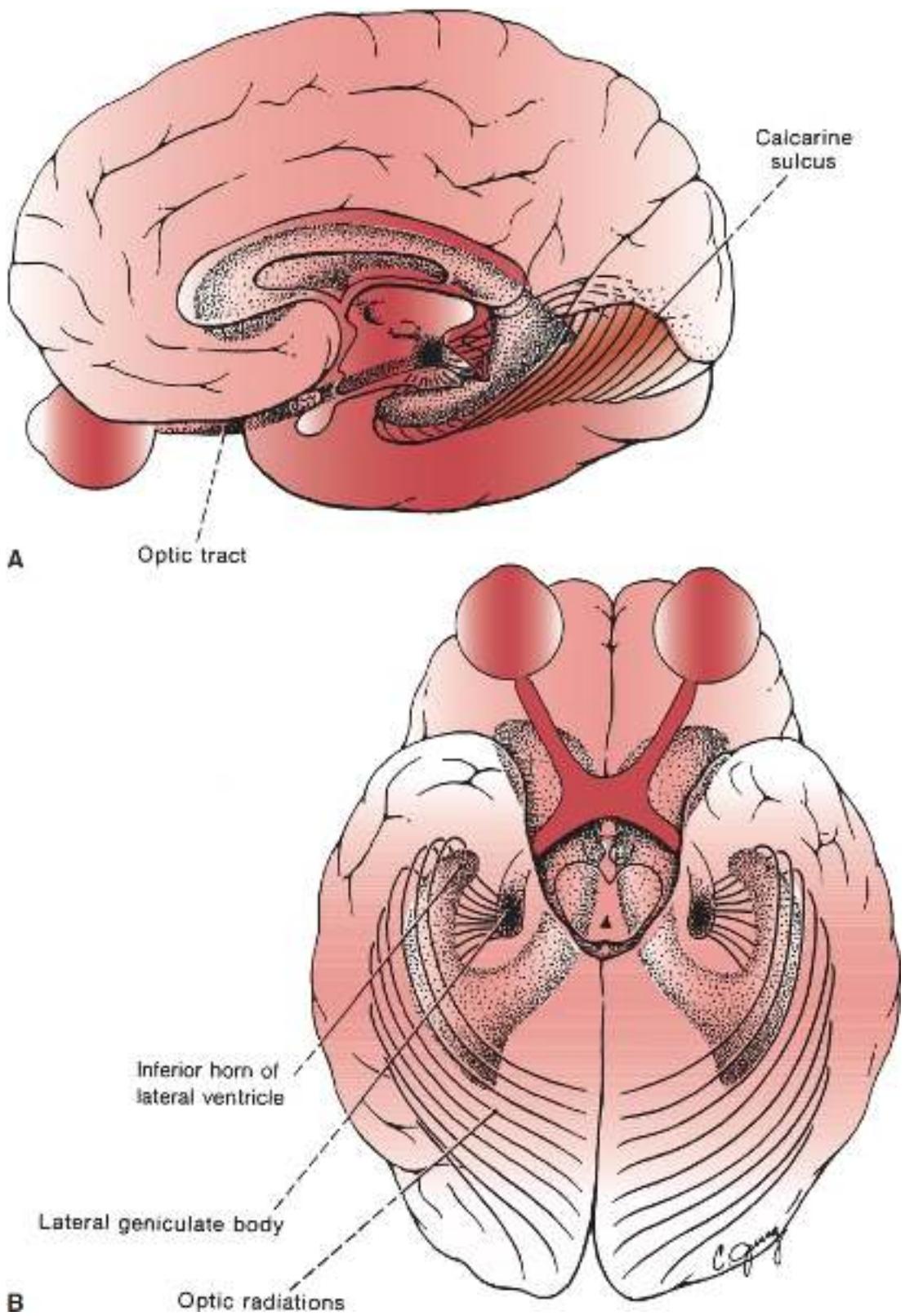


FIGURE 13.11 The course of the geniculocalcarine fibers. **A.** Medial view. **B.** Inferior view.

Approaching the occipital lobe, fibers from the upper and lower retina again converge. The primary visual cortex (calcarine area or striate cortex) lies in Brodmann's area 17 on the medial surface of the occipital lobe. Lower retinal fibers terminate on the lower lip of the calcarine fissure (lingual gyrus) and upper retinal fibers on the upper lip of the calcarine fissure (cuneus). Macular fibers are first lateral and then form the intermediate portion of the geniculocalcarine pathway, continuing to the posterior pole of the occipital lobe. The divergence and convergence of fibers throughout the visual pathway influences the shape and congruity of VF defects, which have localizing value.

Fibers that carry visual impulses from the peripheral portions of the retina terminate on the anterior third or half of the visual cortex of the occipital lobe in concentric zones; macular fibers terminate in the posterior portion ([Figure 13.12](#)). The most peripheral parts of the retina are represented most anteriorly in the calcarine cortex; the closer a retinal point lies to the macula, the more posterior its calcarine representation. This culminates in the representation of the macula at the occipital pole. The nasal hemiretina representation extends farther forward than the temporal (the temporal field is more extensive than the nasal), creating a portion of retina for which no homology exists in the opposite eye. This unpaired nasal retina is represented in the most anterior portion of the calcarine cortex, near the area of the tentorium, just outside the binocular VF, which creates an isolated temporal crescent in each VF. Sparing or selective involvement of this monocular temporal crescent has localizing value. The macula has a wider cortical distribution in the striate cortex than in the peripheral retina. It is represented in a wedge-shaped area with its apex anterior. The central 10 to 15 degrees of the VF occupy 50% to 60% of the visual cortex.

To summarize the retinotopic organization of the visual system, upper retinal fibers remain upper and lower fibers lower throughout except in the tract and LGB where upper becomes medial and lower becomes lateral. The corresponding VF abnormalities can be deduced.

The striate cortex is the sensory visual cortex. It receives afferents via the myelinated stripe or line of Gennari, because of the abundant myelinated fibers in the fourth layer of the calcarine cortex, which gives this area its distinctive appearance and name. Its physiology is complex. Neurons are arranged in parallel, vertically oriented, ocular dominance columns and complex units called hypercolumns. One hypercolumn can process information from a focal region of the VF. There may be interhemispheric connections through the corpus callosum to synchronize information generated from the two sides. Surrounding the striate

cortex are the visual association areas. Area 18, the parastriate or parareceptive cortex, receives and interprets impulses from area 17. Area 19, the peristriate or perireceptive cortex, has connections with areas 17 and 18 and with other portions of the cortex. It functions in more complex visual recognition, perception, revisualization, visual association, size and shape discrimination, color vision, and spatial orientation.

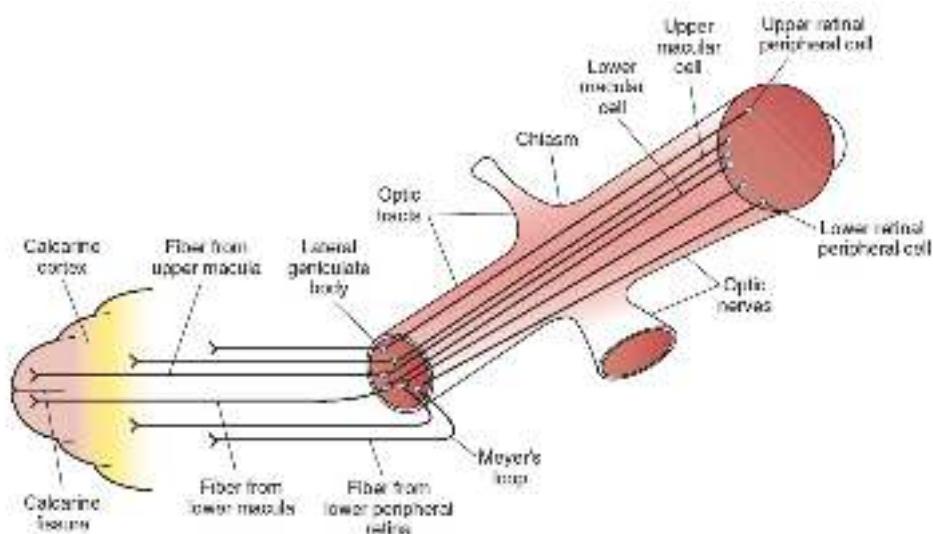


FIGURE 13.12 Fibers from the macula synapse in the geniculate and then project to the occipital tip. The most peripherally located retinal ganglion cells synapse in the geniculate and then loop far forward in Meyer's loop before terminating in the most anterior portion of the calcarine cortex. The most anterior and medial portions of the cortex receive projections from the monocular temporal crescent, which represents the nasal portion of the retina that extends far forward and is the most peripheral part of the retina.

The anterior choroidal artery from the internal carotid and thalamoperforators from the posterior cerebral supply the optic tract. The geniculate is perfused by the anterior choroidal and thalamogeniculate branches from the posterior cerebral. Perhaps because of this redundant blood supply, vascular disease only rarely affects the optic tract or lateral geniculate. Meyer's loop receives blood supply primarily from the inferior division of the middle cerebral artery, whereas the optic radiations in the parietal lobe are perfused via the superior division. The occipital lobe is supplied primarily by the posterior cerebral artery. Collaterals from the anterior and middle cerebral may provide additional perfusion to the macular areas at the occipital tip. The parietal smooth pursuit optomotor center and its projections are supplied by the middle cerebral.

Optic Reflexes

Fibers subserving the pupillary light reflex and other optic reflexes pass through the pregeniculate pathways in the same fashion as fibers subserving vision. They leave the optic tract just before it reaches the LGB. Pupillary light reflex fibers travel to the pretectal nuclei, just rostral to the superior colliculus; from the pretectum, axons are sent to synapse on the Edinger-Westphal nuclei. Some light reflex fibers project to the ipsilateral pretectal nucleus to mediate the direct light reflex; others decussate through the posterior commissure to mediate the consensual light reflex (Figures 13.8 and 13.10). Parasympathetic fibers from the Edinger-Westphal nuclei are carried by the oculomotor nerve to the pupillary sphincter.

Fibers controlling somatic visual reflexes, such as turning of the head and eyes toward a visual stimulus, synapse in the superior colliculus. From there tectospinal tract fibers descend to more caudal brainstem nuclei to execute the reflex response. The internal corticotectal tract is made up of fibers that run from areas 18 and 19 of the occipital cortex to the superior colliculus to subserve reflex reactions through connections with the eye muscle nuclei and other structures. Fibers that carry impulses having to do with visual-palpebral reflexes (such as blinking in response to light) go to the facial nuclei.

CLINICAL EXAMINATION AND DISORDERS OF FUNCTION

Optic nerve function is tested by examining the various modalities of vision: the visual acuity, the VFs, and special components of vision, such as color vision and day and night vision. The optic nerve is the one cranial nerve that can be visualized directly, and no neurologic, or indeed general, physical examination is complete without an ophthalmoscopic inspection of the optic disk and the retina.

Before performing the optic nerve examination, look for local ocular abnormalities such as conjunctival irritation, corneal scarring or opacity, foreign bodies, photophobia, or an ocular prosthesis. The presence of a unilateral arcus senilis with ipsilateral carotid disease has been reported. In Wilson's disease (hepatolenticular degeneration), a yellowish-orange brown coloration 1 to 3 mm wide (Kayser-Fleischer ring) may be seen around the rim of the cornea, more easily in light-eyed individuals (Chapter 30). It is due to copper deposition in the

posterior stroma and in Descemet's membrane and best seen with a slit lamp. Cataracts may be present in patients with myotonic dystrophy, certain rare hereditary conditions with disturbed lipid or amino acid metabolism, and in many other conditions. Lisch nodules are pigmented iris hamartomas that are highly suggestive of NF1 ([Figure 13.13](#)). Proptosis, chemosis, and tortuous ("corkscrew") blood vessels in the conjunctiva occur with carotid cavernous fistula ([Chapter 21](#)). Other causes of unilateral proptosis include thyroid eye disease, meningocele, encephalocele, and histiocytosis X. Other potentially relevant findings might include jaundice, evidence of iritis, dysmorphic changes (e.g., epicanthal folds), xanthelasma due to hypercholesterolemia, corneal clouding from mucopolysaccharidosis, keratoconjunctivitis sicca due to Sjögren's syndrome or other collagen vascular diseases, ocular complications of upper facial paralysis, depositions of amyloid in the conjunctiva, pigmented pingueculae due to Gaucher's disease, tortuous conjunctival vessels in ataxia telangiectasia, scleritis in Wegener's granulomatosis, lens dislocation in Marfan's syndrome, homocystinuria or Ehlers-Danlos syndrome, and nonsyphilitic interstitial keratitis in Cogan's syndrome. Hypertelorism can be seen in a number of neurologic conditions. Blue sclera can occur in Ehlers-Danlos syndrome, osteogenesis imperfecta, and occasionally in Marfan's syndrome. Basal skull fractures often cause bilateral periorbital ecchymosis (raccoon eyes).

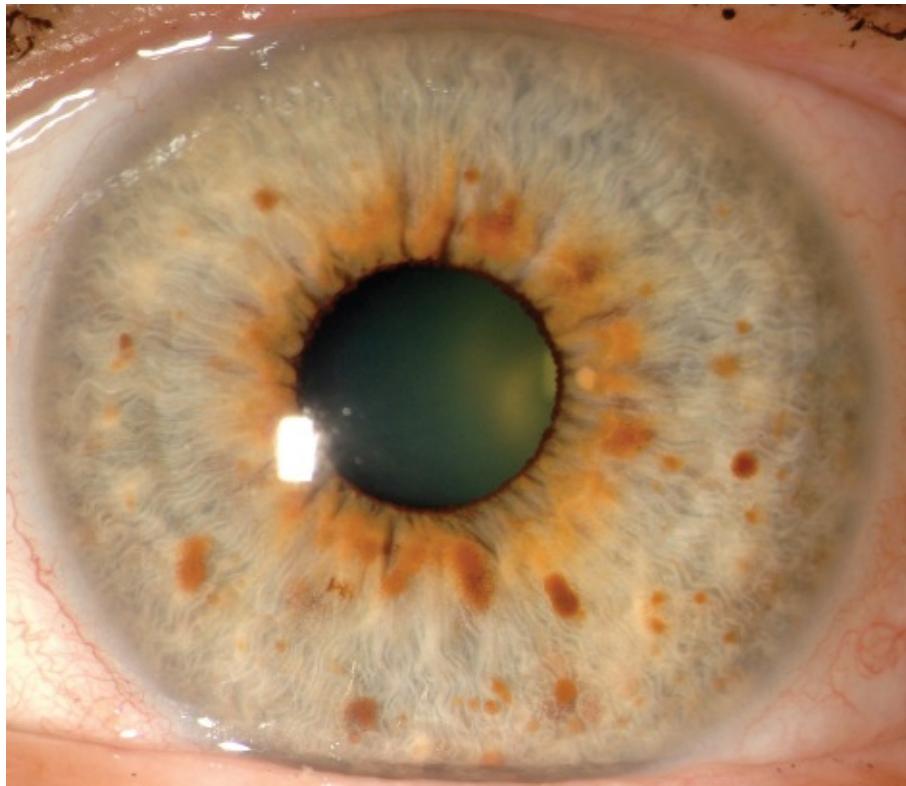


FIGURE 13.13 Lisch nodules are elevated, pale brown lesions that vary in appearance depending on the underlying color of the iris. The prevalence in patients with NF1 increases from birth to about 50% of 5-year-olds, 75% of 15-year-olds, and 95% to 100% of adults over the age of 30. (Reprinted from Gerstenblith AT, Rabinowitz MP. *The Wills Eye Manual: Office and Emergency Room Diagnosis and Treatment of Eye Disease*. 6th ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins, 2012, with permission.)

Visual Acuity

Ideally, the eyes are examined individually. When testing acuity and color vision, it is important to occlude the eye not being tested. Visual acuity is a measure of the eye's ability to resolve details; it depends on several functions. The intensity threshold reflects the sensitivity of the retina to light; the minimum visibility is the smallest area that can be perceived, and the minimum separability is the ability to recognize the separateness of two close points or lines. Visual acuity charts, such as the Snellen chart for distance and the near card for near, consist of letters, numbers, or figures that get progressively smaller and can be read at distances from 10 to 200 ft by normal individuals (Figure 13.14). Snellen charts have certain limitations, the most critical is the nonlinear variation in the sizes of the letters from line to line, and the Early Treatment in

Diabetic Retinopathy Study (ETDRS) charts have become increasingly popular.

The difference between near and distance vision and between vision with and without correction are points of primarily ophthalmologic interest. For neurologic purposes, only the patient's best-corrected visual acuity is pertinent. Near acuity is not as accurate as distant, especially if the card is not held at the required 14 in. Refractive errors, media opacities, and similar optometric problems are irrelevant. Acuity is always measured using the patient's accustomed correction. Ophthalmologists and neuro-ophthalmologists often employ more detailed methods (e.g., full refraction) to clarify the refractive component of a patient's visual impairment. In infants and children, acuity can be estimated by blink to threat or bright light, following movements, and the pupillary reactions. At the age of 4 months, acuity may be 20/400; it gradually increases, reaching normal levels at about age 5.

TEST CHART--SNELLEN RATING
DIRECT READING

E 200
N Z 160
Y L V 120
U F V P 80
N R T S F 60
O C L G T R 50
U P N E S R H 40
T O R E G H B P 30

F N E G H B S C R 25
T V H P R U C F N G 20
P T N U E H V C B O S 15

THE ABOVE CHARACTERS SUBTEND THE VISUAL ANGLE OF 5°
AT THE DESIGNATED DISTANCE IN FEET IN ACCORDANCE
WITH THE SNELLEN NOTATION OF VISUAL ACUITY

BAUSCH & LOMB OPTICAL COMPANY
ROCHESTER 2, N. Y., U. S. A.

FIGURE 13.14 Snellen test chart.

For distance vision measurement in the United States, a Snellen chart or similar is placed 20 ft from the patient; at that distance, there is relaxation of accommodation, and the light rays are nearly parallel. The eyes are tested separately, and by convention, the right eye is tested first. In countries using the metric system, the distance is usually given as 6 m. The ability to resolve test characters (optotypes) approximately 1-in high at 20 ft is normal (20/20 or 6/6) visual acuity. These characters subtend 5 minutes of visual arc at the eye; the components of the characters (e.g., the crossbar on the A) subtend 1 minute of arc. The acuity is the line where more than half of the characters are accurately read. If the patient can read the 20/30 line and two characters on the 20/25 line, the notation is 20/30 + 2. Two mistakes or two extra letters are allowed per line. By conventional notation, the distance from the test chart, 20 or 6, is the numerator, and the distance at which the smallest type read by the patient should be seen by a person with normal acuity is the denominator. An acuity of 20/40 (6/12) means the individual must move in to 20 ft to read letters a normal person can read at 40 ft. This does not mean the patient's acuity is one-half of normal. In fact, an individual with a distance acuity of 20/40 has only a 16.4% loss of vision.

Because few neurology clinics, offices, or hospital rooms have 20-ft eye lanes, testing is commonly done at a closer distance. Neurologists frequently assess vision with a near card. Though examination of distance vision is preferable, the requisite devices are generally not at hand. There are pocket cards designed for testing at 6 ft, a convenient distance that usually eliminates the need for presbyopic correction. Near vision is tested with a near card, such as the Rosenbaum pocket vision screening card, held at the near point (14 in or 35.5 cm). Jaeger reading cards are still used occasionally ([Box 13.1](#)). Good lighting is essential. A penlight shone directly on the line being read is useful for bedside testing.

BOX 13.1

Jaeger Notation

Jaeger's test types are ordinary printer's types, graded from fine (Jaeger 0) to coarse, also used for near testing. The physical optics of the Jaeger system

are crude. The numbers refer to the boxes in the Austrian print shop from which Jaeger selected the type in 1854. Jaeger 0 corresponds approximately to an acuity of 20/20. As a rough approximation of near vision, the examiner may use different sizes of ordinary print. Newspaper want-ad text is approximately J-0, regular newsprint J-6, and newspaper headlines J-17.

If the patient cannot read the 20/200 line at 20 ft, the distance may be shortened and the fraction adjusted. Ability to read the line at 5 ft is vision of 5/200, equivalent to 20/800. Vision worse than the measurable 20/800 is described as count fingers (CFs), hand motion (HM), light perception (LP), or no light perception (NLP). The average finger is approximately the same size as the 20/200 character, so ability to count fingers at 5 ft is equivalent to an acuity of 20/800.

When a patient has impaired vision, an attempt should be made to exclude refractive error by any available means. If the patient has corrective lenses, they should be worn. In the absence of correction, improvement of vision by looking through a pinhole suggests impairment related to a refractive error. Commercial multi-pinhole devices are available. A substitute can be made by making three or four holes with a pin in a 3×5 card in a circle about the size of a quarter. The multiple pinholes help the patient locate one. The patient should then attempt to read further down the acuity card through the pinhole. The pinhole permits only central light rays to enter the eye. These are less likely to be disrupted by refractive errors such as presbyopia and astigmatism. If a pinhole was used, make some notation, such as 20/20 (ph). If the visual impairment is due to a neurologic process, such as optic neuritis (ON), vision will not improve with a pinhole. Under some circumstances, such as with opacities in the media (e.g., cataract), vision may get worse with pinhole.

Other ocular causes of reduced visual acuity include a macular lesion, media opacity such as cataract or vitreous hemorrhage, and corneal opacities or irregularities. Neurologic processes that affect the optic nerve or chiasm may cause impaired acuity. Retrochiasmal lesions affect visual acuity only if they are bilateral. Suspected functional visual loss because of hysteria or malingering is best evaluated by an ophthalmologist, who has the proper tools to answer the question. Clever and determined patients with functional visual loss present a major challenge. There may be certain clues ([Box 13.2](#)).

The term amblyopia refers to impaired vision because of an organic process

in the absence of a demonstrable lesion. The mechanism is poorly understood. Suppression amblyopia is the visual impairment in one eye because of preferential use of the opposite eye in a patient with congenital strabismus. Suppression amblyopia is also referred to as amblyopia ex anopsia (amblyopia from disuse). Many other varieties of amblyopia have been described, including alcoholic, toxic, traumatic, and uremic amblyopia. Amaurosis means blindness of any type, but in general usage, it means blindness without primary eye disease or loss of vision secondary to disease of the optic nerve or brain.

Color Vision; Day and Night Vision

Color blindness (achromatopsia) is an X-linked condition present in about 3% to 4% of males. The most common hereditary dyschromatopsia is an X-linked red-green defect. Disturbances of color vision may also occur in neurologic conditions. Loss of color vision may precede other visual deficits. Color deficits may be partial or total. Color plates or pseudoisochromatic plates (Ishihara, Hardy-Ritter-Rand [HRR], or similar) formally and quantitatively assess color vision. Pseudoisochromatic plates were originally designed to screen for congenital dyschromatopsias. The HRR plates, which contain blue and purple figures that screen for tritan defects, may be more helpful in detecting acquired dyschromatopsia because of some optic neuropathies. Having the patient identify the colors in a fabric, such as a tie or a dress, can provide a crude estimate of color vision.

Acquired dyschromatopsia may result from macular, retinal, optic nerve, chiasmal, or retrochiasmal lesions. Monocular loss of acuity, deficits in color vision, and an afferent pupillary defect (APD) are highly characteristic of an ipsilateral optic neuropathy. Acquired optic nerve diseases usually cause a red/green color deficiency, but there are several exceptions, such as glaucoma and dominant optic atrophy. Impaired color vision with only mildly reduced acuity is suggestive of optic neuropathy; color deficits associated with more severe acuity loss suggest maculopathy.

Fading or bleaching of colors is a real but uncommon complaint in optic nerve disease. Red perception is usually lost first. Desaturation to red, or red washout, describes a graying down or loss of intensity of red. The bright red cap on a bottle of mydriatic drops is a common test object. The patient compares the brightness or redness in right versus left hemifields, temporal versus nasal hemifields, or central versus peripheral fields. No right/left or temporal/nasal

desaturation to red occurs normally. Red does normally look brighter in the center of the VF than off center; reversal of this pattern suggests impairment of central vision. The normal red appears washed out, or changes to pink to orange to yellow to colorless as color perception is lost. Because optic neuropathies affect macular fibers, patients lose the ability to read pseudoisochromatic plates. The flight of colors phenomenon is the series of color perceptions that follows shining a bright light into the eye. With impaired color vision, the flight of colors may be reduced or absent. Patients may also compare the brightness or intensity of an examining light in one eye versus the other. A diminution of brightness on one side suggests optic nerve dysfunction; it is sometimes referred to as a subjective APD, relative APD, or Marcus-Gunn pupil. Its significance is the same as for red desaturation. The APD is discussed in more detail in [Chapter 14](#).

BOX 13.2

Nonorganic (Functional) Visual Loss

A truly blind person can sign his name without difficulty. A functionally blind patient often cannot. A truly blind person asked to look at his hand will look wherever proprioception tells him his hand should be; a functionally blind person may gaze in any direction and perhaps never where the hand actually is (Schmidt-Rimpler test). A truly blind person can touch his forefingers together without difficulty; a functionally blind person may make half-hearted inaccurate thrusts. The presence of normal visual, menace, fixation, and emergency light reflexes (see [Chapter 16](#)) excludes organic blindness. A functionally blind person ignorant of the laws of reflection may have much improved vision reading the image of an acuity chart held to his chest in a mirror 10 ft away compared to reading the actual chart at 20 ft; the acuity in fact should be the same. Some patients with functional blindness can suppress optokinetic nystagmus (OKN) responses and the visual evoked response (VER). An excellent test is to have the patient look into a large mirror that can be held and moved. Tilting and moving the mirror will elicit OKN responses because the entire visual environment is moving. The patient cannot suppress or “blur out” by willfully failing to fixate on a single target, as he may be able to do with OKN or VER.

Day blindness (hemeralopia) is a condition in which vision is better in dim

lighting than in bright. It occurs in various conditions causing a central scotoma, in early cataracts; it is a rare side effect of trimethadione. Night blindness (nyctalopia) is much poorer vision in feeble illumination than occurs normally. It is common in retinitis pigmentosa and can occur in chronic alcoholism, Leber's hereditary optic neuropathy (LHON), and xerophthalmia due to vitamin A deficiency.

The Visual Fields

The VF examination is a very important and, unfortunately, often omitted part of the neurologic examination. The VF is the limit of peripheral vision, the area in which an object can be seen while the eye remains fixed. Macular vision is sharp. Peripheral images are not as distinct, and objects are more visible if they are moving. The normal VF extends to 90 to 100 degrees temporally, about 60 degrees nasally, 50 to 60 degrees superiorly, and 60 to 75 degrees inferiorly. The field is wider in the inferior and temporal quadrants than in the superior and nasal quadrants ([Figure 13.15](#)). There are individual variations in the field of vision, dependent to some extent on the facial configuration, the shape of the orbit, the position of the eye in the orbit, the width of the palpebral fissure, and the amount of brow projection or the size of the nose. However, these changes are seldom clinically relevant. With binocular vision, the VFs of the two eyes overlap except for the unpaired temporal crescent extending from 60 to 90 degrees on the horizontal meridian, which is seen by one eye only. The monocular temporal crescent exists because of the anatomy of the retina. The nasal retina extends farther forward, more peripherally, than the temporal. This is the true reason that the temporal VF is more expansive, not because the nose is blocking the nasal field.

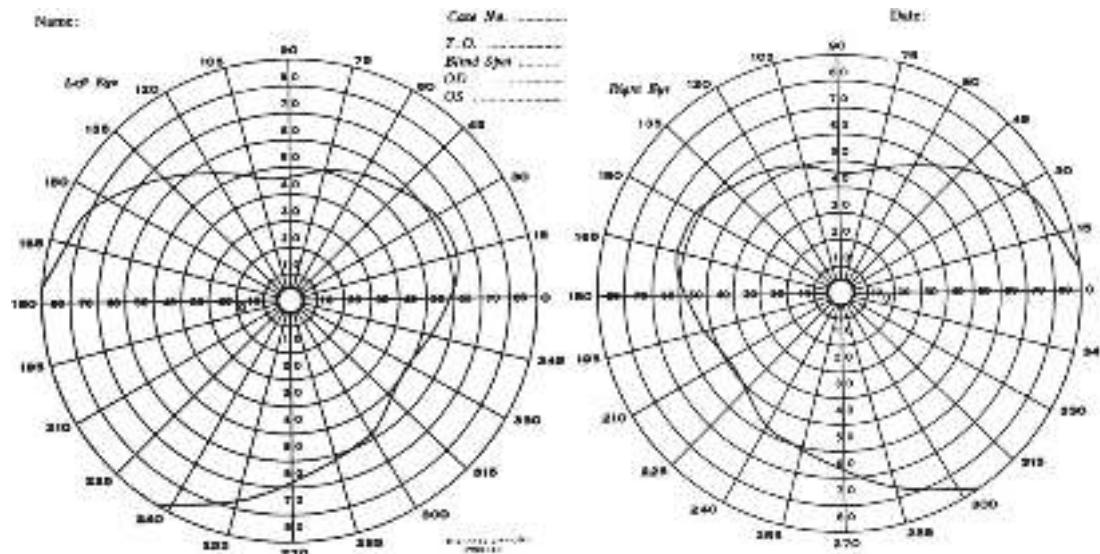


FIGURE 13.15 The normal VFs.

VF examination results are most accurate in an individual who is alert and cooperative and will maintain fixation. Wandering of the eye impairs the evaluation. Crude assessment is possible even in uncooperative patients if the target is interesting enough (e.g., food or paper money). Fatigue and weakness may lengthen the latency between perception of the test object and the response to it, giving a false impression of VF deficit. Close cooperation, good fixation, and adequate illumination are essential for mapping of the blind spot and delineation of scotomas.

Clinicians use several different methods for VF evaluation. The time and energy expended on bedside confrontation testing depends on the patient's history and on the facilities available for formal field testing with tangent (Bjerrum) screen (central 30 degrees) or perimetry (entire field). Even sophisticated confrontation testing cannot approach the accuracy of formal fields.

The confrontation VF exam can be tailored to the circumstances and done as superficially or as thoroughly as the situation requires. Sophisticated bedside techniques can explore the VFs in detail if circumstances warrant. If the patient has no specific visual complaint, and if other aspects of the history and examination do not suggest a field defect is likely, then a screening exam is appropriate. This can be accomplished rapidly and with great sensitivity using small amplitude finger movements in the far periphery of the VF. Recall that the VFs extend temporally to 90+ degrees. Extending elbows and index fingers, the examiner should position the fingers nearly directly lateral to the lateral canthus

at a distance of about 24 in. Superficially, this appears to be a binocular examination, but, properly placed, the finger targets are actually in the unpaired monocular temporal crescent part of the VF. With the targets positioned, make a small amplitude flexion movement with the tip of one index finger, perhaps 2 cm in amplitude. Have the patient “point to the finger that moves.” This language is more efficient than attempting a right-left verbal description where the patient’s and examiner’s rights and lefts are reversed. Stimuli should be delivered in each upper quadrant individually, then both together, and then similarly for the lower quadrants. Including bilateral simultaneous stimuli is necessary to detect subtle defects, which may be manifested only by extinction of one stimulus on double simultaneous stimulation. This technique of small finger movements in the far periphery in both upper and lower quadrants is an excellent screen; when properly done, even binocularly, this technique misses few VF defects. Large amplitude finger wiggles near the center are insensitive. Always bear in mind that primary ophthalmologic disorders such as glaucoma, diabetic retinopathy, and retinal detachment can also alter the VFs.

With any hint of abnormality, or if the patient has or could be expected to have a visual problem, higher-level testing is in order. Examining monocularly, techniques include having the patient assess the brightness and clarity of the examiner’s hands as they are held in the right and left hemifields, in both upper and lower quadrants, or having the patient count fingers fleetingly presented in various parts of the field. Because of the over-representation of central vision in the CNS, assessing each quadrant within the central 10 to 20 degrees is important.

More exacting techniques compare the patient’s field dimensions with the examiner’s, using various targets—still or moving fingers, the head of a cotton swab, colored pinheads, or similar objects. Impairment of color perception also occurs with lesions of the posterior visual pathways. Loss of VF to testing with a red object may be apparent even when the fields are intact to a white object. Positioning the patient and examiner at the same eye level, and gazing eyeball to eyeball over an 18- to 24-in span, targets introduced midway between and brought into the VF along various meridians should appear to both people simultaneously in all parts of the field except temporally, where the examiner must simply develop a feel for the extent of a normal field ([Figure 13.16](#)). Even in expert hands, confrontation fields are relatively gross and more precision required perimetry.

For obtunded, uncooperative, or aphasic patients, paper money (the larger the

denomination the better) makes a compelling target. Even if the examiner has only a \$1 bill, suggest to the patient that it might be \$100. The patient who can see will glance at or reach for the object. Children may respond to keys (no jingling), candy, or other visually interesting objects. Infants may turn the head and eyes toward a diffuse light within a few days after birth. Moving a penlight into the VF and noting when the patient blinks is sometimes useful. Checking for blink to threat—the menace reflex—provides a crude last resort method. The examiner’s hand or fingers are brought in rapidly from the side, as if to strike the patient or poke him in the eye. The patient may wince, drawback, or blink. The threatening movement should be deliberate enough to avoid stimulating the cornea with an induced air current.

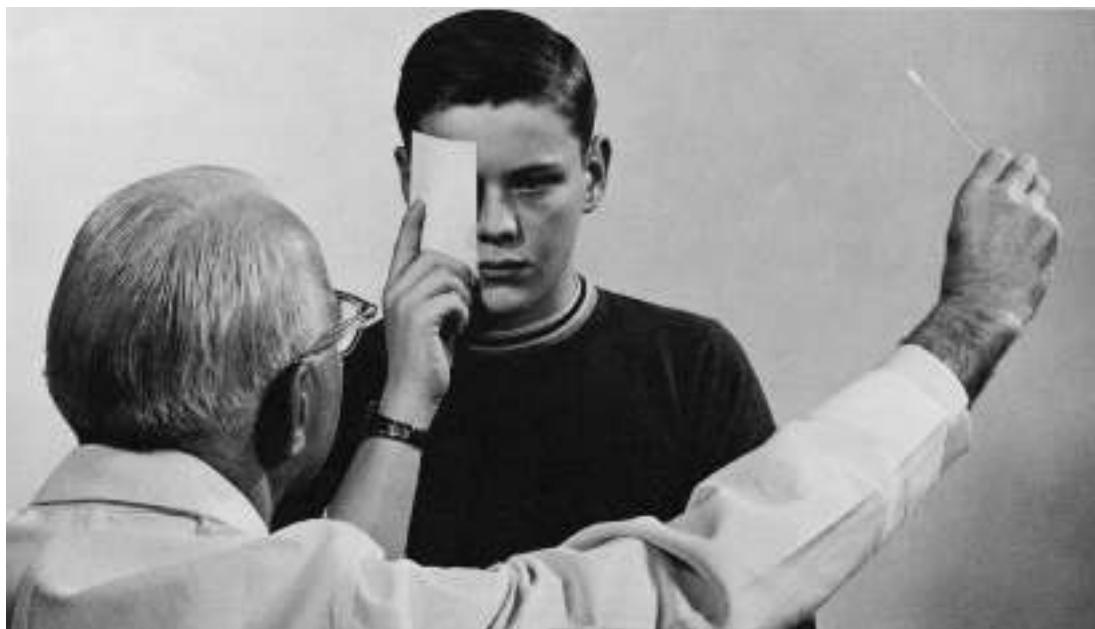


FIGURE 13.16 Confrontation method of testing the VFs.

Testing central fields can include having the patient gaze at the examiner’s face and report any defects, such as a missing or blurred nose. Having the patient survey a grid work (Amsler grid, graph paper, or a quickly sketched homemade version) while fixing on a central point is a sensitive method to detect scotomas ([Figure 13.17](#)). Probing the central field with a small white or red object may detect moderate or large scotomas. With a cooperative patient, one can estimate the size of the blind spot. Amsler grid testing is helpful in detecting central and paracentral scotomas. Small deficits suggest macular disease and may be missed on perimetry.

Pandit et al. compared the sensitivity of seven confrontation VF examining methods in patients whose formal fields showed small or shallow defects. The most sensitive method was examining the central VF with a 5-mm red target; the next most sensitive was comparing red color intensity. These together had a sensitivity of 76%. Description of the examiner's face and quadrant finger counting were the least sensitive. All of the confrontation methods had high specificity. In a similar study, Kerr et al. compared seven common confrontation VF tests to Humphrey VF in 301 eyes in patients recruited from a neuro-ophthalmology clinic, and therefore at high risk for having a VF defect. Anterior visual pathway lesions accounted for 78% of the defects, and of these, glaucoma was the underlying cause in 81%; how applicable the findings are to a general neurologic practice is debatable. Most confrontation tests were relatively insensitive. All tests were more sensitive for posterior than anterior lesions. Although very commonly done, finger counting had a sensitivity of only 35%, but a specificity of 100%. The most sensitive single test was red comparison. Testing with a kinetic red target had the highest combined sensitivity and specificity of any individual test. The combination of kinetic testing with a red target combined with static finger wiggle was the best combination, with a sensitivity of 78% while retaining a specificity of 90%. The combination was significantly better than any single test. Description of the examiner's face and finger counting, while simple tests, had low sensitivity and negative predictive values; it was recommended these tests not be used in isolation to exclude VF loss.

By convention, VFs are depicted as seen by the patient (i.e., right eye drawn on the right). This convention is backward from most things in clinical medicine, and violations of the rule occur sufficiently often that labeling notations are prudent. When confrontation fields are not adequate for the clinical circumstances, formal fields are done. These might include tangent screen examination, kinetic perimetry, or computerized automated static perimetry ([Box 13.3](#)).

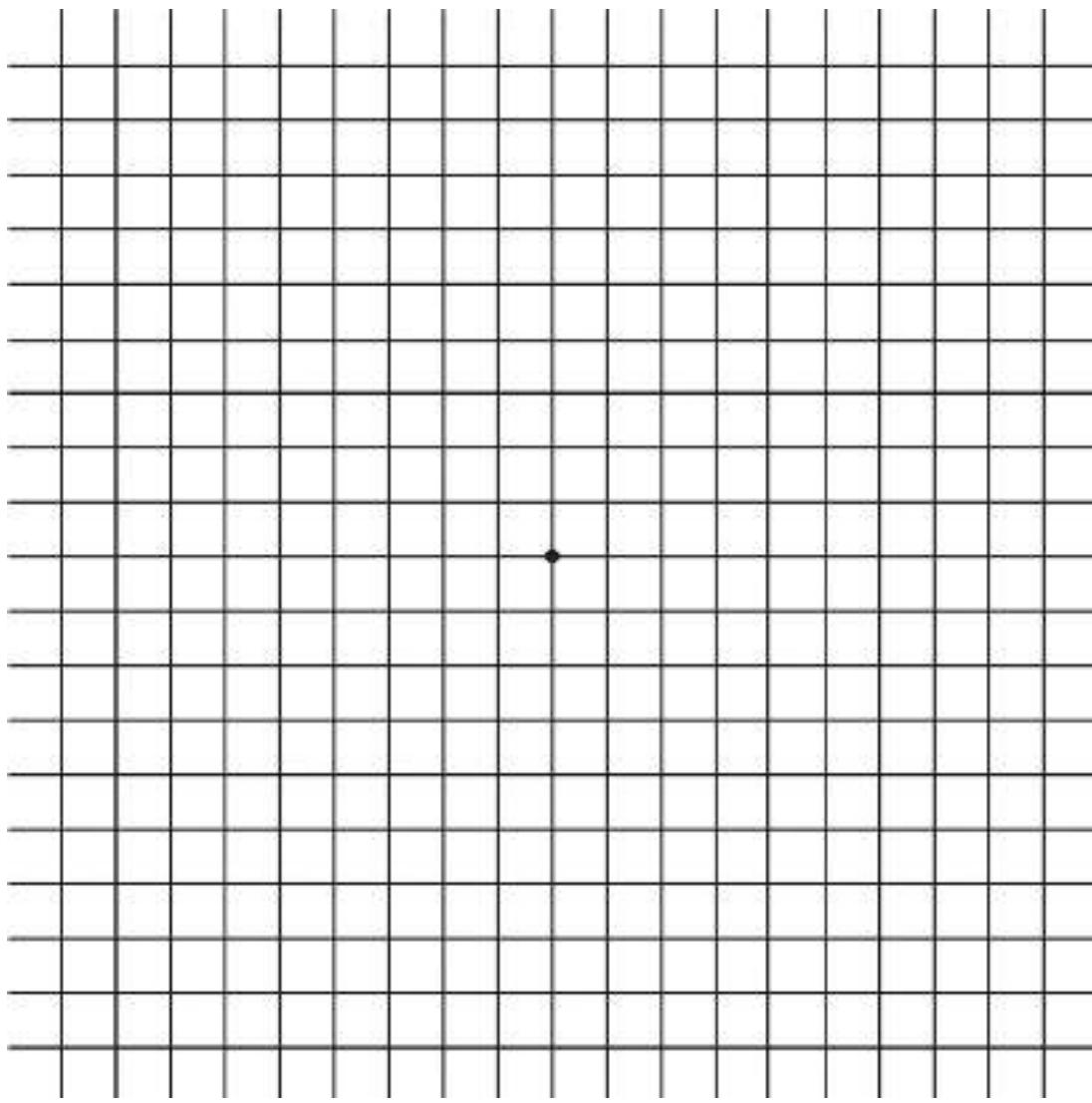


FIGURE 13.17 The Amsler grid for testing the central VFs. (1) Test vision with one eye at a time, and use normal glasses for reading. (2) Hold chart at normal reading distance. (3) Stare at *central dot* and look for distortion or blind spots in the grid.

Visual Field Abnormalities

For neurologic purposes, VF abnormalities can be divided into scotomas, hemianopias, altitudinal defects, and concentric constriction or contraction of the fields. [Figure 13.19](#) depicts some examples of different types of field defects. Because of the anatomy and organization of the visual system, neurologic disorders tend to produce straight-edged defects that respect either the horizontal or vertical meridian or have a characteristic shape because of the arrangement of the NFL. Respect of the horizontal meridian may occur because of the horizontal temporal raphe and the arching sweep of NFL axons above and below the

macula. This pattern is characteristic of optic nerve, optic disk, and NFL lesions. The vascular supply of the retina consists of superior and inferior branches of the central retinal artery, which supply the upper and lower retina, respectively. Vascular disease characteristically causes altitudinal field defects that are sharply demarcated horizontally. The calcarine cortex is organized into a superior and an inferior bank, and lesions involving only one bank may produce VF defects that respect the horizontal meridian. The vertical meridian is respected because of the division into nasal and temporal hemiretinas that occurs at the chiasmal decussation and is maintained through the retrochiasmal visual pathways.

BOX 13.3

Formal Visual Field Testing

Perimetry is the measurement of the visual field (VF) on a curved surface. Campimetry is the measurement of the VF on a flat surface. The tangent screen is the standard method for performing campimetry. For tangent screen examination, a black screen, blackboard, or other flat surface is used to examine the central 30 degrees of vision. The central fields can be evaluated more accurately with the tangent screen, the peripheral fields more accurately with perimetry. The patient is seated 1 to 2 m from the tangent screen; objects of various sizes and colors are brought into view using a black wand that blends into the background. Testing is now often done with a laser pointer. The test object is the only thing of visual interest against the black background. As with perimetry, the notation numerator is the test object size and the denominator the distance from the screen, often followed by a letter to indicate the target color. A field notation of 2/1,000 r indicates the field was done with a 2-mm red test object, and the patient was seated 1 m away from the screen. The tangent screen is especially valuable for measuring the size of the physiologic blind spot and for demonstrating central defects. Defects may be easier to detect when the VF is done at 2 m, because the dimensions of the field and the dimensions of the defect are doubled. The Amsler grid is another sensitive method for testing the central 10 degrees of the VF ([Figure 13.17](#)).

A perimeter is useful for testing the peripheral VFs, which cannot be done by tangent screen. Many different types of perimeters and perimetric techniques have been described. Perimetry may be kinetic or static. Kinetic

perimetry entails moving a test object along various meridians and noting when it is detected. For standard kinetic perimetry (e.g., Goldmann), the patient gazes at a fixation point and various test objects are brought into the field of vision through multiple meridians in a hemispheric dome. White and colored test objects varying in size from 1 to 5 mm are used. The points at which a target of given size and color is first seen are recorded, and a line is drawn joining these points to outline the VF. The line representing the limits of the field for a given size and color test object is called an isopter. The smaller the test object, the smaller the VF. Mapping isopters for test objects of varying sizes and colors creates an image resembling a topographic map. Perimetric readings are expressed in fractions; the numerator indicates the target size and the denominator the distance away from the patient in millimeters. If the size of a VF defect is the same with all test objects, it is said to have steep, or abrupt, margins. If the defect is larger with smaller test objects, its margins are said to be gradual, or sloping, in character.

Limits of the VF vary according to the size, color, and brightness of the test object, the intensity of illumination, the state of adaptation of the eye, and the cooperation of the patient. The VF for a colored test object is smaller than the VF for a white object of the same size. The size of the VF is different for different colors. Changes in color fields precede gross field changes (color desaturation). Altered responses to color may help differentiate between retinal lesions and neurologic conditions. Formal fields provide permanent objective documentation of the VFs. They may be repeated periodically to look for progression or improvement.

The Goldmann perimeter uses a kinetic paradigm. Modern quantitative automated perimetry uses static perimeters, and automated perimetry has largely replaced manual perimetry. Static perimetry measures the threshold for perception of various targets at various locations in the VF with the aid of a computer and statistical analysis. The Humphrey Visual Field Analyzer is in widespread use in the United States. Statistical analysis of the VF data allows determination of the probability that a VF is normal. Automated perimetry is very sensitive for detecting VF defects. However, normal patients may appear to have an abnormal VF because of the large number of erroneous responses that can occur during automated testing. The instruments include reliability indices determined by the false-positive and false-negative responses ([Figure 13.18](#)).

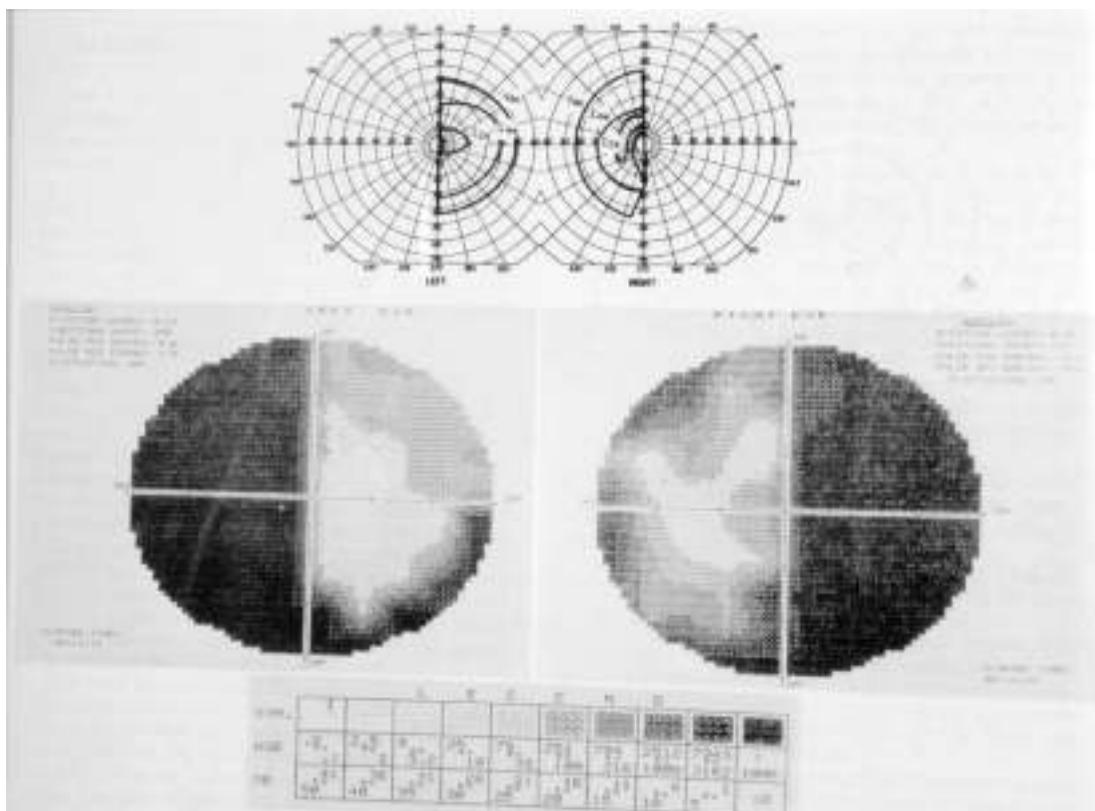


FIGURE 13.18 **Top.** VF performed on a Goldmann perimeter in a patient with a chiasmal lesion. **Bottom.** Humphrey perimeter field in the same patient. (Reprinted from Beck RW, Bergstrom TJ, Lichter PR. A clinical comparison of visual field testing with a new automated perimeter, the Humphrey Field Analyzer, and the Goldmann perimeter. *Ophthalmology* 1985;92[1]:77–82. Copyright © 1985 American Academy of Ophthalmology, Inc. With permission.)

Scotomas

A scotoma (Gr. “darkness”) is an area of impaired vision in the field, with normal surrounding vision. With an absolute scotoma, there is no visual function within the scotoma to testing with all sizes and colors of objects. With a relative scotoma, visual function is depressed but not absent; smaller objects and colored objects are more likely to detect the abnormality. A positive scotoma causes blackness or a sense of blockage of vision, as though an object were interposed; it suggests disease of the retina, especially the macula or choroid. Positive scotomas are often due to exudate or hemorrhage involving the retina or opacity in the media. A negative scotoma is an absence of vision, a blank spot as if part of the field had been erased; it suggests optic nerve disease but can occur with lesions more posteriorly. With a negative scotoma, the defect may not be perceived until a VF examination is done.

A scotoma can often be demonstrated on confrontation VF testing using small objects and carefully exploring the central fields, but they are best demonstrated by the use of the tangent screen. The physiologic blind spot (Mariotte's spot) is a scotoma corresponding to the optic nerve head, which contains no rods or cones and is blind to all visual impressions. The physiologic blind spot is situated 15 degrees lateral to and just below the center of fixation because the disk lies nasal to the macula and the blind spot is projected into the temporal field. Elliptical in shape, it averages 7 to 7½ degrees vertically and 5 to 5½ degrees horizontally and extends 2 degrees above and 5 degrees below the horizontal meridian. On a tangent screen with the patient 1 m away using a 1-mm white object, the average measurements for the blind spot are from 9 to 12 cm horizontally and 15 to 18 cm vertically. The blind spot is enlarged in papilledema and ON.

Scotomas are described by their location or their shape. A central scotoma involves the fixation point and is seen in macular or optic nerve disease. It is typical for ON but can occur in vascular and compressive lesions ([Figure 13.19A](#)). A paracentral scotoma involves the areas adjacent to the fixation point, and it has the same implications as for a central scotoma. A cecocentral scotoma extends from the blind spot to fixation. It is usually accompanied by loss of all central vision with preservation of a small amount of peripheral vision, and it strongly suggests optic nerve disease ([Figures 13.19B](#) and [13.20](#)). Central, paracentral, and cecocentral scotomas are all suggestive of a process involving the PMB. Any scotoma involving the blind spot implies optic neuropathy.

An arcuate scotoma is a crescent defect arching out of the blind spot, usually because of optic neuropathy with the brunt of damage falling on the fibers forming the superior and inferior NFL arcades. A nasal step defect is a scotoma that involves the nasal part of the VF away from fixation, usually respecting the horizontal meridian, which is due to optic neuropathy and often progresses to become a broad arcuate scotoma. Nasal step defects are common, especially in optic neuropathy because of glaucoma. A junctional scotoma is an optic nerve defect in one eye (central, paracentral, or cecocentral scotoma) and a superior temporal defect in the opposite eye (syndrome of Traquair). This is due to a lesion (usually a mass) that involves one optic nerve close to the chiasm, which damages the inferior nasal fibers from the opposite eye (Wilbrand's knee) as they loop forward into the proximal optic nerve on the side of the lesion ([Figures 13.9](#) and [13.19C](#)). The temporal VF defect in the contralateral eye may be subtle and easily missed. The anatomic evidence supporting the existence of Wilbrand's knee has been questioned, but clinical cases continue to suggest it exists. No

junctional scotoma could be detected in three patients whose optic nerves were surgically divided at the optic nerve-chiasm junction.

Although scotomas most often result from disease of the retina or optic nerve, they may also be caused by cerebral lesions. Occipital pole lesions primarily affecting the macular area can produce contralateral homonymous hemianopic scotomas ([Figure 13.19D](#)). Because the bulk of fibers in the chiasm come from the macula, early compression may preferentially affect central vision producing bitemporal heteronymous paracentral scotomas ([Figure 13.19E](#)); with progression of the lesion, a full blown bitemporal hemianopia will appear ([Figure 13.19G](#)). Optic nerve lesions such as glioma and drusen (hyaline excrescences that may be buried in or on the surface of the nerve) may cause scotomas, contraction of the VFs, or sector defects. Enlargement of the physiologic blind spot is referred to as a peripapillary scotoma.

Other types of scotomas occur from primary ocular disease, such as retinitis, chorioretinitis, and glaucoma, which are not related directly to disease of the nervous system ([Box 13.4](#)).

Subjective scotomas cannot be delineated in the field examination. Subjective scotomas include the scintillating scotomas, or teichopsias, of migraine, and the annoying but harmless vitreous floaters that many normal individuals experience.

Hemianopia

Hemianopia is impaired vision in half the VF of each eye; hemianopic defects do not cross the vertical meridian. Hemianopias may be homonymous or heteronymous. A homonymous hemianopia causes impaired vision in corresponding halves of each eye (e.g., a right homonymous hemianopia is a defect in the right half of each eye). Homonymous hemianopias are caused by lesions posterior to the optic chiasm, with interruption of the fibers from the temporal half of the ipsilateral retina and the nasal half of the contralateral retina. Vision is lost in the ipsilateral nasal field and the contralateral temporal field ([Figure 13.21](#)). A heteronymous hemianopia is impaired vision in opposite halves of each eye (e.g., the right half in one eye and the left half in the other). Unilateral homonymous hemianopias, even those with macular splitting, do not affect visual acuity. Patients can read normally with the preserved half of the macula, but those with left-sided hemianopias may have trouble finding the line to be read. Occasionally, patients with homonymous hemianopia will read only half of the line on the acuity chart.

A homonymous hemianopia may be complete or incomplete. If incomplete, it may be congruous or incongruous. A congruous hemianopia shows similar-shaped defects in each eye ([Figure 13.19H](#)). The closer the optic radiations get to the occipital lobe, the closer lie corresponding visual fibers from the two eyes. The more congruous the field defect, the more posterior the lesion is likely to be. An incongruous hemianopia is differently shaped defects in the two eyes ([Figure 13.19I](#)). The more incongruous the defect, the more anterior the lesion. The most incongruous hemianopias occur with optic tract and lateral geniculate lesions. With a complete hemianopia, congruity cannot be assessed; the only localization possible is to identify the lesion as contralateral and retrochiasmal. A superior quadrantanopia implies a lesion in the temporal lobe affecting Meyer's loop (inferior retinal fibers): “pie in the sky” ([Figure 13.19J](#)). Such a defect may occur after temporal lobe epilepsy surgery because of damage to the anteriorly looping fibers. An inferior quadrantanopia (“pie on the floor”) implies a parietal lobe lesion affecting superior retinal fibers ([Figure 13.19K](#)). A macular-sparing hemianopia is one that spares the area immediately around fixation; it implies an occipital lobe lesion ([Figure 13.19L](#)). The explanation for macular sparing remains unclear. There has been conjecture about dual representation of the macula in each occipital pole, but this has never been confirmed anatomically. More likely it is collateral blood supply from the anterior or middle cerebral artery, which protects the macular region from ischemia. Or it could simply be that the extensive cortical representation of the macula both at the occipital pole and anteriorly in the depths of the calcarine fissure makes it difficult for a single lesion to affect all macular function. A small amount of macular sparing may be due to fixation shifts during testing.

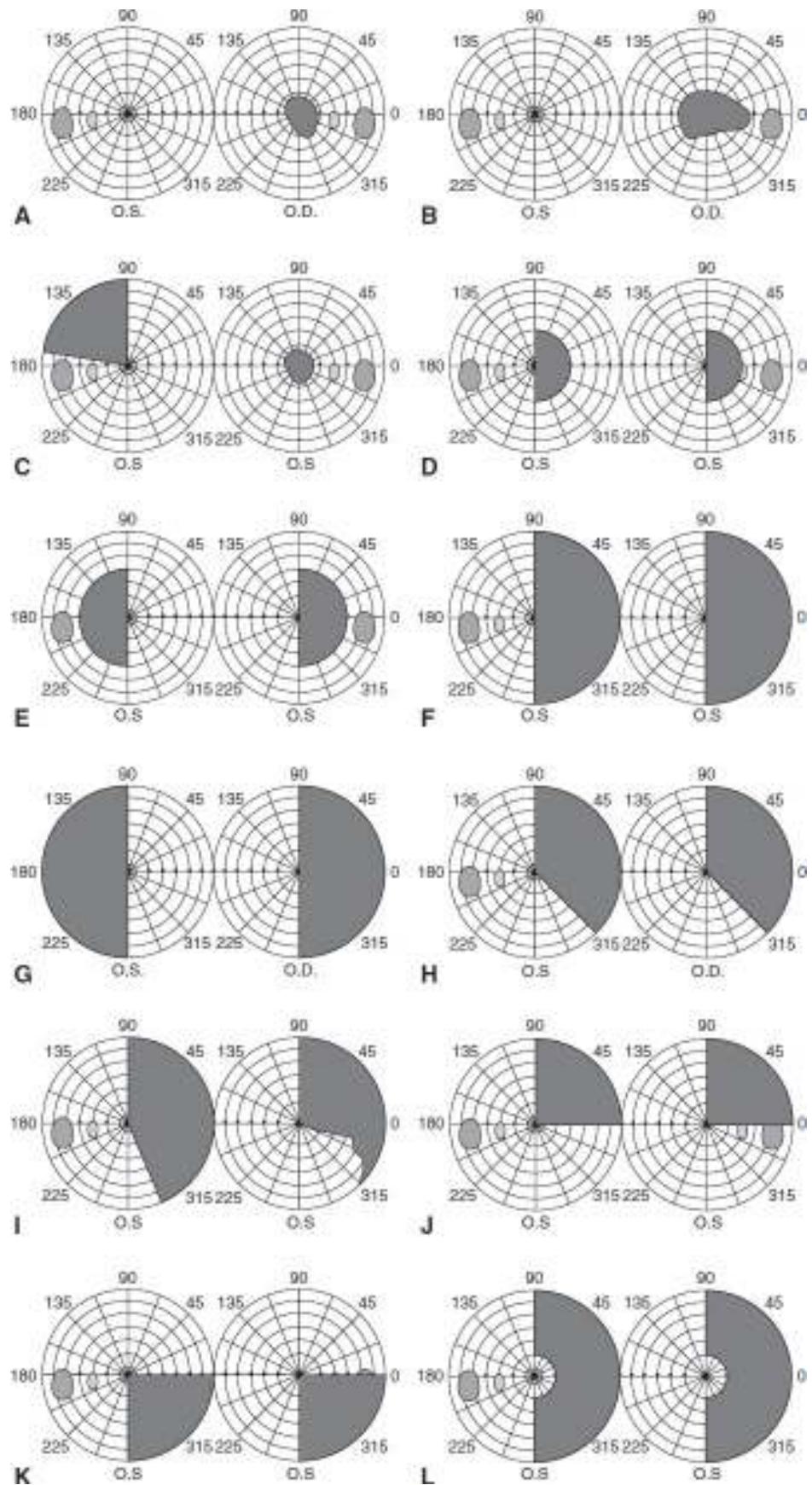


FIGURE 13.19 Types of VF defects. **A.** Central scotoma. **B.** Cecocentral scotoma. **C.** Junctional scotoma. **D.** Homonymous scotomas. **E.** Heteronymous scotomas. **F.** Right homonymous hemianopia. **G.** Bitemporal hemianopia. **H.** Congruous right homonymous hemianopia. **I.** Incongruous right homonymous hemianopia. **J.** Right superior quadrantanopia (“pie in the sky”). **K.** Right inferior quadrantanopia. **L.** Macular-sparing right homonymous hemianopia.

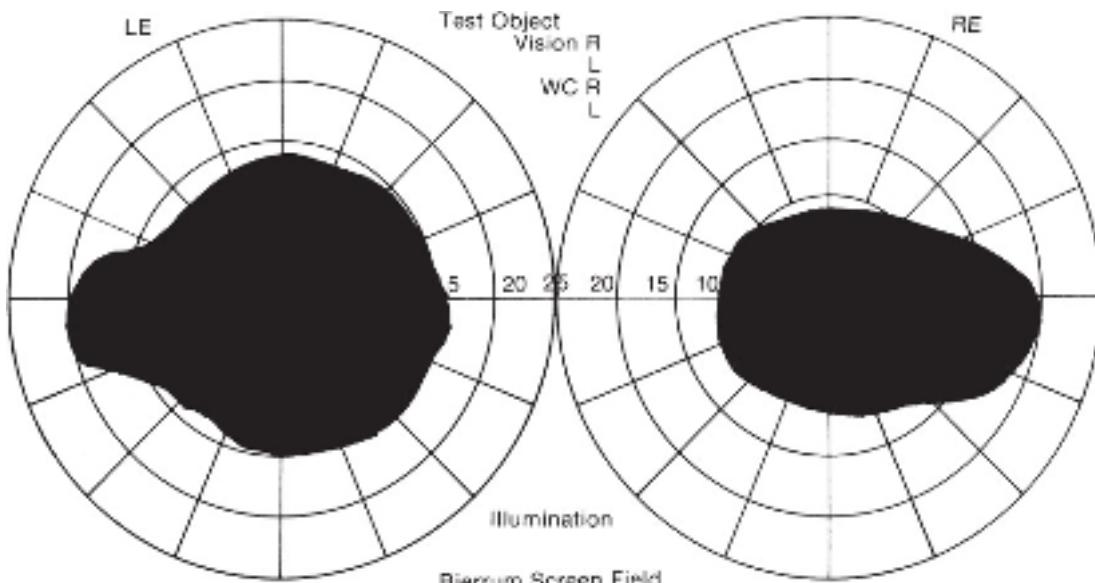


FIGURE 13.20 Bilateral cecocentral scotomas in a patient with bilateral optic neuritis.

BOX 13.4

Other Types of Scotomas

Glaucoma may cause arcuate, cuneate, comma-shaped, or other partially ring-shaped scotomas. A Seidel scotoma arises from the blind spot and has a thin and well-demarcated arcuate tail, the shape resembling a comma. A Bjerrum scotoma is shaped like a bow, extending from the blind spot to near fixation. Both are common in glaucoma. Peripheral scotomas may be present anywhere in the field of vision. In annular, or ring, scotomas, there is a loss of vision in a doughnut shape with relative sparing of fixation and of the far periphery. These types of scotomas are typically due to retinitis pigmentosa, a condition primarily affecting the rods that are concentrated in the midzone of the retina. Ring scotomas also occur in optic neuropathy, macular lesions, cancer-associated retinopathy, choroiditis, and myopia. Many ophthalmologic conditions produce a global depression of retinal function and concentric constriction of the VF, rather than a discrete defect.

Ophthalmoscopic examination generally reveals the nature of such conditions.

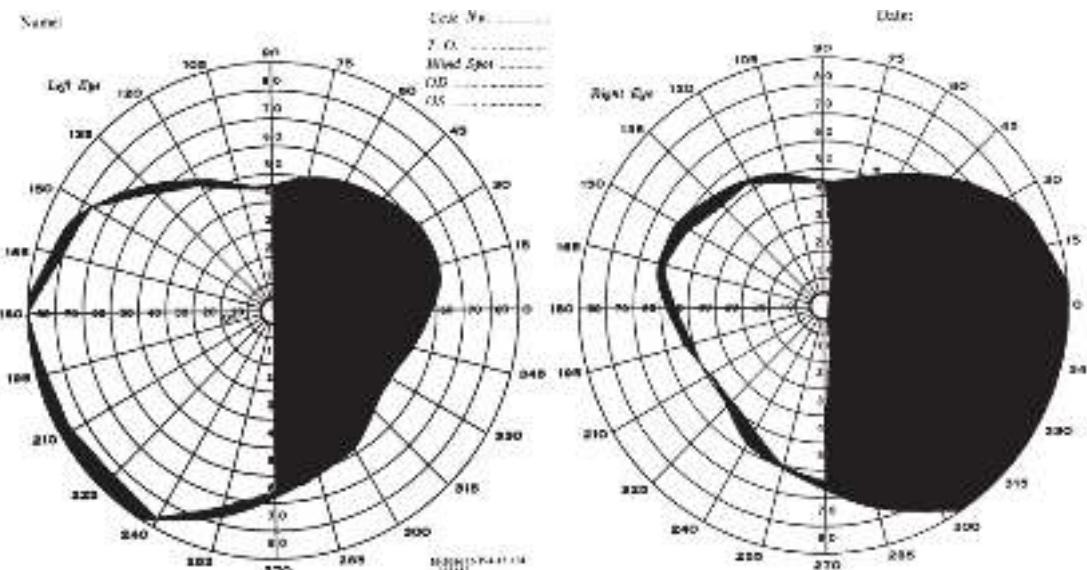


FIGURE 13.21 Macular-splitting right homonymous hemianopia in a patient with a neoplasm of the left occipital lobe.

Incomplete homonymous VF defects are common. These include partial or irregular defects in one or both of the hemifields, relative rather than absolute loss of vision, an inability to localize the visual stimulus, and hemianopia only for objects of a certain color (hemiachromatopsia). Extinction (visual inattention) is hemianopic suppression of the visual stimulus in the involved hemifield when bilateral simultaneous stimuli are delivered. Visual extinction is most characteristic of lesions involving the nondominant parietooccipital region. Riddoch's phenomenon is a dissociation between the perception of static and kinetic stimuli. The patient may not perceive a stationary object but detect it instantly when it moves.

Heteronymous hemianopias are usually bitemporal; only rarely are they binasal. A bitemporal hemianopia is usually due to chiasmatic disease, such as a pituitary tumor growing up out of the sella turcica and pressing on the underside of the chiasm ([Figure 13.18](#)). Bitemporal field defects can usually be detected earliest by demonstrating bitemporal desaturation to red. Because of the anterior inferior position of decussating inferior nasal fibers, lesions impinging from below produce upper temporal field defects, which evolve into a bitemporal hemianopia ([Figure 13.6](#)). Lesions encroaching from above tend to cause inferior

temporal defects initially. The defect will be first and worst in the upper quadrants with infrachiasmatic masses (e.g., pituitary adenoma), and it will be first and worst in the lower quadrants with suprachiasmatic masses (e.g., craniopharyngioma). Patients with postfixed chiasms and pituitary tumors may present with optic nerve defects, and those with prefixed chiasms may have optic tract defects.

The most common cause of bitemporal hemianopia is a pituitary adenoma; occasionally, it results from other parasellar or suprasellar lesions such as meningioma and craniopharyngioma, as well as glioma of the optic chiasm, aneurysms, trauma, and hydrocephalus. Other VF defects that may simulate bitemporal hemianopia include tilted optic disks, bilateral cecocentral scotomas, and bilaterally enlarged blind spots. Binasal hemianopias may occur from disease impinging on the lateral aspect of the chiasm bilaterally (e.g., bilateral intracavernous carotid aneurysms), but they are more likely to be due to bilateral optic neuropathy.

An altitudinal VF defect is one involving the upper or lower half of vision, usually in one eye, and usually due to retinal vascular disease (central retinal artery or branch occlusion or anterior ischemic optic neuropathy [AION]). A partial altitudinal defect may approximate a quadrantanopia. Altitudinal defects do not cross the horizontal meridian.

Constriction of the VFs is characterized by a narrowing of the range of vision, which may affect one or all parts of the periphery. Constriction may be regular or irregular, concentric or eccentric, temporal or nasal, and upper or lower. Symmetric concentric contraction is most frequent and is characterized by a more or less even, progressive reduction in field diameter through all meridians. Such constriction is referred to as funnel vision, as opposed to tunnel vision (see below). Concentric constriction of the VFs may occur with optic atrophy, especially secondary to papilledema or late glaucoma, or with retinal disease, especially retinitis pigmentosa. Narrowing of the fields because of fatigue, poor attention, or inadequate illumination must be excluded, as must spurious constriction because of decreased visual acuity or delayed reaction time. Slight constriction of the VF may occur when there is a significant refractive error. Diffuse depression is the static perimeter equivalent of constriction on kinetic perimetry.

Concentric constriction of the fields is sometimes seen in hysteria. A suspicious finding is when the fields fail to enlarge as expected with testing at increasing distance (tubular or tunnel fields). Normally, the field of vision

widens progressively as the test objects are held farther away from the eye. However, in nonorganicity, this normal widening is not seen, and the entire width of the field is as great at 1 ft from the eye as it is at 2, 5, 10, or 15 ft. The normal VF is a funnel; the nonorganic VF is a tunnel. The tubular field can be demonstrated either by testing the extent of the VF at varying distances from the patient, or it can be shown by using test objects of different sizes at a constant distance. Spiral contraction is a progressive narrowing of the VF during the process of testing. It may be a sign of nonorganicity, but it is probably more suggestive of fatigue. A similar pattern field is the star-shaped VF, where there is an irregularity of outline. This may be seen in nonorganicity, fatigue, or poor attention.

The Ophthalmoscopic Examination

The physician using a direct ophthalmoscope is like a one-eyed Eskimo peering into a dark igloo from the entryway with a flashlight. Only a narrow sector of the posterior pole is visible, and there is no stereopsis. Pupil dilation significantly increases the field of view. Indirect ophthalmoscopy, used by ophthalmologists, can stereoscopically view almost the entire vista of the fundus. PanOptic direct ophthalmoscopes (Welch-Allyn) give the advantage of a broader view but still reveal only the posterior pole. See [Box 13.5](#) for a brief discussion of the techniques of direct ophthalmoscopy. It is important to become facile by practicing direct ophthalmoscopy on all patients, as the examination is inevitably most technically difficult in situations where fundus examination is most critical.

BOX 13.5

Direct Ophthalmoscopy

The standard direct ophthalmoscope has dials that adjust the light apertures and filters and allow the examiner to focus. The small aperture is for examining an undilated pupil, the large aperture for examining a dilated pupil. Using the small aperture may help minimize reflections from the cornea. The red-free filter is useful for examining blood vessels, looking for hemorrhages, and examining the nerve fiber layer (NFL). The red reflex can be assessed from a distance of 12 to 15 in. Opacities in the media (e.g., cataract) appear as black dots against the red background. The ocular fundus

is the only place in the body where blood vessels can be visualized directly. Changes in the retinal vasculature in conditions such as diabetes and hypertension mirror the status of the systemic circulation. The fundus may also reveal important findings in systemic diseases such as endocarditis and AIDS.

In the neurologic examination, the areas of primary concern are the disk, the macula, and the arteries. The disk is normally round or a vertically oriented slight oval. The nasal margin is normally slightly blurred compared to the temporal. The disk consists of a peripheral neuroretinal rim and a central cup. The neuroretinal rim consists of axons streaming from the retina to enter the optic nerve. The physiologic cup is a slight depression in the center of the disk that is less pinkish than the rim and shows a faint latticework because of the underlying lamina cribrosa. The rim is elevated slightly above the cup. The cup normally occupies about a third of the temporal aspect of the disk. To locate the disk, a helpful technique is to find a retinal blood vessel, focus on it, and then follow it to the disk. In severe myopia, the disk may appear larger and paler than normal. In the aphakic eye, the disk looks small and far away.

The myelinated axons making up its substance render the normal optic disk yellowish-white. It is paler temporally where the papillomacular bundle (PMB) enters. The normal disk lies flat and well demarcated against the surrounding retina, with arteries and veins crossing the margins and capillaries staining the surface a faint pink. The size of the scleral opening varies from individual to individual. When the opening is small, the disk consists entirely of neuroretinal tissue, and the cup is inconspicuous or nonexistent. Such a small cupless disk is more vulnerable to anterior ischemic optic neuropathy and is termed a disk at risk. The normal cup-to-disk ratio is about 0.1 to 0.5. In patients with glaucoma, the cup-to-disk ratio is increased and the cup is more prominent and often nasally displaced.

The central retinal artery enters the eye through the physiologic cup and divides into superior and inferior branches, which in turn divide into nasal and temporal branches, yielding four prominent arterial trunks emanating from the disk. Beyond the second branch, the retinal vessels are arterioles, visible because of the 14 \times magnification provided by the patient's lens and cornea. Cilioretinal arteries are present in many normal individuals. These vessels arise from posterior ciliary arteries, enter the eye along the disk margin, and perfuse the peripapillary retina. They may become prominent as

shunt vessels when there is optic nerve compression. Varying amounts of pigmentation are present in the retina near the temporal border of the disk, especially in dark-skinned persons. At times a pigment ring may completely surround the disk. White scleral and dark choroidal rings may sometimes be seen.

The macula is a dark area that lies about two disk diameters temporal to and slightly below the disk. The macula appears darker than the surrounding retina because the depression of the macula and fovea means the retina is thinner in that area, allowing more of the deeply colored choroid to show through. The area of the macula is devoid of large blood vessels. The fovea centralis appears as a pinpoint of light reflected from the center of the macula. The macula may be seen more easily with a red-free filter. It is sometimes easier to visualize the macula if the patient looks directly into the light.

The routine fundus examination in neurologic patients is generally done through the undilated pupil. The fundus examination is more challenging when the patient has a small pupil, myopia, or opacities in the media such as cataract. One or more of these are commonly present in older individuals. In some circumstances, the benefits of an adequate fundus exam outweigh the minimal risk of precipitating an attack of acute narrow angle glaucoma by using mydriatic drops. A crude estimate of the narrowness of the iridocorneal angle can be made by shining a light from the temporal side to see if a shadow is cast on the nasal side of the iris and sclera. The risk of an attack of acute narrow-angle glaucoma because of the use of mydriatic drops has been estimated at 0.1%. Mydriatic drops are best avoided in situations where assessment of pupillary function is critical, such as patients with head injury or other causes of depressed consciousness. Their use in such situations must be obtrusively documented, even to the point of writing “eye drops in” on the patient’s forehead.

LOCALIZATION AND DISORDERS OF VISUAL FUNCTION

Disorders of the afferent visual system can be divided into prechiasmal, chiasmal, and retrochiasmal. Disease in each of these locations has characteristic

features that usually permit its localization. The etiologic processes affecting these different segments of the afferent visual system are quite different. As a generalization, prechiasmal lesions cause monocular visual loss; impaired color perception; a central, paracentral, or cecocentral VF defect; and an APD. The disk may or may not appear abnormal depending on the exact location of the lesion. Chiasmal lesions cause heteronymous VF defects, most often bitemporal hemianopia, with preservation of visual acuity and color perception and a normal appearing optic disk. Retrochiasmal lesions cause a contralateral homonymous hemianopia and have no effect on acuity or disk appearance. There is usually no effect on color vision, but some central lesions may cause achromatopsia. A summary of the features of disease involving the macula, optic nerve, chiasm, optic tract, LGB, optic radiations, and calcarine cortex can be found in Table 13.1.

TABLE 13.1 Clinical Characteristics of Acute Lesions Involving Different Parts of the Afferent Visual Pathway

	Visual Acuity	Color Vision	Visual Field Defect	Pupillary Function	Disk Appearance	Causation
Macula	Decr.	Decr.	Bitemporal central scotoma	Normal or APD	Normal	May have retinopathy; macula may be obscured on ophtalmoscopy; common etiologies: age-related macular degeneration, central serous retinopathy, macular hole, cystoid macular edema, trauma, toxic retinopathy
Optic Nerve Proximally	Decr.	Decr.	Bitemporal central, paracentral, or cecocentral scotoma	APD	Edema	With ON may have pain in eye movement; common etiologies: idiopathic ON, MS, ADEM, vasculitis, sarcoid, LHMN, collagen vascular disease, sarcoidosis, diabetes, papillopathy
Retrobulbar neuropathy	Decr.	Decr.	Same as proximally	APD	Normal	May have proptosis; common etiologies: ON, MS, myopathy, compression, glioma, infiltrative lesions, trauma, infection, sarcoid, collagen vascular disease, infection, posterior ischaemic optic neuropathy
Distal optic nerve, near chiasm	Decr.	Decr.	Bitemporal scotoma	APD	Normal	May have evidence of a solitary/pansolitary lesion; common etiology: sarcoid
Chiasm	Normal	Normal	Bitemporal hemianopsia	Normal	Normal	May develop bitemporal hemianopsia; APD can occur in eyes with greatest VF loss; common etiologies: tumor (e.g., pituitary adenoma, craniopharyngioma), demyelination, trauma, sarcoid, sarcoidosis, sarcoiditis, chorioretinitis, sarcoid, lymphomatous arachnoiditis
Optic tract	Normal	Normal	Contralateral incongruous homonymous hemianopsia	Mid/APD in contralateral eye	Normal	May be involved with disease involving the posterior chiasm; common etiologies: dominantly acting disease, trauma, mass lesion, stroke
Lateral geniculate body	Normal	Normal	Contralateral incongruous homonymous hemianopsia	Normal	Normal	Common etiologies: ischemia, trauma, mass lesion
Optic Radiations						
Temporal lobe	Normal	Normal	Contralateral superior quadrantanopsia	Normal	Normal	May have visual hallucinations at the affected hemifield; common etiologies: tumor, stroke, hemiatrophy, trauma, mass lesion
Parietal lobe	Normal	Normal	Contralateral inferior quadrantanopsia	Normal	Normal	May have contralateral ON; patient may be unaware of the deficit, especially with nondominant hemisphere lesions; common etiologies: tumor, stroke, trauma, hemiatrophy
Calcarine cortex	Normal	Normal	Contralateral congruous homonymous hemianopsia	Normal	Normal	Macula sparing frequent; common etiologies: stroke, trauma, tumor, demyelinating disease

ADEM, acute disseminated encephalomyelitis; APD, afferent pupillary defect; decr., decreased; LHMN, lateral hemispheric optic neuropathy; MS, multiple sclerosis; ON, optic neuritis; sarcoid; OPT, optic neuritis.

Prechiasmal Lesions

Prechiasmal disorders affect the optic nerve. Disorders can be divided into those that affect the disk (papillopathy) and those that affect the retrobulbar segment between the globe and the chiasm. The macula gives rise to the majority of the fibers in the optic nerve, and disease of the macula itself can cause a clinical picture that is at times difficult to distinguish from optic neuropathy. Common causes of maculopathy include age-related macular degeneration and central serous retinopathy ([Table 13.1](#)). Macular disease causes marked impairment of central acuity and impaired color vision. There may be a central scotoma. A distinct central scotoma with normal field between the central defect and the blind spot is more common in macular than in optic nerve disease. Macular disease often causes metamorphopsia, a distortion of visual images. When severe, maculopathy can cause an APD. Prolongation of the time to recover vision after direct, intense light stimulation (photostress test) can sometimes help to distinguish macular from optic nerve disease ([Box 13.6](#)). Other retinal lesions severe enough to cause monocular VF defects are almost all visible ophthalmoscopically.

A macular star is a radial pattern of exudates in the perimacular retina. They are common in hypertension, papilledema, and in other conditions. Neuroretinitis refers to the association of ON with a macular star and is commonly of viral origin. Chorioretinitis is inflammation involving choroid and retina, which is most often due to infections such as tuberculosis, syphilis, toxoplasmosis, cytomegalovirus, and HIV. Chorioretinitis often leaves whitish scars surrounded by clumps of pigment. Cytomegalovirus chorioretinitis is common in AIDS.

BOX 13.6

The Photostress Test

In macular disease, the photoreceptors require longer to recover from bleaching of the retinal pigments after exposure to a bright light. The photostress test is done by determining a baseline visual acuity, then shining a bright light (e.g., a fresh penlight) into the eye for 10 seconds, and then determining the time required for the visual acuity to return to baseline. Reliable reference values are not available; the test is mainly useful with unilateral disease when the unaffected eye can be used for comparison. In optic nerve disease, the photostress test is normal. Recovery times may reach

several minutes in macular disorders such as macular edema, central serous retinopathy, and macular degeneration.

Monocular altitudinal defects are characteristic of disease in the distribution of the central retinal artery. Central vision may be spared because the macula is often perfused by the cilioretinal arteries. AION (see below) is another cause of an altitudinal defect. Bilateral altitudinal defects may occur with bilateral lesions in certain parts of the visual pathway, for example, bilateral occipital infarction or a large prechiasmal lesion compressing both optic nerves. A checkerboard pattern is a superior altitudinal defect in one eye and an inferior altitudinal defect in the other eye.

Disorders of the Optic Disk

The color and appearance of the disk may change in a variety of circumstances. The disk may change color—to abnormally pale in optic atrophy or to abnormally red with disk edema. The margins may become obscured because of disk edema or the presence of anomalies. Edema of the disk is nonspecific. It may reflect increased intracranial pressure, or it may occur because of optic nerve inflammation, ischemia, or other local processes. By convention, disk swelling because of increased intracranial pressure is referred to as papilledema; under all other circumstances, the noncommittal terms disk edema or disk swelling are preferred. Visual function provides a critical clue to the nature of disk abnormalities. Patients with acute papilledema and those with disk anomalies have normal visual acuity, VFs, and color perception. Impairment of these functions is the rule in patients suffering from optic neuropathies of any etiology. The first step in evaluating a questionably abnormal disk is therefore a careful assessment of vision.

Papilledema

Increased intracranial pressure exerts pressure on the optic nerves, which impairs axoplasmic flow and produces axonal edema and an increased volume of axoplasm at the disk. The swollen axons impair venous return from the retina, engorging first the capillaries on the disk surface, then the retinal veins, and ultimately causing splinter- and flame-shaped hemorrhages as well as cotton wool exudates in the retinal NFL. Further axonal swelling eventually leads to elevation of the disk above the retinal surface. Transient visual obscurations,

momentary graying out or blacking out of vision, often precipitated by postural changes, are classical symptoms of papilledema, especially in pseudotumor cerebri (idiopathic intracranial hypertension [IIH]). Obscurations may be due to microvascular compromise at the nerve head.

The four stages of papilledema are early, fully developed, chronic, and atrophic. Fully developed papilledema is obvious, with elevation of the disk surface, humping of vessels crossing the disk margin, obliteration of disk margins, peripapillary hemorrhages, cotton wool exudates, engorged and tortuous retinal veins, and marked disk hyperemia. The recognition of early papilledema is much more problematic ([Figure 13.22](#)). Occasionally, the only way to resolve the question of early papilledema is by serial observation. The earliest change is loss of previously observed spontaneous venous pulsations (SVPs). Venous pulsations are best seen where the large veins dive into the disk centrally. The movement is a back-and-forth rhythmic oscillation of the tip of the blood column, which resembles a slowly darting snake's tongue. Side-to-side expansion of a vein is much more difficult to see. The presence of SVPs indicates an intracranial pressure less than approximately 200 mm H₂O. However, because they are absent in 10% to 20% of normals, only the disappearance of previously observed SVPs is clearly pathologic.

As papilledema develops, increased venous back pressure dilates the capillaries on the disk surface, transforming its normal yellowish-pink color to fiery red. Blurring of the superior and inferior margins evolves soon after. However, because these margins are normally the least distinct areas of the disk, blurry margins alone are not enough to diagnose papilledema. There is no alteration of the physiologic cup with early papilledema. With further evolution, the patient with early papilledema will develop diffuse disk edema, cup obscuration, hemorrhages, exudates, and venous engorgement. Frank disk elevation then ensues as the fundus ripens into fully developed papilledema ([Figure 13.23](#)). In chronic papilledema, hemorrhages and exudates resolve and leave a markedly swollen "champagne cork" disk bulging up from the plane of the retina. If unrelieved, impaired axoplasmic flow eventually leads to death of axons and visual impairment, which evolves into the stage of atrophic papilledema, or secondary optic atrophy. Papilledema ordinarily develops over days to weeks. With acutely increased intracranial pressure because of subarachnoid or intracranial hemorrhage, it may develop within hours. Measuring diopters of disk elevation ophthalmoscopically has little utility.



FIGURE 13.22 Early papilledema.

The changes in the optic nerve head in papilledema are both mechanical and vascular in nature. The mechanical signs of disk edema include blurring of the disk margins, filling in of the physiologic cup, protrusion of the nerve head, edema of the NFL and retinal or choroidal folds, or both. The vascular signs include venous congestion, hyperemia of the nerve head, papillary and peripapillary hemorrhages, NFL infarcts (cotton-wool spots), and hard exudates of the optic disk.

Acute papilledema causes no impairment of visual acuity or color vision. The typical patient has no symptoms related to its presence except for obscurations. The blind spot may be enlarged, but VF testing is otherwise normal. In patients who develop optic atrophy following papilledema, the visual morbidity can be severe and may include blindness.



FIGURE 13.23 Severe papilledema.

With current technology, imaging has usually detected intracranial mass lesions before the development of increased intracranial pressure. As a result, IIH is the most common cause of papilledema in the developed world. IIH can occur without papilledema, or with asymmetric papilledema, rarely with unilateral papilledema. The typical patient with IIH is an obese, young female with headaches, no focal findings on neurologic examination, normal imaging except for small ventricles, and normal CSF except for elevated opening pressure. Without adequate treatment, visual loss is a common sequel.

Other Causes of Disk Edema

Changes ophthalmoscopically indistinguishable from papilledema occur when conditions primarily affecting the optic nerve papilla cause disk edema. Papilledema is usually bilateral; other causes of disk edema are often unilateral ([Table 13.2](#)). Optic neuropathies generally cause marked visual impairment, including loss of acuity, central or cecocentral scotoma, loss of color perception, and an APD. Disease of the optic nerve head is usually due to demyelination, ischemia, inflammation, or compression. ON and AION are two common conditions that cause impaired vision and disk edema. Both are usually unilateral. Compressive lesions of the optic nerve in the orbit may cause disk

edema, but intracanalicular and intracranial compression usually does not. ON with disk edema is sometimes called papillitis. Papillitis may occur as an isolated abnormality, as a manifestation of multiple sclerosis (MS), or as a complication of some systemic illness. Demyelinating optic neuropathies causing papillopathy are common as a feature of MS, but they also can occur as an independent disease process or complicate other disorders such as acute disseminated encephalomyelitis and neuromyelitis optica (NMO), which includes Devic's disease. There are many other causes of optic neuropathy; some of the more common conditions are listed in [Table 13.3](#).

TABLE 13.2 Some Causes of Unilateral Disk Edema

- Optic neuritis
- Anterior ischemic optic neuropathy
- Compression of the optic nerve in the orbit
- Central retinal vein occlusion
- Optic nerve infiltration
- Diabetic papillopathy
- Syphilis
- Leber's hereditary optic neuropathy (LHON)

TABLE 13.3 Some Causes of Optic Neuropathy

- Optic neuritis
- Ischemic optic neuropathy
- Optic nerve compression
- Papillophlebitis
- Optic nerve infiltration (carcinomatous, lymphomatous)

Sarcoidosis

Diabetic papillopathy

Tobacco-alcohol amblyopia

Nutritional deficiency, especially vitamin B₁₂

Drugs

Toxins

Hereditary optic neuropathy (Leber, Kjer)

Glaucoma

Optic Neuritis

Inflammation or demyelination of the optic nerve can occur in a variety of conditions, including MS, postviral syndromes, sarcoidosis, collagen vascular disease, neurosyphilis, and others. Many cases are idiopathic. The majority of patients are women in the 20 to 50 age range. ON occurs sometime during the course of MS in 70% of patients and is the presenting feature in 25%. Some 50% to 70% of patients presenting with ON eventually develop other evidence of MS. Factors that increase the likelihood of underlying MS in patients with ON include the presence of Uhthoff's phenomenon (increased symptoms with elevation of body temperature or after exercise), HLA-DR2 positivity, and a recurrent episode. Decreased acuity, impaired color perception, central or cecocentral scotoma, disk edema, and an APD are the typical findings. For a video of an APD, see [Video Link 13.1](#) (from Kathleen B. Digre, MD at the University of Utah Neuro-Ophthalmology Virtual Education Library: NOVEL). Color vision loss usually parallels acuity loss, but in ON, the loss of color vision may be more severe than expected for the loss of acuity. Visual loss in ON occurs suddenly and tends to progress over 1 to 2 weeks, with substantial recovery over 2 to 12 weeks. Severe visual loss acutely does not necessarily portend poor recovery. Eye pain is present in 90% of patients, and many have positive visual phenomena with colors or flashing lights (photopsias, phosphenes). The eye pain is usually mild but can become severe and more debilitating than the visual loss. The pain may precede or begin concomitantly

with the visual loss and is usually worsened with eye movement, particularly upgaze. The absence of pain suggests a noninflammatory type of optic neuropathy. In about 65% of cases of ON, the disk appears normal; in the remainder, there is mild disk edema and occasional NFL hemorrhages. Pain can occur whether or not there is disk edema. Optic atrophy ensues over the next several weeks in 50% of patients. Improvement to normal or near normal acuity occurs in 90% of patients. ON may rarely involve the chiasm (chiasmal neuritis).

In NMO, there are lesions of the optic nerves and the spinal cord. It is a distinct entity from MS, but separating the two clinically may be difficult. The spinal cord lesion extends over three or more vertebral segments (longitudinally extensive transverse myelitis [LETM]). The spinal cord syndrome is usually sudden and severe and may be permanent. In one series of 60 patients, ON was the initial feature in 53.3%.

NMO is increasingly being seen as a spectrum of neurologic conditions defined by serologic tests. The term NMO spectrum disorder (NMOSD) emphasizes that patients with ON or LETM alone are often antibody positive and that some patients have brain lesions. The brain MRI abnormalities differ from those typical of MS. Autoantibodies against aquaporin-4 and myelin-oligodendrocyte glycoprotein have been identified so far.

Anterior Ischemic Optic Neuropathy

AION is the most common syndrome of optic nerve ischemia, and the most common optic neuropathy in adults over 50 after glaucoma. In AION, microangiopathy produces occlusion of the short posterior ciliary arteries and infarction of all or part of the disk. Visual loss is sudden, painless, nonprogressive, and generally does not improve. Decreased acuity, impaired color perception, an altitudinal field defect, usually inferior, and pallid disk edema are the typical findings acutely; evolving subsequently into optic atrophy. In the acute phase, a pale disk with hemorrhage will virtually always be due to AION. Other useful findings suggesting AION are altitudinal swelling and arterial attenuation.

AION is due to disease involving the posterior ciliary arteries, not the central retinal artery, and is divided into two forms: arteritic and nonarteritic. Arteritic AION most commonly complicates giant cell arteritis (GCA), accounting for about 10% to 15% of patients. Usually, these patients are over 65 and have more severe visual loss than patients with nonarteritic AION. A history of headache, jaw claudication, and scalp tenderness is very suspicious. Evidence of

polymyalgia rheumatica, such as malaise, weight loss, myalgias, and an elevated ESR, increases the likelihood that AION is due to GCA. In a meta-analysis of 21 studies, jaw claudication and diplopia were the only historical features that substantially increased the likelihood of GCA. Predictive physical findings included temporal artery beading, prominence, and tenderness; the absence of any temporal artery abnormality was the only clinical factor that modestly reduced the likelihood of disease. There is evidence that varicella-zoster virus infection may trigger the inflammatory cascade that characterizes GCA.

Premonitory amaurosis fugax is more common in the arteritic form. They do not have a small disk in the fellow eye (disk at risk, see below). Involvement of the opposite eye occurs in approximately 15% of patients within 5 years. Although no treatment affects the outcome in the involved eye, recognition and management of underlying vasculitis may prevent a future attack in the opposite eye.

Nonarteritic AION is most often caused by a microvasculopathy related to hypertension, diabetes, tobacco use, arteriosclerosis, or atherosclerosis. Some cases are due to impaired microvascular perfusion related to systemic hypotension or increased intraocular pressure. There is a syndrome of posterior ischemic optic neuropathy, lacking disk edema, but it is rare and much less well defined than the anterior ischemic syndromes. It may be difficult to distinguish ON from ischemic optic neuropathy. In contrast to ON, the visual loss in AION is usually permanent, although one-third of patients may improve somewhat.

Other Optic Neuropathies

Numerous other conditions may affect the optic nerve head, causing visual loss and disk abnormalities (e.g., glaucoma; LHON and other hereditary optic atrophies; toxins and drugs; primary and metastatic tumors; malnutrition and deficiency states; neurodegenerative disorders; leukodystrophies; sarcoid; optic perineuritis; and congenital anomalies). Dysthyroid optic neuropathy occurs as a late complication of thyroid orbitopathy when enlarged ocular muscles compress the nerve at the orbital apex. See [Table 13.3](#). It is important to distinguish ON from compressive lesions of the optic nerve. One characteristic feature of compressive optic neuropathy is that the condition continues to progress, often insidiously. Large, abnormal-appearing veins on the disk surface because of collateral venous drainage between the retinal and ciliary venous systems (optociliary shunt vessels) may provide a telltale clue to a compressive lesion ([Figure 13.24](#)). The triad of progressive visual loss, optic atrophy, and

optociliary shunt vessels is highly suggestive.



FIGURE 13.24 Pale, elevated optic disk with optociliary shunt vessels in a blind eye; the typical findings of an optic nerve meningioma. (Reprinted from Savino PJ, Danesh-Meyer HV; Wills Eye Hospital [Philadelphia, PA]. *Neuro-Ophthalmology*. 2nd ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins, 2012, with permission.)

Pseudopapilledema

Some conditions affecting the nerve head cause striking disk changes of little or no clinical import. This circumstance arises frequently when routine ophthalmoscopy unexpectedly reveals an abnormal-looking disk in a patient with migraine or some seemingly benign neurologic complaint. Such patients generally have normal vision and no visual complaints. Common causes of pseudopapilledema include optic nerve drusen and myelinated nerve fibers.

Optic nerve drusen, or hyaloid bodies, are acellular, calcified hyaline deposits within the optic nerve that may elevate and distort the disk (Figure 13.25). Drusen occur in about 2% of the population and are bilateral in 70% of cases. They are familial, inherited as an irregular dominant with incomplete penetrance, and occur almost exclusively in Caucasians. On the disk surface, drusen have a highly refractile, rock-candy appearance. But when buried beneath the surface,

drusen may produce only disk elevation and blurred margins, causing confusion with papilledema. Optic nerve drusen are not to be confused with retinal drusen, which are an age-related abnormality consisting of yellowish-white, round spots of variable size concentrated at the posterior pole. Myelinated nerve fibers occasionally extend beyond the disk margin into the retina, which causes a very striking disk picture but signifies nothing ([Figure 13.26](#)). Other causes of pseudopapilledema include remnants of the primitive hyaloid artery (Bergmeister's papilla), tilted disks ([Figure 13.27](#)), and extreme hyperopia.

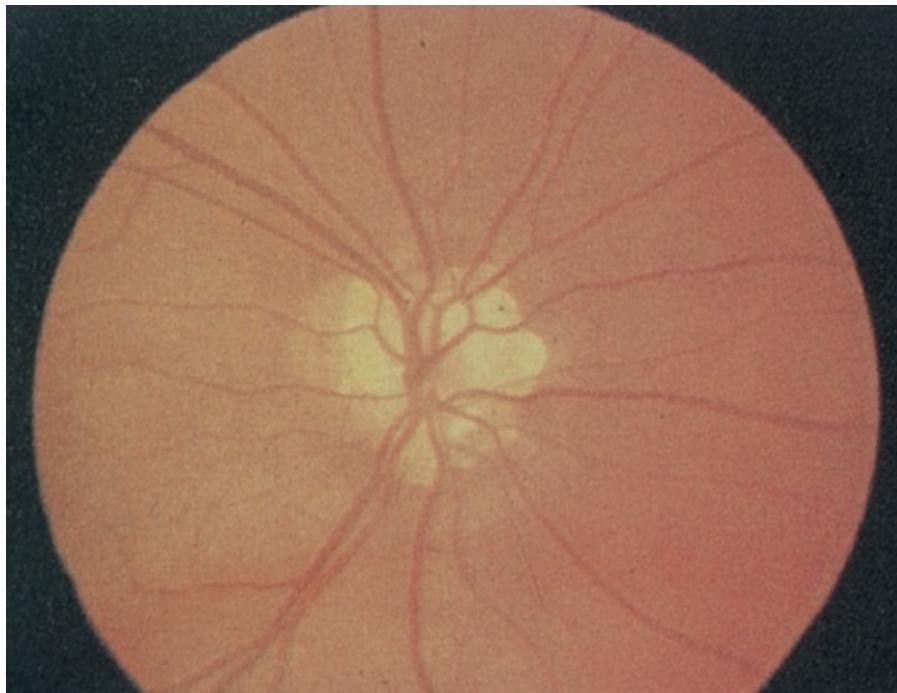


FIGURE 13.25 Drusen of the optic nerve head simulating papilledema.



FIGURE 13.26 Myelinated nerve fibers.

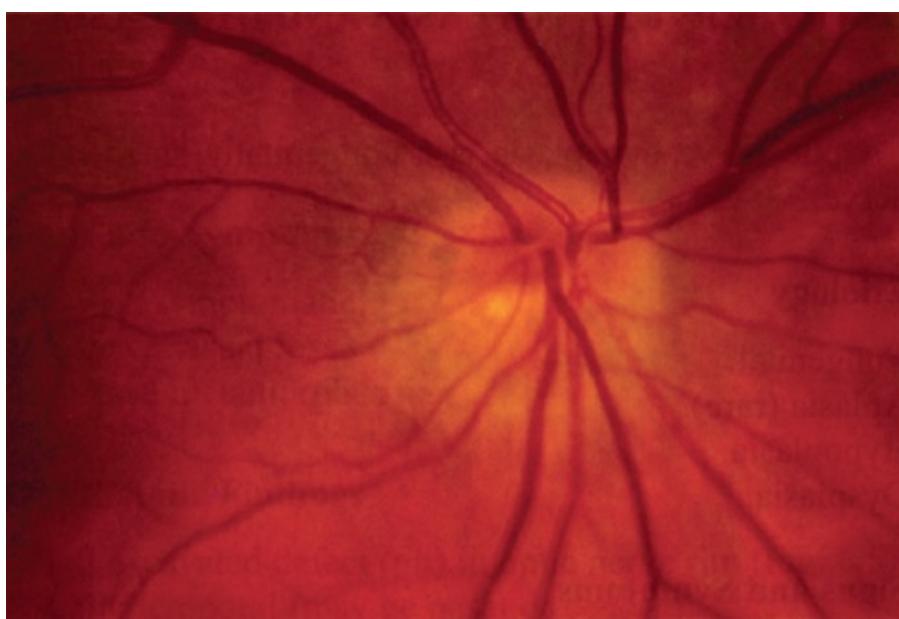


FIGURE 13.27 The congenital tilted optic disk is apparent as the oval of nerve tissue superiorly. There is no apparent optic cup. (Reprinted from Chern KC, Saidel MA.

Distinguishing pseudopapilledema from acquired disk edema can be difficult. Features that may be helpful include the following: in papilledema, the disk is usually hyperemic; the disk margin blurriness is at the superior and inferior poles early in the process; blood vessels look normal except for fullness of the veins; SVPs are absent; and the NFL is dull with the retinal blood vessels obscured because of retinal edema. In pseudopapilledema, the disk color remains normal; blurriness of the disk margin may be irregular, and the disk may have a lumpy appearance; SVPs are usually present; the blood vessels on the disk frequently look anomalous; and the NFL is clear. Hemorrhages are common in papilledema and extremely rare in pseudopapilledema. If in doubt, consult an ophthalmologist.

Optic Atrophy

In optic atrophy, the disk is paler than normal and more sharply demarcated from the surrounding retina, sometimes having a punched-out appearance ([Figure 13.28](#)). The disk margins stand out distinctly; the physiologic cup may be abnormally prominent and extend to the margin of the disk. Loss of myelinated axons and their supporting capillaries with replacement by gliotic scar produce the lack of color, which may vary from a dirty gray to a blue-white color to stark white. Loss of axons causes involution of the capillary bed of the disk and allows the sclera to show through, contributing to the pallor. Dark choroidal pigment deposits may be present about the margin of the disk. The depth of color of the choroid will influence the perception of the degree of contrast between the disk and retina. An atrophic disk may appear perceptibly smaller. Pallor of the temporal portion of the disk—a classical finding in MS—may precede definite atrophy, but normal physiologic temporal pallor makes this finding often equivocal.



FIGURE 13.28 Primary optic atrophy.

Optic atrophy may follow some other condition (ON, AION, or papilledema) and is then referred to as secondary or consecutive optic atrophy. Primary optic atrophy, appearing *de novo*, occurs as a heredofamilial condition (e.g., LHON) or after toxic, metabolic, nutritional, compressive, or glaucomatous insult to the nerve. Some causes of optic atrophy are listed in [Table 13.4](#). The term cavernous, or pseudoglaucomatous, optic atrophy is used if there is marked recession of the disk. Glaucoma is a common cause of optic atrophy; it produces both an increase in the depth of the physiologic cup and atrophy of the nerve ([Figure 13.29](#)). LHON is an uncommon mitochondrialopathy that affects only males; it may cause the appearance of disk edema acutely but evolves into optic atrophy. It typically affects young men and causes sudden unilateral visual loss with involvement of the fellow eye within days to months. Characteristic peripapillary telangiectasias are frequently present, even in the uninvolved eye. Bow-tie or band optic atrophy refers to pallor of the disk that may develop in an eye with temporal VF loss following a lesion of the optic chiasm or tract ([Box 13.7](#), [Figure 13.30](#)).

TABLE 13.4**Some Causes of Optic Atrophy**

Optic neuritis

Glaucoma

Trauma

Chronic papilledema

Ischemic optic neuropathy

LHON

Drugs

Toxins

Optic nerve compression

Deficiency states

Central nervous system syphilis

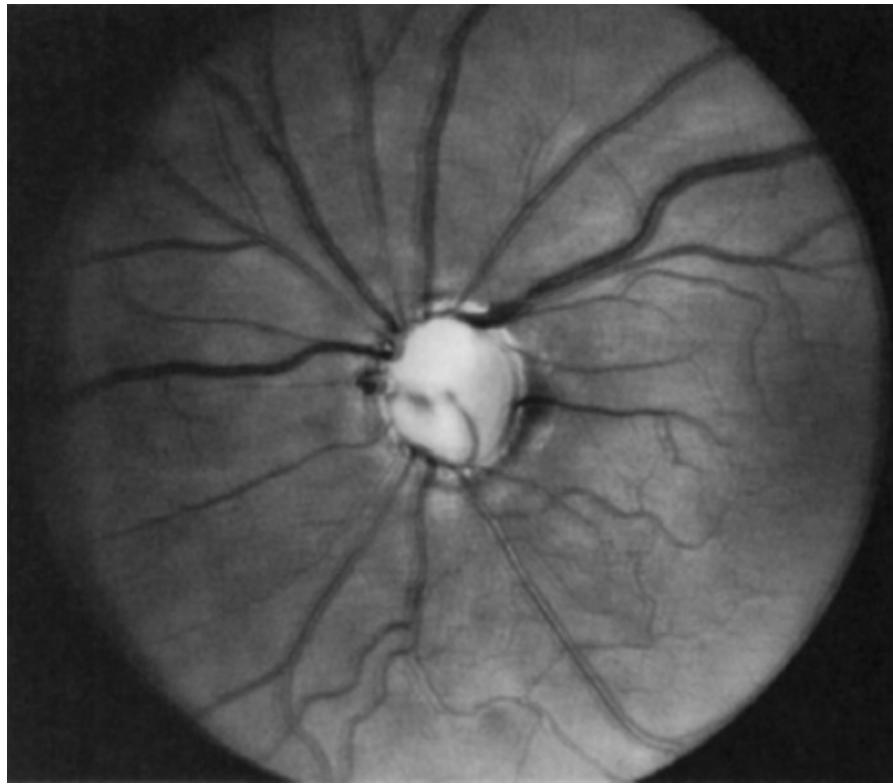


FIGURE 13.29 Glaucomatous optic atrophy. (Courtesy Richard A. Lewis.)

BOX 13.7

Bow-Tie (Band) Optic Atrophy

The macula lies temporal to the disk, and fibers from the nasal hemimacula enter the temporal aspect of the disk. These papillomacular fibers are responsible for the normal pallor of the temporal aspect of the disk, and the pallor is accentuated with NFL axon loss. There is also atrophy of the nasal hemiretinal NFL. Fibers from the peripheral nasal hemiretina enter the nasal aspect of the disk, and axon loss causes nasal disk pallor. With axon loss involving both nasal hemimacula and nasal hemiretina, the result is a transverse band of atrophy across the disk. The appearance is reminiscent of a white bow tie.



FIGURE 13.30 “Band” or “bow-tie” atrophy of the right optic disk in a patient with a temporal hemianopia caused by a pituitary adenoma. Note horizontal band of atrophy across the right disk, with preservation of the superior and inferior portions of the disk. (Reprinted from Miller NR, Bioussse V, Newman NJ, et al. *Walsh and Hoyt’s Clinical Neuro-Ophthalmology: The Essentials*. 2nd ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins, 2008, with permission.)

A patient may have disk edema in one eye and optic atrophy in the other eye. Foster Kennedy syndrome is due to an olfactory groove meningioma, causing anosmia (see [Chapter 12](#)), with optic atrophy because of direct compression ipsilateral to the neoplasm, and late contralateral papilledema because of increased intracranial pressure. Optic atrophy in one eye with disk edema in the other eye is now much more commonly seen with AION or ON (pseudo–Foster Kennedy syndrome), when the disease strikes the opposite eye weeks to months after an initial episode renders the originally affected disk atrophic.

Retrobulbar Optic Neuropathy

The retrobulbar portion of the nerve may be affected by most of the diseases that

affect the optic disk. The clinical picture is similar except that there is no disk edema acutely, but optic atrophy may follow later. When ON strikes the retrobulbar portion of the nerve, marked visual impairment occurs, but the disk appearance remains normal, because the pathology is posterior to the papilla. Optic papillopathy thus causes impaired vision and an abnormal disk; retrobulbar optic neuropathy causes impaired vision and a normal disk; and papilledema causes an abnormal disk but does not affect vision acutely. An old saw describes these differences aptly: when the patient sees (has normal vision) and the doctor sees (observes disk abnormalities), it is papilledema; when the patient doesn't see (has impaired vision) and the doctor sees (observes disk abnormalities), it is papillitis; when the patient doesn't see (has impaired vision) and the doctor doesn't see (observes no disk abnormality), it is retrobulbar neuritis.

A major difference between retrobulbar neuropathy and papillopathy is the increased incidence of compression as an etiology in the former. Mass lesions of many types, particularly neoplasms, can affect the retrobulbar optic nerve. Common causes include meningiomas of the optic nerve sheath or sphenoid wing, pituitary tumors, and distal carotid aneurysms. The possibility of compression always figures prominently in the differential diagnosis of patients with optic neuropathy. Insidious visual loss producing decreased acuity; impaired color perception; and central, cecocentral, or arcuate scotoma is typical. Compressive neuropathies may evolve more acutely in patients with metastatic lesions, particularly lymphoma. The optic neuropathy in low-pressure glaucoma may simulate the picture of compression.

Distal (Prechiasmal) Optic Neuropathy

Disorders that affect the distal portion of the optic nerve near its junction with the chiasm are similar to other retrobulbar optic neuropathies except that involvement of the Wilbrand's knee fibers may produce a junctional scotoma, which is highly localizing when present ([Figure 13.19C](#)). For this reason, it is important to pay particular attention to the temporal field of the opposite eye when examining a patient with optic neuropathy. The most common cause is pituitary tumor.

Chiasmal Lesions

Pituitary tumors, craniopharyngiomas, meningiomas, gliomas, and carotid aneurysms are the lesions that commonly involve the chiasm. Uncommon causes include demyelination, ischemia, radionecrosis, and a host of other conditions. Because the chiasm lies about a centimeter above the diaphragma sella, visual system involvement indicates suprasellar extension; chiasmatic mass effect is a late, not an early, manifestation of a pituitary tumor ([Figure 13.6](#)). Involvement of macular fibers may produce bitemporal scotomas. Chiasmal lesions rarely produce textbook bitemporal hemianopias. There is often a combination of chiasm and optic nerve or optic tract defects depending on whether the chiasm is prefixed, postfixed, or in normal position and the particular attributes of the mass and its force vectors ([Figure 13.7](#)). Generally, the defects are binocular and usually heteronymous. The deficit may develop so slowly as to pass unnoticed by the patient. Acuity, color vision, and pupillary function are not affected unless there is optic nerve involvement. Although binasal hemianopias can occur from chiasmal disease, optic neuropathy, glaucoma, and congenital anomalies are more common causes.

Retrochiasmal Lesions

Retrochiasmal lesions produce contralateral homonymous VF defects that respect the vertical meridian. Except for optic tract lesions, they do not cause any deficit of visual acuity, color perception, pupillary reactions, or disk appearance.

Optic tract and LGB lesions occur rarely, perhaps because of generous collateral blood supply; they are characterized by incongruous homonymous hemianopias that split the macula. Optic tract lesions may be accompanied by a mild APD in the contralateral eye because of a greater percentage of crossed pupillomotor fibers (see [Chapter 14](#)). Tract lesions may also result in bow-tie pattern disk pallor in the contralateral eye ([Box 13.7](#)) and more generalized pallor in the ipsilateral eye. Visual acuity remains normal. Etiologies of optic tract lesions include masses (e.g., meningioma, glioma, craniopharyngioma), aneurysms, AVMs, demyelinating disease, and trauma. Rarely, an APD can be seen with lesions elsewhere in the retrochiasmal pathways and even in the midbrain. Behr's pupil refers to a slightly dilated pupil because of an optic tract lesion, usually associated with a contralateral hemiparesis.

LGB lesions are rare and usually because of vascular disease. They cause a contralateral homonymous hemianopia that is somewhat incongruous,

occasionally with a wedge-shaped or hour-glass pattern along the horizontal meridian pointing to fixation (sectoranopia or keyhole defect) and splits the macula. The unusual pattern is due to the organization of the LGB and to its dual blood supply. Etiologies of an LGB lesion include ischemia, neoplasm, AVM, demyelinating disease, and trauma.

In geniculocalcarine pathway (optic radiation) lesions, temporal lobe pathology typically produces contralateral superior quadrantanopias, or homonymous hemianopia, worse in the upper quadrants; and parietal lobe processes contralateral inferior quadrantanopias, or homonymous hemianopia, worse in the lower quadrants ([Figure 13.19](#)). The more posterior the lesion, the more congruous the defect. Parietal lesions are associated with asymmetric OKN responses. Parietal lobe lesions may be accompanied by other evidence of parietal lobe dysfunction, such as cortical sensory loss, aphasia, apraxia, agnosia, anosognosia, and hemispatial neglect ([Chapters 9, 10, and 35](#)).

In the occipital lobe, the upper retinal fibers (lower VF) synapse on the upper bank, and the lower retinal fibers synapse on the lower bank of the calcarine cortex, which is separated by the calcarine fissure ([Figure 13.12](#)). The macular representation is massive, taking up the occipital pole and about 40% to 50% of the contiguous cortex. Occipital lobe lesions cause contralateral homonymous hemianopias that are highly congruous, tend to spare the macula, and do not affect OKN responses. Macular sparing is thought to be due in part to middle cerebral artery collaterals that help to preserve macular function despite a posterior cerebral artery territory infarct. Conversely, the occipital pole is an area of border zone perfusion between the middle and posterior cerebral arteries, and hypotensive watershed infarctions may cause contralateral homonymous paracentral scotomas because of ischemia limited to the macular cortex ([Figure 13.19D](#)). Bilateral occipital lobe lesions causing bilateral hemianopias may cause decreased visual acuity. Bilateral occipital infarcts with macular sparing may leave only constricted tunnels of central vision, as though looking through pipes. Although acuity may be normal, the functional visual impairment is extreme because of the constricted peripheral vision, analogous to end-stage retinitis pigmentosa. Occipital lobe lesions may spare the monocular temporal crescent if the damage does not involve the anterior part of the cortex. Conversely, small far anteriorly placed lesions may involve only the temporal crescent in the contralateral eye (half [quarter might be more appropriate] moon or temporal crescent syndrome). Preservation of the temporal crescent results in strikingly incongruous fields. Preservation of the temporal crescent has been

called an “endangered” finding because it requires the now seldom used kinetic (Goldmann) perimetry; the currently used static perimetric techniques that concentrate on the central 30 degrees of the VF tend to miss this phenomenon ([Figure 13.31](#)).

Bilateral occipital lesions may also cause some dramatic defects of cortical function in addition to the visual loss. Anton’s syndrome is cortical blindness because of bilateral homonymous hemianopias, with extreme visual impairment in which the patient is unaware of, and denies the existence of, the deficit. Anton’s syndrome and related disorders are discussed in [Chapter 10](#).

Most occipital lesions are vascular. Many anterior temporal lobe lesions are neoplastic. Parietal lesions may be either. The greater likelihood of tumor in the parietal lobe gives rise to Cogan’s rule regarding OKNs (see [Chapter 14](#)). Trauma, vascular malformations, abscesses, demyelinating disease, metastases, and other pathologic processes can occur in any location.

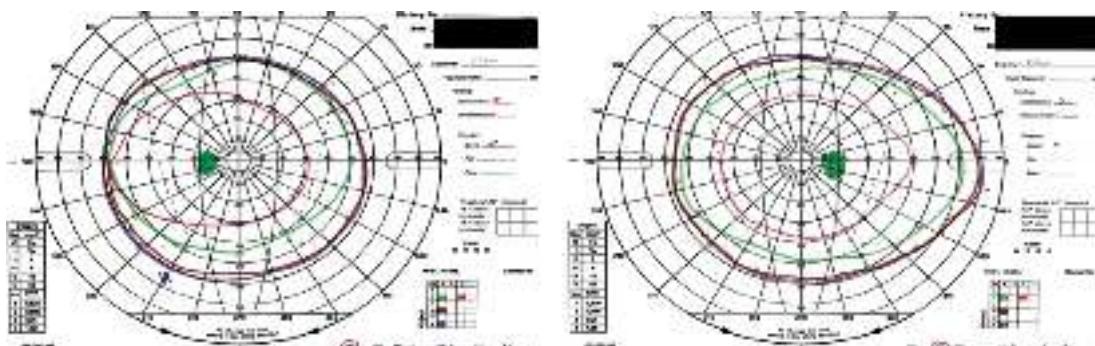


FIGURE 13.31 Loss of the temporal crescent in a patient with an infarct in the right anterior occipital lobe. Kinetic perimetry demonstrates a full peripheral field in the right eye (right), but there is loss of the far temporal field (the temporal crescent) in the left eye (left). (Reprinted from Miller NR, Bioussse V, Newman NJ, et al. *Walsh and Hoyt’s Clinical Neuro-Ophthalmology: The Essentials*. 3rd ed. Philadelphia: Wolters Kluwer, 2016, with permission.)

Other Abnormalities of the Ocular Fundus

Other abnormalities of the fundus are also important to detect in neurologic patients. The fundus may reveal evidence of hypertensive retinopathy in the patient with stroke, especially in the lacunar syndromes. In the patient with hypertensive encephalopathy, there may be spasm of retinal arterioles. Retinal emboli may be seen in the patient with possible cerebrovascular disease. In the patient with acute severe headache, the finding of subhyaloid (preretinal) hemorrhage is pathognomonic for subarachnoid hemorrhage ([Figure 13.32](#)). The

presence of a cherry red spot indicates a condition such as gangliosidosis, lipid storage disease or mucopolysaccharidosis in the younger patient (e.g., Tay-Sachs disease), or a central retinal artery occlusion in the older patient ([Figure 13.33](#)). In storage diseases, the cherry red spot is seen because of the accumulation of abnormal material within the cell layers of the retina. Because of the relative transparency of the macula, the underlying choroid is visible. In central retinal artery occlusion, the preservation of blood supply to the macula from the choroidal circulation makes it stand out against the retina made pale by ischemia. Pigmentary retinopathy is seen in such conditions as Kearns-Sayre syndrome and other mitochondrialopathies.



FIGURE 13.32 Subhyaloid hemorrhage in a patient with subarachnoid hemorrhage (Terson's syndrome). The hemorrhage occurs between the posterior layer of the vitreous and the retina, is globular, and often forms a meniscus.

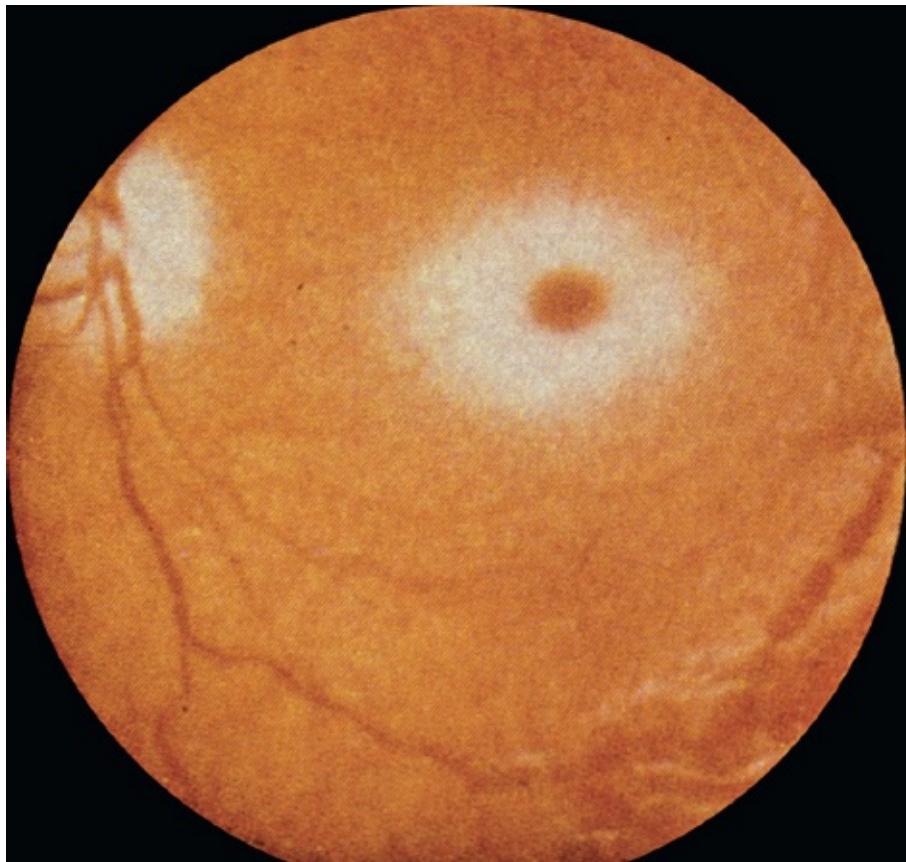


FIGURE 13.33 Cherry red spot in a patient with a lipid storage retinopathy.

Video Links

Video Link 13.1. Afferent pupillary defect.

https://collections.lib.utah.edu/details?id=180307&q=sort_type_t-%3A%2AMovingImage%2A+AND+afferent+pupillary+defect&f%2Csubject_t%2Ccollection_t&rows=50&sort=sort_title_t+asc&c

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CHAPTER 14

The Ocular Motor Nerves

ANATOMY AND PHYSIOLOGY

By convention, the phrase ocular motor nerves refers to cranial nerves (CNs) III, IV, and VI, and the term oculomotor nerve refers specifically to CN III. The orbits and the globes lie in the skull divergently, making the anatomic axes of the eyes diverge slightly from the visual axes, which lie straight ahead for distance vision and convergently for near vision. In sleep and coma, the eyes rest in the divergent position of anatomic neutrality. In wakefulness, cerebral cortical activity influencing the extraocular muscles lines the eyes up for efficient, binocular vision. Phorias and tropias are manifestations of the latent or manifest tendency, respectively, of the eyes to drift away from the visual axis (see [Box 14.4](#)).

The four rectus muscles arise from a common structure in the orbital apex, the annulus of Zinn. The annulus is a thickening of the periosteum that forms a circular tendon, its center pierced by the optic nerve, central retinal artery and CNs III and VI, and the recti arising from its body. The rectus muscles insert on the sclera 5 to 7 mm posterior to the limbus.

The nervous system attempts to maintain visual fusion of images by controlling precisely the movements of the two eyes. The extraocular muscles work in pairs that are yoked together and work in concert to perform a certain action. The superior and inferior recti lie in the orbit, and insert into the globe, along the anatomic axis, exerting their maximally efficient pull when the eye is slightly abducted ([Figure 14.1](#)). The superior and inferior obliques insert into the globe at an angle of about 30 degrees from medial to lateral; they exert maximal pull with the eye slightly adducted. The obliques insert posteriorly into the globe: the superior oblique pulls the back of the eye up, producing downgaze; the inferior oblique pulls the back of the eye down, producing upgaze. The

superior oblique therefore works as a depressor of the adducted eye, the inferior oblique as an elevator; they move the globe in the direction opposite their names ([Figure 14.2](#)).

To achieve conjugate downgaze to one side, the superior oblique of the adducting eye is yoked to the inferior rectus of the abducting eye ([Figure 14.3](#)). In fact, even in adduction, most of ocular elevation and depression is accomplished by the superior and inferior rectus, and the major action of both obliques is torsional (cyclotorsional, rotational). The primary action—some contend the only action—of the superior oblique is to intort (incyclotort) and of the inferior oblique to extort (excyclotort). Because of its angle of insertion along the anatomic axis, when the eye is in primary gaze, the inferior rectus acts not only to depress the eye but also to extort it. The yoked superior oblique, through its intorsion action, counteracts the extorsion effect of the inferior rectus so that downgaze is smooth and linear. Likewise, the superior rectus and the inferior oblique.

Because of the anatomical arrangement of the obliques and vertically acting recti, examination of extraocular movement should include gaze to the right and left plus upgaze and downgaze in eccentric position to both sides: the six cardinal directions of gaze ([Figure 14.3](#)). The levator palpebrae superioris supplies the striated muscles of the eyelid and elevates the lid.

THE OCULOMOTOR NERVE

The oculomotor, or third cranial nerve (CN III), arises from the oculomotor nuclear complex in the midbrain and conveys motor fibers to extraocular muscles, plus parasympathetic fibers to the pupil and ciliary body. These nuclear centers are situated in the periaqueductal gray matter just anterior to the aqueduct of Sylvius, at the level of the superior colliculi (anterior quadrigeminal bodies). The median longitudinal fasciculus (MLF) abuts the nucleus laterally and ventrally ([Figure 14.4](#)). Each oculomotor nucleus consists of multiple adjacent subnuclei that innervate specific ocular muscles. The neurons are somatic motor (general somatic efferent). The paired lateral nuclei are the largest and are situated anterior and lateral to the others; their medial portions are fused into an unpaired mass. CN III has a superior and an inferior division. The superior division supplies the levator palpebrae superioris and superior rectus muscles. The inferior division supplies the medial and inferior recti, the inferior

oblique, and the pupil. The lateral subnucleus innervates the ipsilateral inferior oblique and medial and inferior recti; its axons make up the inferior division of CN III. The superior rectus muscle is innervated by the contralateral medial subnucleus. Because of its crossed innervation, a major clue to the presence of a nuclear third nerve palsy is superior rectus weakness in the opposite eye.

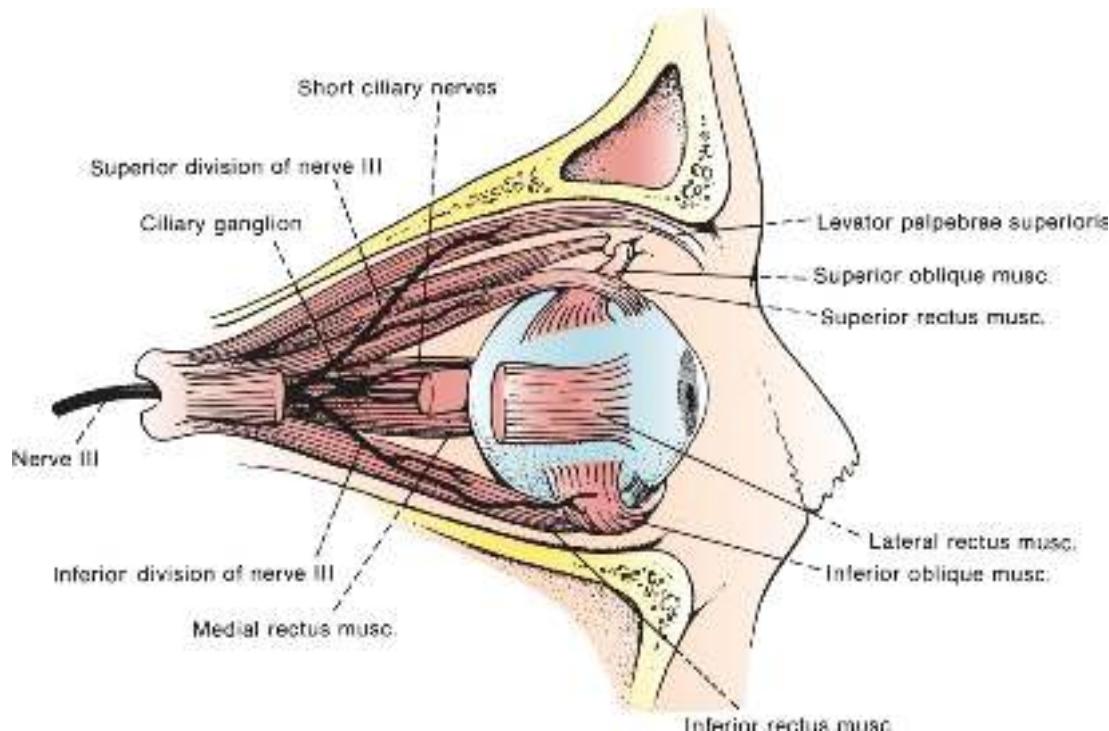


FIGURE 14.1 The extraocular muscles and the third nerve in the orbit.

A single midline structure, the central caudal nucleus, supplies the levator palpebrae muscles on both sides. The periaqueductal gray matter is also involved with eyelid function; destructive lesions there may cause ptosis. A supraoculomotor area in the ventral periaqueductal gray matter controlling levator function has been proposed. The Edinger-Westphal (EW) nuclei are part of the craniosacral, or parasympathetic, division of the autonomic nervous system. The EW subnucleus is a single structure that provides parasympathetic innervation to both sides. It is spread throughout the length of the oculomotor complex with a paired rostral portion and an unpaired medial and caudal portion. Preganglionic fibers from the EW nuclei go to the ciliary ganglion (Figure 13.9). Postganglionic fibers derived from cells in the rostral part of the subnucleus supply the pupillary sphincter; those derived from the anteromedial nucleus supply the ciliary muscle and function in accommodation. Fibers from the

medial, EW, and central caudal subnuclei form the superior division of CN III.
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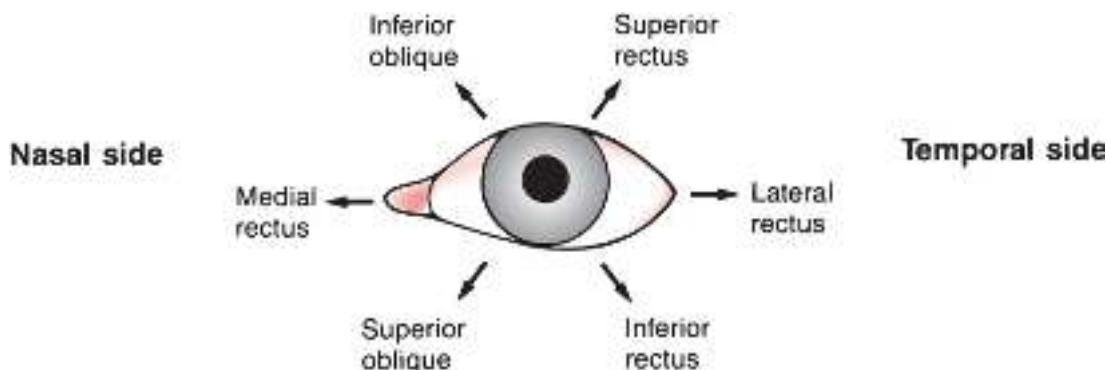


FIGURE 14.2 Actions of the extraocular muscles on the left eye. Arrows denote the main directions of action for each muscle, resulting from a combination of movements of the globe in the three dimensions.

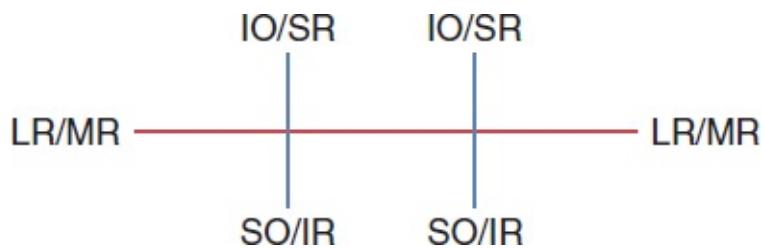


FIGURE 14.3 The yoke muscles control extraocular movement in the six cardinal directions of gaze.

Fibers from the ipsilateral lateral subnucleus, from the contralateral medial subnucleus (superior rectus), and from both central caudal (levator palpebrae) and EW (parasympathetics) nuclei join to form the filaments of CN III, which course anteriorly through the mesencephalon, traversing the medial portion of the red nucleus and the substantia nigra. The nerve exits from the interpeduncular fossa on the anterior surface of the midbrain just above the pons ([Figure 11.3](#)). It travels anteriorly and passes between the superior cerebellar and posterior cerebral arteries ([Figure 14.5](#)). It runs forward parallel to the posterior communicating artery. Third nerve palsy is a classic and important sign of posterior communicating aneurysm. In its course toward the cavernous sinus, it lies on the free edge of the tentorium cerebelli, medial to the temporal lobe. Here, it is at risk of compression because of uncal herniation. Through the nerve's subarachnoid course, the parasympathetic fibers lie superficially on the dorsomedial surface. The location of these fibers influences whether a third nerve palsy will or will not involve the pupil, an important differential diagnostic

point. CN III penetrates the dura just lateral and anterior to the posterior clinoid processes and enters the cavernous sinus, where it lies in the upper aspect, close to the lateral wall ([Figure 14.6](#)). In the cavernous sinus, CN III has important relationships with the carotid artery, ascending pericarotid sympathetics, and CNs IV, V, and VI. CN III separates into its superior and inferior divisions in the anterior cavernous sinus, then enters the orbit through the superior orbital fissure, and passes through the annulus of Zinn. It sends a short root to the ciliary ganglion, from which postganglionic fibers go as the short ciliary nerves to supply the ciliary muscle and the sphincter pupillae ([Figure 14.1](#)). The sphincter pupillae causes constriction of the pupil. Contraction of the ciliary muscle causes relaxation of the ciliary zonule, decreasing the tension on the lens capsule and allowing it to become more convex to accommodate for near vision. Pupillary constriction, convergence, and accommodation are all part of the near reflex.

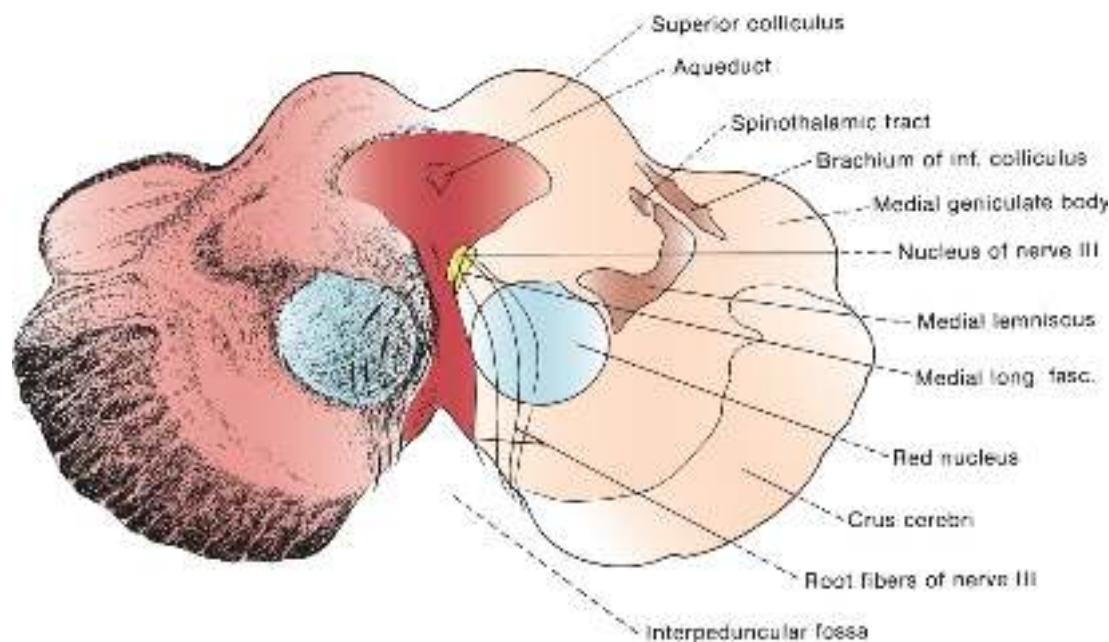


FIGURE 14.4 Section through the mesencephalon at the level of the superior colliculus and oculomotor nucleus.

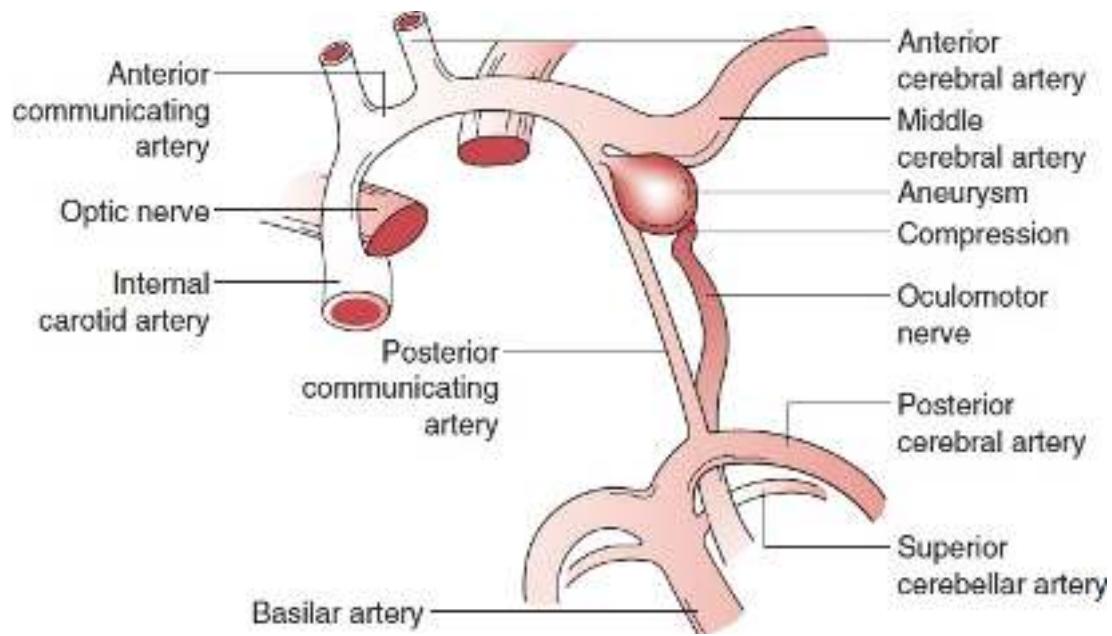


FIGURE 14.5 Anatomy of the oculomotor nerve in relation to the major arteries at the base of the brain. An aneurysm arising from the posterior communicating artery is compressing and distorting the nerve.

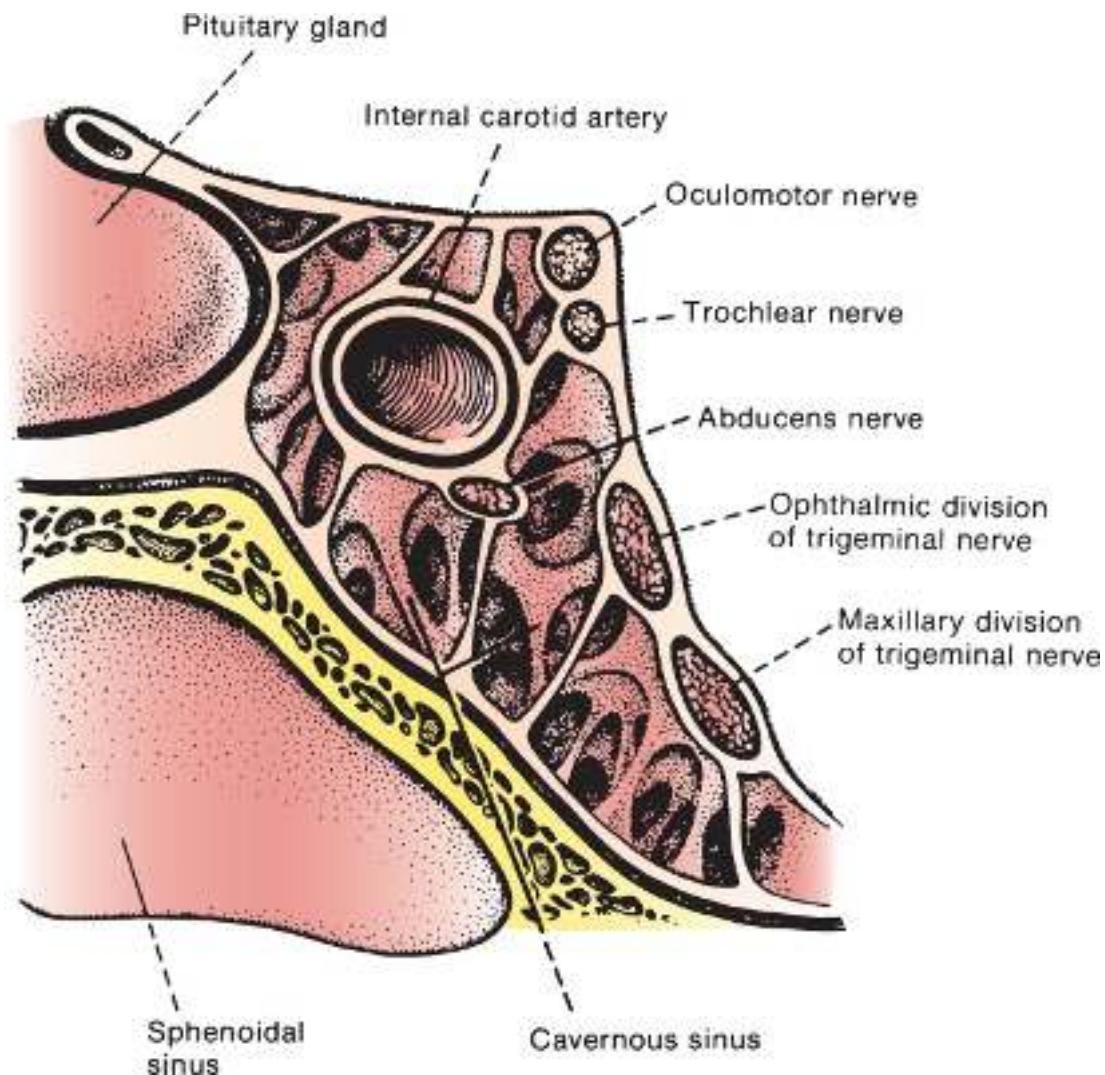


FIGURE 14.6 Oblique section through the cavernous sinus.

THE TROCHLEAR NERVE

The trochlear, or fourth cranial nerve (CN IV), is the smallest CN. It arises from the trochlear nucleus located just anterior to the aqueduct in the gray matter of the lower mesencephalon at the level of the inferior colliculus, immediately above the pons (Figure 14.7) and caudal to the lateral nucleus of CN III but separated by a short distance. The nucleus contains somatic motor neurons. The nerve filaments curve posteriorly around the aqueduct, decussate in the anterior medullary velum, and exit through the tectum. It is the only CN to exit from the brainstem posteriorly, and because of this extra distance, CN IV has the longest intracranial course of any of the CNs. The nerve circles the brainstem, then turns

and runs forward, passing between the posterior cerebral and superior cerebellar arteries, and then courses along the tentorium. It penetrates the dura just behind and lateral to the posterior clinoid processes and enters the cavernous sinus in proximity to CN III. In the sinus, it is located superolaterally, below CN III but above the trigeminal branches. Leaving the cavernous sinus, it traverses the superior orbital fissure, enters the orbit, and crosses over CN III to supply the superior oblique. It does not pass through the annulus of Zinn.

CN IV terminates on the superior oblique muscle on the side opposite the nucleus of origin. In a nuclear lesion of the fourth nerve, the contralateral superior oblique muscle is weakened; in an extramedullary lesion along the course of the nerve, the ipsilateral muscle is involved.

THE ABDUCENS NERVE

The nucleus of the abducens, or sixth cranial nerve (CN VI), lies in the mid to lower pons, in the gray matter of the dorsal pontine tegmentum in the floor of the fourth ventricle, encircled by the looping fibers of the facial nerve ([Figure 14.8](#)). The nucleus is made up of somatic motor neurons. The nerve exits anteriorly at the pontomedullary junction, crosses the internal auditory artery, and then ascends the clivus in the prepontine cistern. It passes near the gasserian ganglion, makes a sharp turn over the petrous apex, pierces the dura at the dorsum sellae, and traverses the Dorello's canal between the posterior clinoid process and the petrous apex. The petroclinoid ligament forms the roof of the canal. The nerve enters the cavernous sinus in company with CNs III and IV, where it lies below and medial to CN III and just lateral to the internal carotid artery. CN VI is the only nerve that lies free in the lumen of the sinus; the others are in the wall ([Figure 14.6](#)). It enters the orbit through the superior orbital fissure and the annulus of Zinn to innervate the lateral rectus.

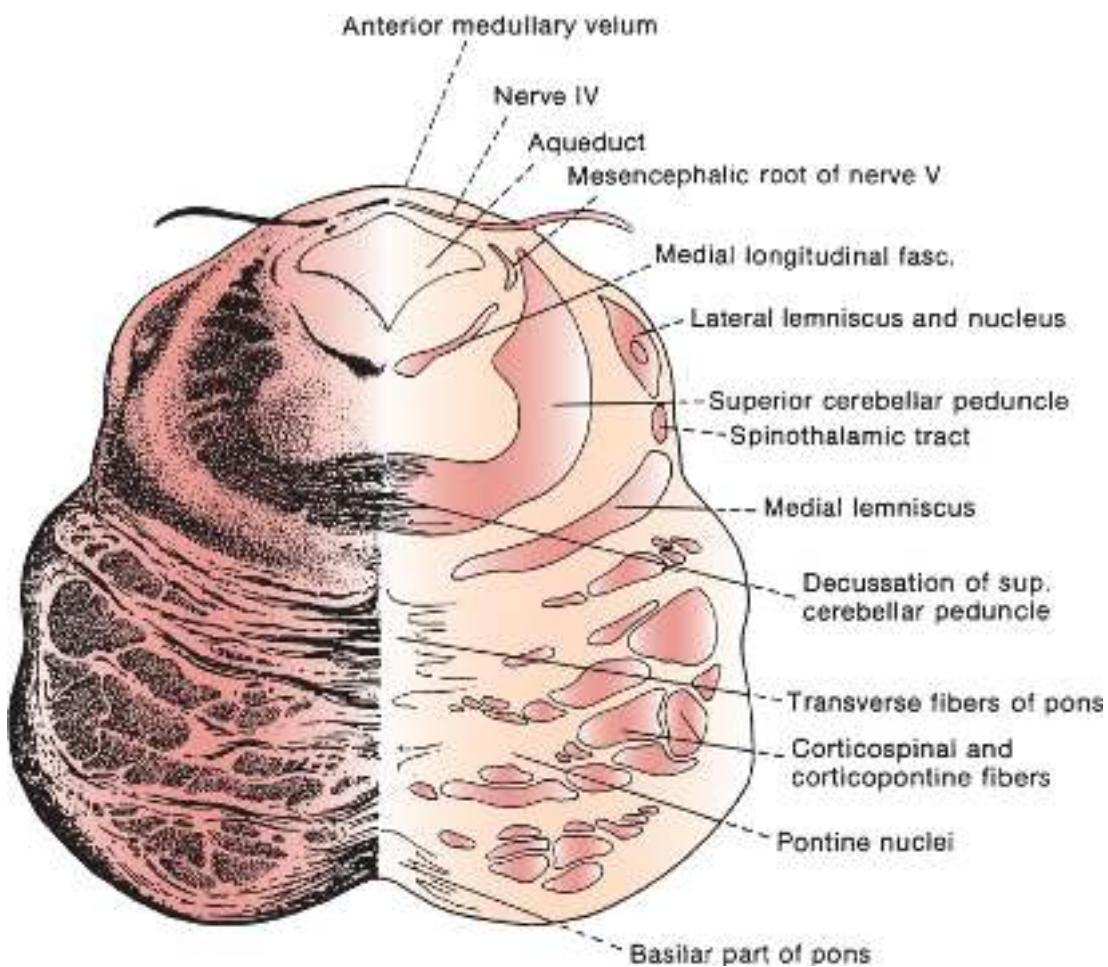


FIGURE 14.7 Section through the mesencephalon at the border of the pons, showing the trochlear nerve.

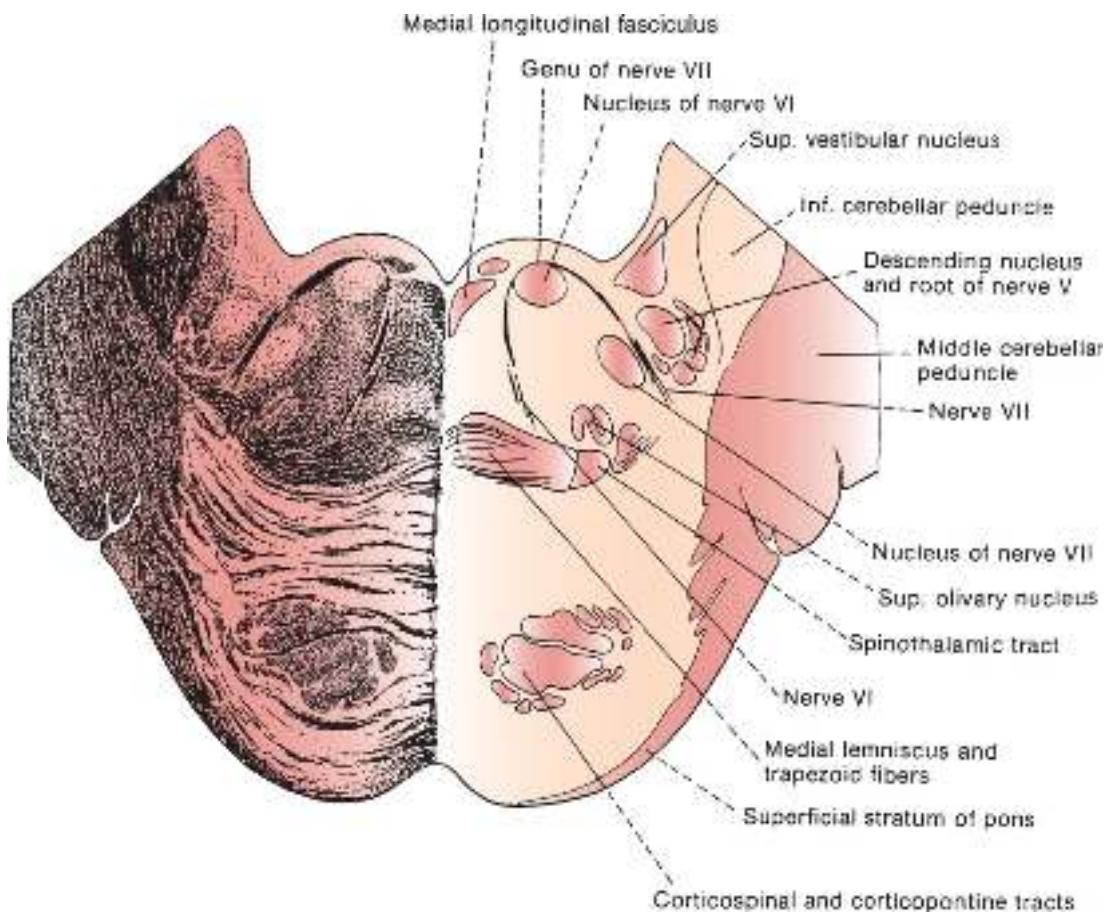


FIGURE 14.8 Section through the pons showing fibers of the abducens and facial nerves.

SUPRANUCLEAR CONTROL OF GAZE

The supranuclear mechanisms that control gaze are designed to ensure that the fovea maintains fixation on the object of interest despite movements of the object, the eyes, or the head. A saccade (Fr. “jerk”) is a quick, small-amplitude eye movement used to acquire a target. Smooth pursuit mechanisms use slower eye movements to track a target once acquired. Saccades are designed to rapidly shift gaze to the target; pursuit movements are designed to maintain foveation of a moving target. The CN VI nucleus is the final common pathway controlling horizontal eye movements. The vertical gaze centers lie in the midbrain. There are six currently recognized eye movement control systems: saccadic, smooth pursuit, vergence, fixation, optokinetic, and vestibuloocular reflex (VOR).

Four interconnected cortical areas are involved in the generation of saccades: the frontal eye field (FEF), which lies anterior to the motor strip in the premotor

cortex in the second frontal gyrus; the supplementary eye field, which lies in the supplementary motor area; the dorsolateral prefrontal cortex, which lies anterior to the FEF in the second frontal gyrus; and the posterior eye field, which lies in the parietal lobe.

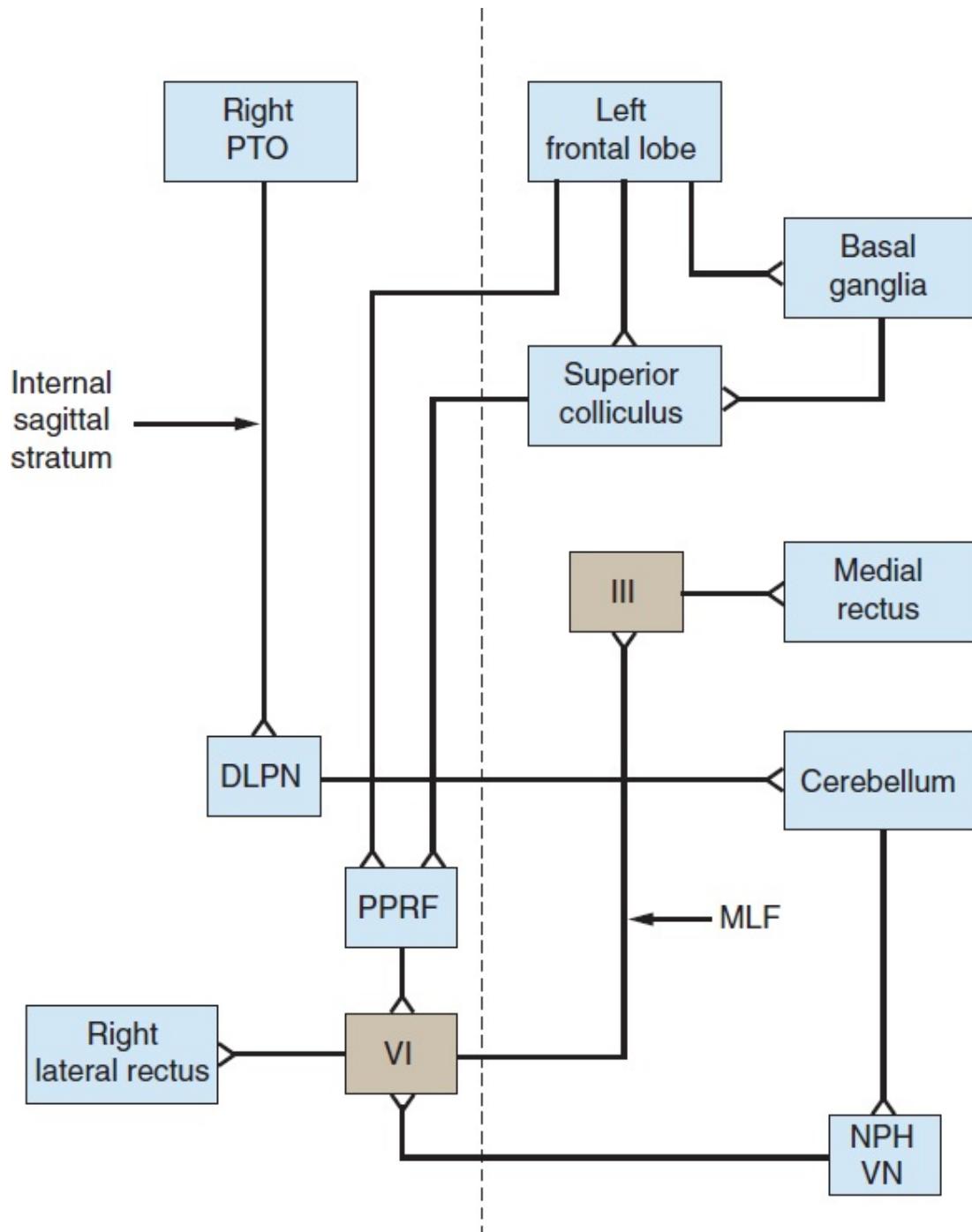


FIGURE 14.9 Diagram of the major supranuclear gaze pathways. The saccadic pathway arises in the frontal lobe and descends to the contralateral pons. The pursuit

pathway arises in the region of the parietotemporal-occipital junction (PTOJ) and descends to the ipsilateral pons. Vertical dashed line represents the midline. III, nucleus of CN III; VI, nucleus of cranial nerve (CN) VI; DLPN, dorsolateral pontine nuclei; MLF, medial longitudinal fasciculus; NPH, nucleus prepositus hypoglossi; PPRF, pontine paramedian reticular formation; VN, vestibular nuclei.

The FEF controls horizontal conjugate saccades to the opposite side. Fibers descend and decussate en route to the pontine paramedian reticular formation (PPRF) (Figure 14.9). Other fibers descend to the superior colliculus and are then relayed to the contralateral PPRF. The FEF to the superior colliculus pathway and the posterior eye fields are likely involved in reflex saccades. The PPRF (horizontal gaze center, lateral gaze center, pontine gaze center) is a premotor area that consists of cells lying ventrolateral to the MLF from the level of the abducens nucleus extending rostrally to near the trochlear nucleus. Signals from the PPRF activate both motor neurons and interneurons in the adjacent CN VI nucleus. The CN VI motor neurons activate the ipsilateral lateral rectus, whereas the interneurons simultaneously send impulses up the MLF, which decussates just rostral to the PPRF and runs to the medial rectus subnucleus of the contralateral oculomotor nuclear complex in the midbrain to activate the medial rectus. The ipsilateral lateral rectus and contralateral medial rectus then contract synchronously to produce conjugate horizontal gaze. A left FEF-initiated command to look right is thus transmitted down to the right PPRF, which simultaneously influences the right sixth nerve to contract the lateral rectus and the left third nerve to contract the yoked medial rectus—both contract, according to Hering's law, exactly the same amount.

The PPRF contains burst and pause neurons. The burst neurons fire a high-frequency pulse of discharges to initiate an ipsilateral saccade. The burst neurons determine saccadic velocity. The pause neurons lie in the nucleus raphe interpositus. Their tonic discharges prevent the burst cells from initiating extraneous saccades, and the tonic firing pauses just before and during saccades. Smooth pursuit signals to the PPRF come from the vestibular nuclei and the nucleus prepositus hypoglossi, which lies in the perihypoglossal nuclear complex. Step cells in the perihypoglossal nuclei control the impulses that maintain the eyes in an eccentric position following a saccade. To acquire and maintain an eccentric stationary target, the CN VI motor neurons would have a pulse of activity generated by the burst cells to create the saccade, followed by a step-up of firing generated by the step cells to maintain the new position. All movements would be conjugate and synchronous because of coordination with

the fellow eye by the MLF.

The dorsolateral prefrontal cortical area may be involved in mechanisms responsible for inhibiting unwanted saccades. Antisaccades are voluntary saccades away from a target. Patients with frontal lobe disease, progressive supranuclear palsy (PSP), Parkinson's disease, Alzheimer's disease, and schizophrenia, when asked to look away from a visual stimulus, may be unable to inhibit a saccade toward the target (prosaccade) and are therefore unable to make an antisaccade or make it only after a prosaccade. Another system involved in saccades works through the basal ganglia. Collaterals from the FEF go to the head of the caudate and putamen, which send fibers to the ipsilateral substantia nigra. Neurons in the pars reticulata project to the superior colliculus, which then projects to the PPRF. Disturbances in this system may explain some of the abnormalities of ocular motor control that occur in basal ganglia disorders, particularly Parkinson's disease.

The FEF to the contralateral PPRF system controls saccadic eye movements. The smooth pursuit system originates ipsilaterally in the region of the parietotemporal-occipital junction (PTOJ) and functions to maintain foveation of a moving target. The visual cortex sends information about the target to the extrastriate cortex at the PTOJ. From there, fibers descend in the internal sagittal stratum adjacent to the atrium of the lateral ventricle down to the ipsilateral dorsolateral pontine nuclei. The system then double decussates. The dorsolateral pontine nuclei project to the contralateral cerebellum. Signals from the cerebellum then activate the medial vestibular nucleus and the nucleus prepositus hypoglossi, which in turn project to the contralateral PPRF. The PPRF then coordinates conjugate horizontal pursuit movements. The PTOJ also sends corticocortical fibers to the ipsilateral frontal lobe. Smooth pursuit to the right is controlled by the right occipital region. Quick refixation saccades back to the left are mediated by the right FEF, so the process of following a series of moving objects (as in optokinetic nystagmus [OKN], or railroad nystagmus) is all accomplished in the same cerebral hemisphere.

The vergence system controls the degree of convergence or divergence of the eyes, maintaining macular fixation no matter what the distance to the target. The vestibular system has a large input into the oculomotor system in order to maintain proper eye orientation in relation to head and body position. The VOR produces conjugate eye movements of equal magnitude but in the opposite direction to compensate for head movements in order to maintain foveation during motion of the head. The VOR is discussed in more detail in [Chapter 17](#).

The pathways controlling upgaze and downgaze course in the region of the rostral midbrain, pretectum, and posterior commissure. The vertical gaze equivalent of the PPRF is the rostral interstitial nucleus of the MLF (riMLF), which lies in the midbrain near the red nucleus. The lateral portion of the riMLF is concerned with upgaze, the medial portion with downgaze. The riMLF send impulses to the nuclei of CNs III and IV. Connections via the posterior commissure coordinate the activity on the two sides. The interstitial nucleus of Cajal (INC) lies caudal to the riMLF. Its neurons connect to the riMLF and are involved in vertical pursuit and gaze holding. Upgaze and downgaze pathways occupy different positions, and abnormalities may affect one without the other. The upgaze centers lie more dorsally. Lesions in the region of the posterior commissure may disturb vertical gaze, especially upgaze (Parinaud's syndrome). The downgaze centers lie more ventrally, and lesions there may primarily affect downgaze.

Bhidayasiri et al. developed a hypothetical scheme to account for clinical disorders of vertical gaze based on recent insights gained from experimental studies. Vertical saccades are generated by burst neurons in the riMLF, with unilateral innervation of depressor muscles but bilateral innervation of elevator muscles. The riMLF is also a torsional saccade generator. Torsional deviation during an attempted vertical saccade, together with a vertical gaze palsy, occurs with lesions involving the riMLF. The INC acts similar to the step neurons in the PPRF, holding the eye in the new position after a vertical saccade. The INC projects to ocular motoneurons via the posterior commissure. Bilateral INC or posterior commissure lesions cause defects of vertical gaze.

Reflex upgaze occurs with forceful eyelid closure (Bell's phenomenon), and in some conditions, reflex upgaze may be preserved when upgaze is otherwise paralyzed. Levator palpebrae and superior rectus muscle tone are normally matched. In extreme downgaze, both are maximally inhibited, but in reflex upgaze, the normal parallel innervation becomes reversed.

THE MEDIAL LONGITUDINAL FASCICULUS

The oculomotor, trochlear, and abducens nuclei make up one more or less continuous cell column. They are united for coordinated and conjugate action by the MLF, an extensive and prominent fiber tract that runs in the midline in the dorsal tegmentum of the brainstem. The MLF extends from the midbrain down

to the upper thoracic spinal cord. It has many connections. Its primary function is to coordinate lateral gaze by connecting the sixth nerve nucleus on one side with the third and fourth nerve nuclei on the opposite side in order to allow the two eyes to move synchronously. Signals from the PPRF activate interneurons in the adjacent sixth nerve nucleus, which send axons up the MLF. The MLF crosses in the pons, soon after beginning its ascent to the contralateral third nerve complex. Lesions of the MLF disrupt communication between the two nuclei, causing internuclear ophthalmoplegia (INO). The MLF also has extensive connections with CNs V, VII, VIII, XI, and XII, and with the motor nuclei of the upper cervical nerves. Nuclear groups in the rostral midbrain are involved in MLF function, including the nucleus of the posterior commissure (nucleus of Darkshevich), INC (the nucleus of the MLF), and the riMLF. These connections coordinate movement of the two eyes, as well as head and eye, and even body movements. The MLF mediates reflex head and eye movements in response to various stimuli and is important in auditory-ocular, vestibular-ocular, and righting reflexes.

SYMPATHETIC INNERVATION

The sympathetic pathway to the eye begins in the hypothalamus. Fibers of the first-order neuron descend through the brainstem and upper cervical spinal cord. The second-order neuron lies in the intermediolateral gray column at C8-T2 of the upper thoracic spinal cord (ciliospinal center of Budge). Axons exit through the anterior roots and transverse the gray rami communicantes, and then arch over the apex of the lung and beneath the subclavian artery to enter the cervical sympathetic chain, where they ascend to synapse on the third-order neuron in the superior cervical ganglion at the level of the carotid bifurcation.

Postganglionic fibers of the third-order neuron lie on the wall of the common carotid artery, forming the pericarotid sympathetic plexus. Sympathetic fibers innervating facial structures follow the external carotid at the bifurcation. Sympathetic fibers destined for the eye follow the internal carotid artery. A lesion proximal to the carotid bifurcation causes Horner's syndrome (ptosis, miosis, and anhidrosis), and a lesion distal to the bifurcation causes oculosympathetic paresis (Horner's syndrome minus facial anhidrosis). The effects on the eye of oculosympathetic paresis and Horner's syndrome are the same, and the terms are often used interchangeably; subsequent discussion refers

to Horner's syndrome. The pericarotid sympathetic plexus continues along the internal carotid artery in its course through the cavernous sinus. Sympathetic fibers migrate to CN VI for a short distance, then join the nasociliary branch of CN V₁, and enter the orbit through the superior orbital fissure. They continue as long ciliary nerves to the pupillodilator muscle ([Figure 14.10](#)).

Sympathetically innervated smooth muscle is present in both the upper and lower lids to serve as accessory retractors. The upper lid muscle is better organized and identified, and it is referred to as the accessory levator palpebrae superioris, superior tarsal muscle, or Müller's muscle. The inferior tarsal muscle in the lower lid is less distinct.

CLINICAL EXAMINATION AND DISORDERS OF FUNCTION OF THE OCULAR MOTOR NERVES AND THE CERVICAL SYMPATHETIC SYSTEM

Examination of the eyes begins with inspection—looking for any obvious ocular malalignment, abnormal lid position, or abnormalities of the position of the globe within the orbit. Abnormalities of the external eye may occasionally be of diagnostic significance in neurologic patients (see [Chapter 13](#)).

EXOPHTHALMOS AND ENOPHTHALMOS

The globe may be abnormally positioned within the orbit so that it protrudes (exophthalmos, proptosis) or recedes (enophthalmos). Subtle proptosis can often be better appreciated by looking down at both eyes from above the vertex of the head or by comparing side views. Exophthalmos is usually bilateral and most commonly due to thyroid eye disease (TED, Graves' ophthalmopathy, Graves' orbitopathy). Other conditions associated with neurologic complications and exophthalmos include the craniosynostosis syndromes and Hand-Schüller-Christian disease. Although TED can occasionally cause unilateral exophthalmos, the likelihood of other conditions increases in this situation. Orbital pseudotumor is an idiopathic inflammatory condition that affects the tissues of the orbit. It is common, and second only to TED as a cause of unilateral proptosis. Some of the neurologically significant causes of unilateral proptosis include orbital mass lesion, carotid cavernous fistula ([Figure 14.11](#)),

cavernous sinus thrombosis, sphenoid wing meningioma, meningocele, and mucormycosis.

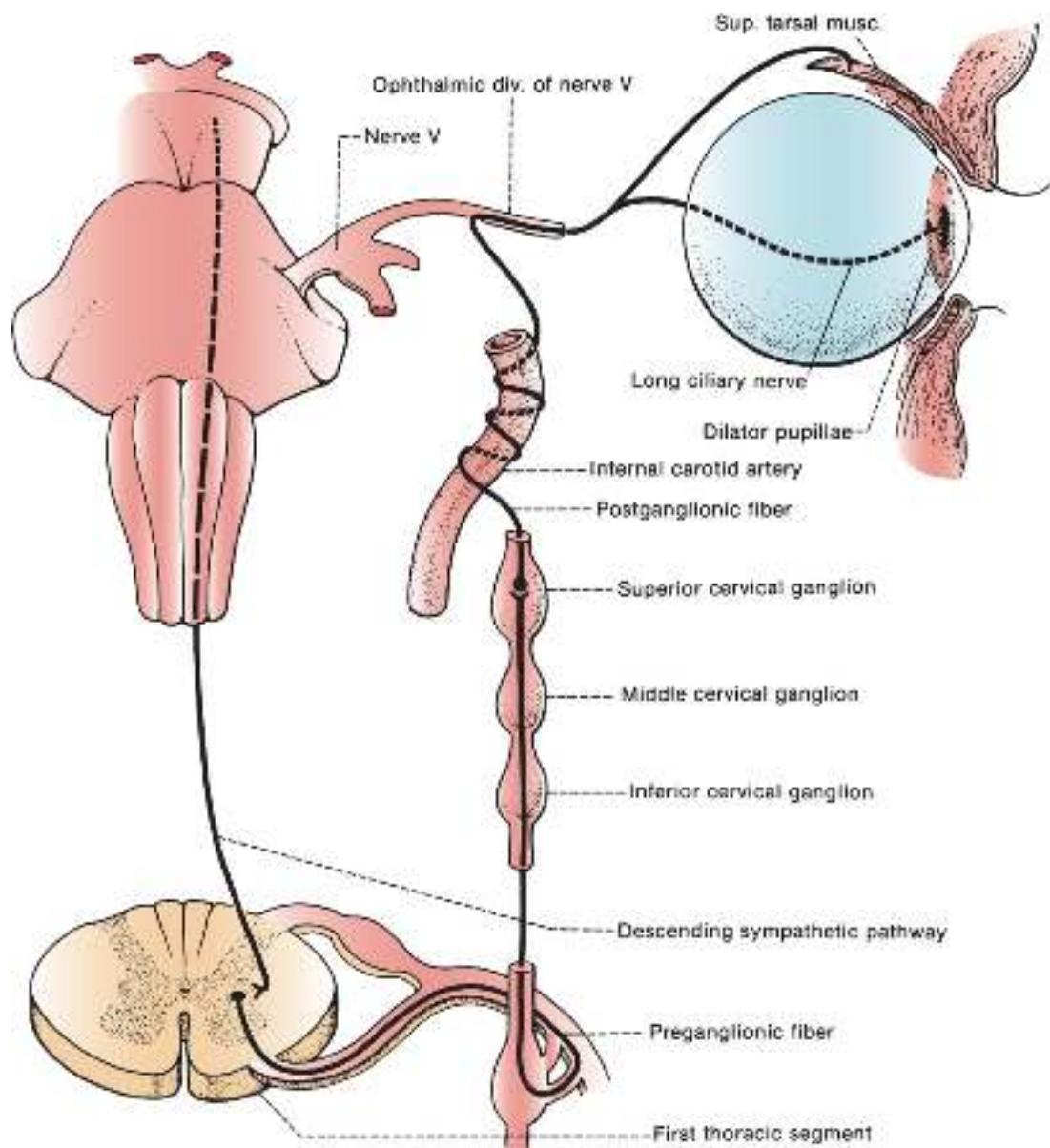


FIGURE 14.10 The cervical portion of the sympathetic division of the autonomic nervous system.

Other causes of exophthalmos include orbital neoplasm and vascular malformation of the orbit. Intraorbital varicosities may cause intermittent, positional exophthalmos because of decreased venous return in certain head postures. Pulsatile proptosis may occur with an orbital vascular malformation or when there is a defect in the orbital roof that transmits cerebral pulsations, which

can occur in neurofibromatosis. Diplopia can occur in conditions where the movement of the eyeball is restricted. Pseudoproptosis is the appearance of proptosis in the absence of any orbital disease; it may occur with lid retraction or high myopia.



FIGURE 14.11 Proptosis and chemosis in a direct, high-flow, right carotid cavernous fistula following trauma. (Courtesy N. Schatz. Reprinted from Gold DH, MD, and Weingeist TA, MD, PhD. *Color Atlas of the Eye in Systemic Disease*. Baltimore: Lippincott Williams & Wilkins, 2001, with permission.)

Few conditions of neurologic interest cause enophthalmos. Horner's syndrome causes apparent enophthalmos because the upper lid is ptotic and the lower lid elevated because of hypotonicity of the accessory eyelid retractors. This may cause the eye to appear sunken in the orbit, but it is an optical illusion and the actual globe position is normal.

THE EYELIDS

Patients may couch the complaint of ptosis (blepharoptosis) in ways other than droopy eyelid (e.g., eye has shrunk). Fluctuating ptosis may suggest myasthenia gravis (MG), although many varieties of ptosis, as in Horner's syndrome, may get worse when the patient is fatigued. Ptosis may have been present for a very long time before coming to the patient's attention. Looking at old photographs is often helpful. The eyes on a driver's license photo can be seen quite well by

using the ophthalmoscope on magnification.

The position of the eyelids is important and can reveal significant information. Note the position of the eyelids and the width of the palpebral fissures bilaterally. The width of the palpebral fissures should be equal on both sides, although a slight difference occurs in many normal individuals. Any asymmetry of lid position should be noted, such as ptosis or lid retraction. Note the amount of iris or pupil covered by the lid. Patients may compensate for ptosis by contracting the frontalis muscle. If the examiner fixes the frontalis muscle with her finger, the patient may be unable to raise the eyelid. Ptosis may cause an artefactual superior altitudinal visual field defect that disappears when the eyelid is raised.

The normal upper eyelid in primary position crosses the iris between the limbus (junction of the iris and sclera) and the pupil, usually 1 to 2 mm below the limbus; the lower lid touches or crosses slightly above the limbus. Normally, there is no sclera showing above the iris. The palpebral fissures are normally 9 to 12 mm from upper to lower lid margin at the midpoint. Measurement can also be made from the lid margin to the corneal light reflex. The upper lid margin is normally 3 to 4 mm above the light reflex. Levator function can be assessed by measuring the upper lid excursion from full downgaze to full upgaze just to the point where the frontalis begins to contract. This excursion is typically 10 to 12 mm. Upper lid excursion of 4 mm or less indicates poor levator function; 8 mm or more indicates good function.

With ptosis, the lid droops down and may cross at the upper margin of the pupil or cover the pupil partially or totally. With complete ptosis, the eyelid is down and the eye appears closed ([Figure 14.12](#)). Patients with ptosis often display telltale wrinkling of the ipsilateral forehead as they attempt to hold the eye open using the frontalis muscle. Ptosis may be unilateral or bilateral, partial or complete, and occurs in many neurologic conditions ([Figure 14.13](#)). With eyelid retraction, the upper lid pulls back and frequently exposes a thin crescent of sclera between the upper limbus and the lower lid margin. Lid retraction is a classic sign of thyroid disease but occurs in neurologic disorders as well.

The width of the palpebral fissures is normally equal on the two sides. Sometimes, inequality results from subtle lid retraction or a widened palpebral fissure on one side, not to be confused with ptosis on the other side. When in doubt, measure the width of the palpebral fissures with a ruler, in both primary position and in upgaze. In addition to observing the lid position at rest, notice the relationships of the lid to the globe during eye movement. CN VII, via

contraction of the orbicularis oculi, closes the eye. Facial weakness never causes ptosis. In fact, the palpebral fissure on the weak side is often wider than normal, and unilateral widening of one palpebral fissure may be an early sign of facial palsy.

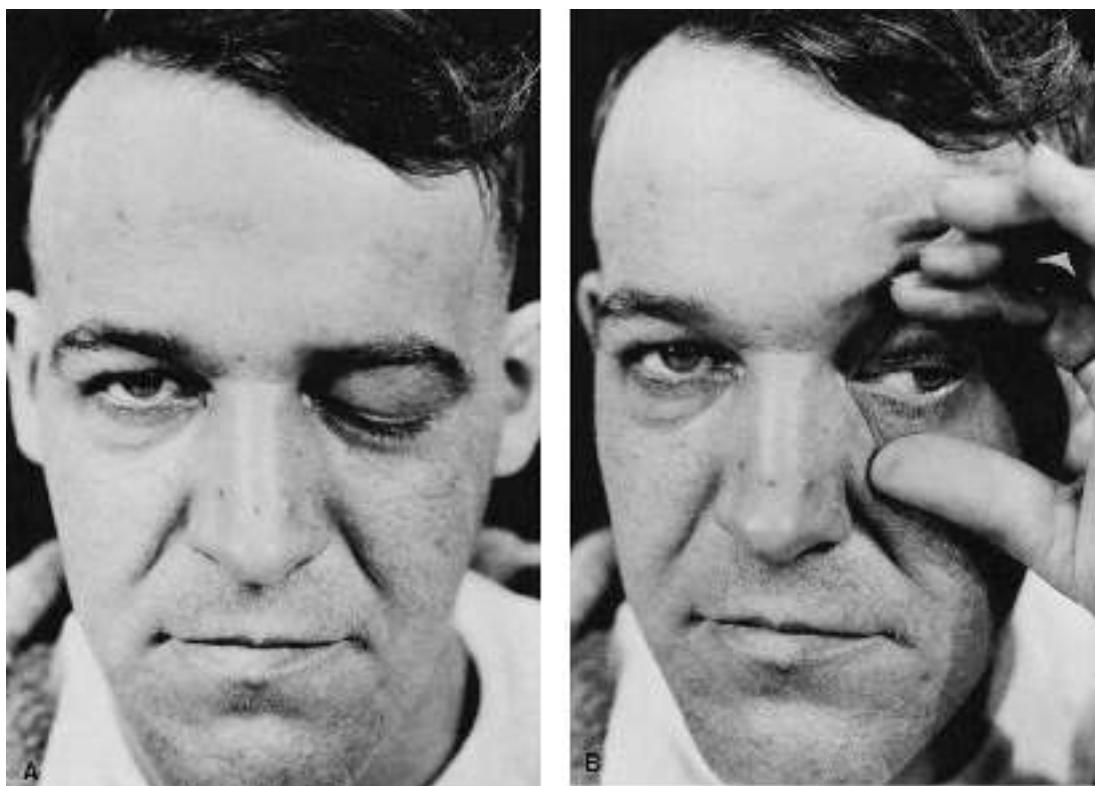


FIGURE 14.12 Paralysis of the left oculomotor nerve in a patient with an aneurysm of the left internal carotid artery. **A.** Only ptosis can be seen. **B.** On elevating the eyelid, it is seen that the pupil is dilated and the eyeball is deviated laterally.

Total unilateral ptosis only occurs with complete third nerve palsy. Mild to moderate unilateral ptosis occurs as part of Horner's syndrome, or with partial third nerve palsy. Ptosis may rarely be the only manifestation of an oculomotor nerve palsy. Mild to moderate bilateral ptosis occurs in some neuromuscular disorders, such as MG, muscular dystrophy, or ocular myopathy. The ptosis in MG is frequently asymmetric and may be unilateral, though it will tend to shift from side to side (Figure 14.14). It characteristically fluctuates from moment to moment and is worsened by prolonged upgaze (fatigable ptosis). Cogan's lid twitch sign, characteristic of myasthenia, consists of a brief overshoot twitch of lid retraction following sudden return of the eyes to primary position after a period of downgaze (see [Video Link 14.1](#)). In a series of 117 patients, the

specificity of the lid twitch sign was 99%, the sensitivity was 75%, and the false-positive rate was 1%. A similar upward twitch may occur on glancing quickly to the side from primary position (eyelid hopping). When the ptosis is asymmetric, the driving discharges attempting to keep the more ptotic eyelid open are also transmitted, per Hering's law, to the less ptotic eyelid. Manually raising the more ptotic lid causes relaxation, and the eye with less ptosis, sometimes even no ptosis, may suddenly crash (curtain sign, seesaw ptosis, enhanced ptosis, see [Video Link 14.2](#)). Because of the law of equal innervation, compensation for mild ptosis on one side may cause the involved eye to appear normal and the other eye to have lid retraction. Ptosis in MG may respond dramatically to edrophonium ([Figure 14.15](#), also see *Bilateral Ptosis* from Dr. Shirley Wray, Neuro-ophthalmology Virtual Education Library [NOVEL], University of Utah, [Video Link 14.3](#)).

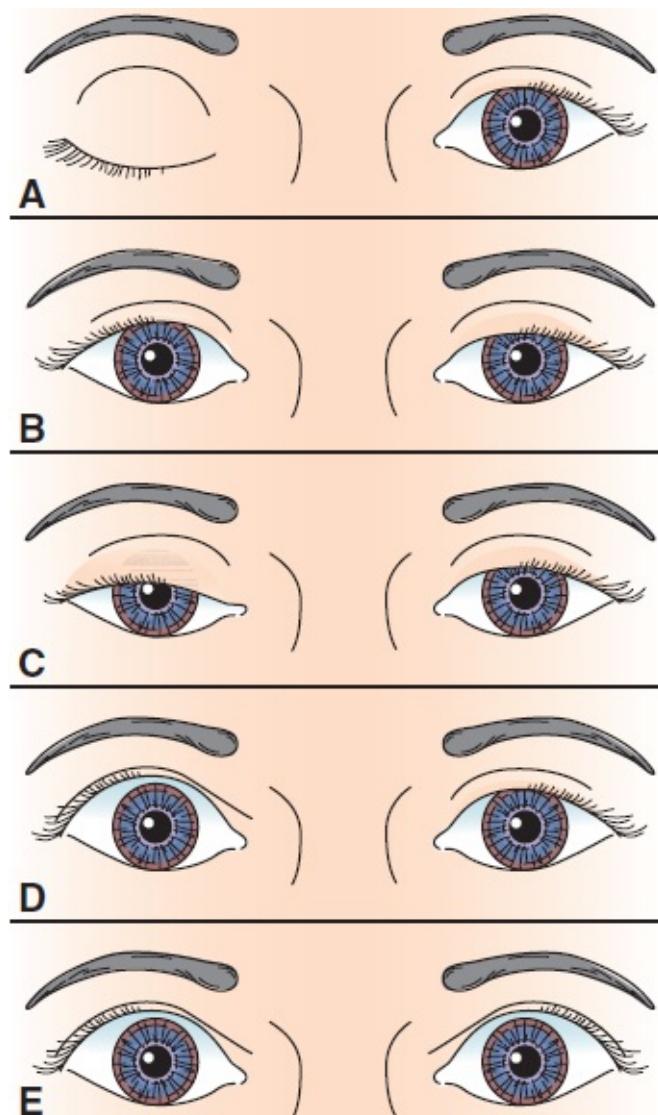


FIGURE 14.13 Characteristics of different causes of abnormal lid position. **A.** Right third CN palsy with complete ptosis. **B.** Left Horner's syndrome with drooping of upper lid and slight elevation of lower lid. **C.** Bilateral, asymmetric ptosis in myasthenia gravis (MG). **D.** Right lid retraction in thyroid eye disease. **E.** Bilateral lid retraction with a lesion in the region of the posterior commissure (Collier's sign).

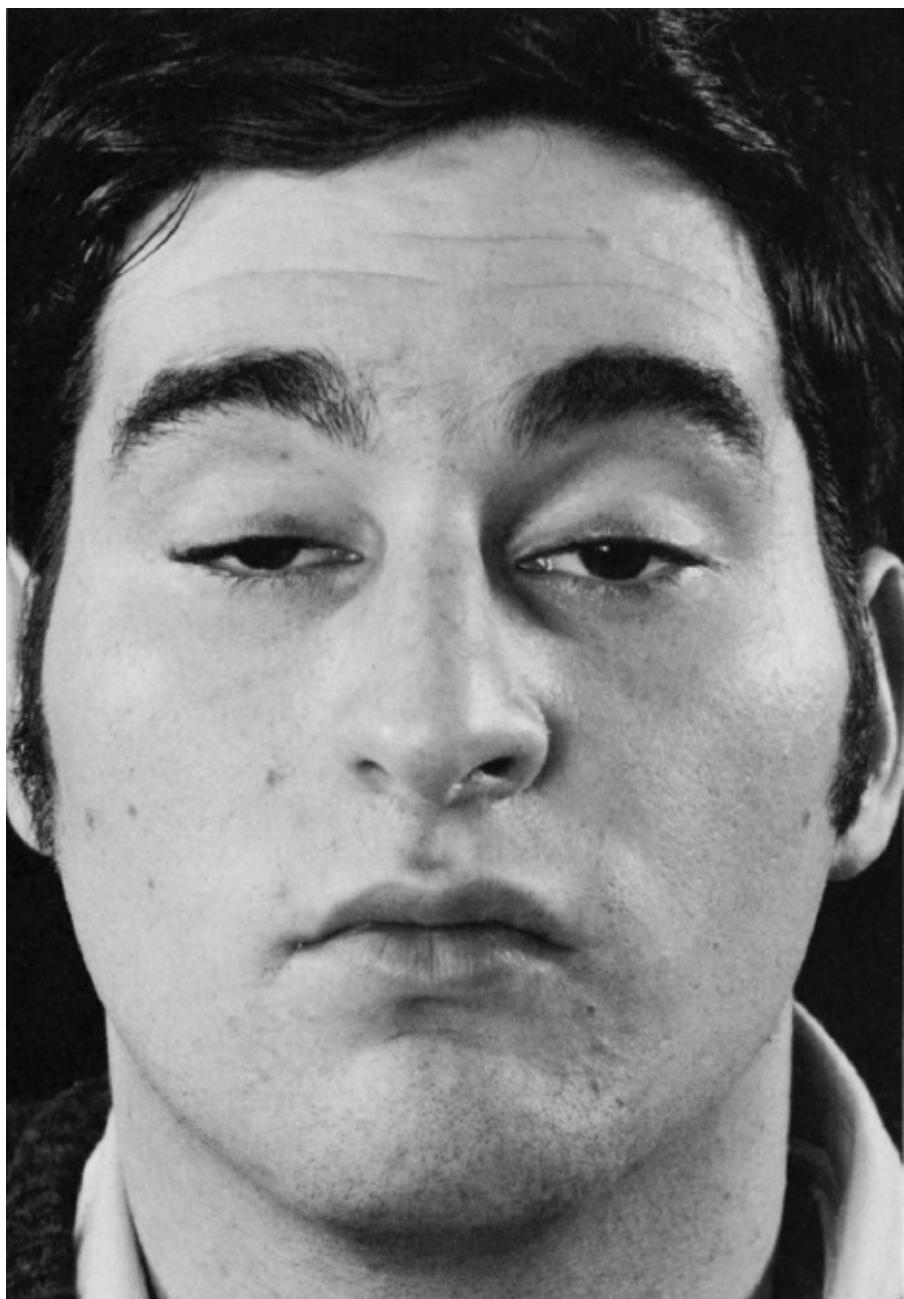


FIGURE 14.14 Bilateral ptosis in a patient with MG.

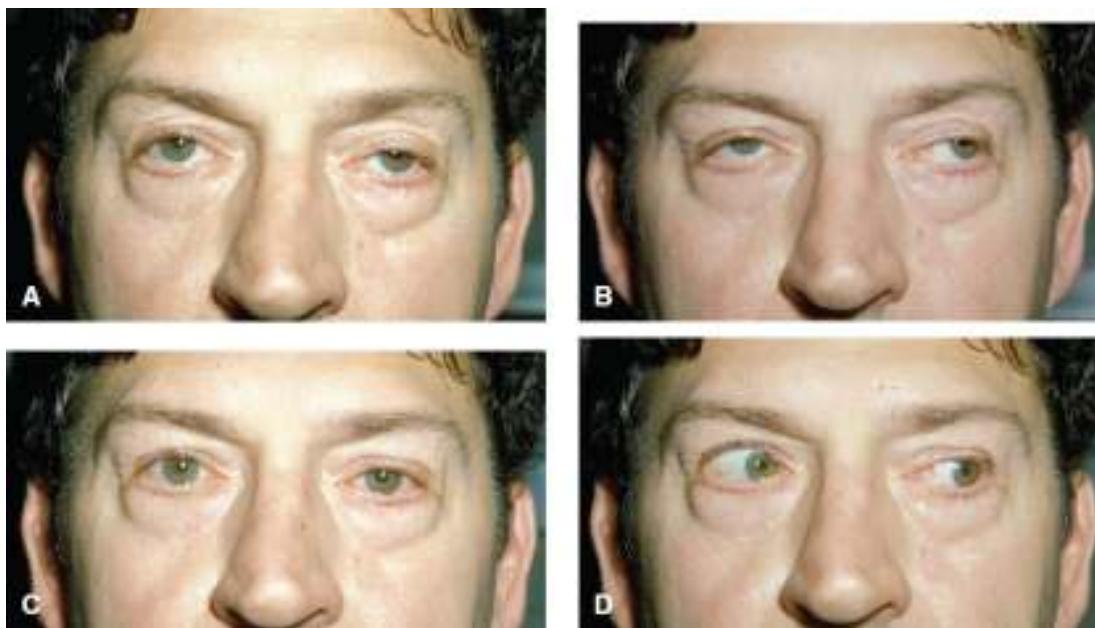


FIGURE 14.15 Results of a Tensilon (edrophonium chloride) test in a 34-year-old man with recent onset of ptosis and diplopia. **A.** The patient has bilateral ptosis, left more than right. Note also bilateral inferior scleral show from laxity of the lower eyelids. **B.** The patient can adduct the right eye only to the midline when attempting to look to the left (pseudointernuclear ophthalmoplegia). **C.** One minute after intravenous injection of 2 mg of Tensilon, the patient's ptosis has markedly improved and the inferior scleral show has resolved. **D.** At the same time, the patient's right eye adduction has become full. (Reprinted from Miller NR, Subramanian PS, Patel VR. *Walsh and Hoyt's Clinical Neuro-ophthalmology: The Essentials*. 3rd ed. Philadelphia: Wolters Kluwer, 2016, with permission).

Cerebral ptosis is due to supranuclear lesions. Unilateral cerebral ptosis occurs with lesions, usually ischemic, of the opposite hemisphere, and is more common with right hemisphere lesions. Bilateral supranuclear ptosis may occur with unilateral or bilateral hemispheric lesions. Ptosis has been reported in as many as 37.5% of patients with hemispheric strokes. Because of the anatomy of the central caudal nucleus, bilateral ptosis can occur as the only ocular motility abnormality with some midbrain lesions.

Senile or involutional ptosis is very common. Asymmetric lids and redundant lid tissue are more the rule than the exception in the elderly. The levator aponeurosis attaches the levator muscle to the tarsal plate, which forms the eyelid. The lid crease, or upper lid fold, is the skin fold at the upper part of the lid at the site of levator insertion. Aging may cause levator dehiscence-disinsertion (LDD)—with stretching, thinning, or detachment of the aponeurosis. Normally, with the eyelids gently closed, the upper lid margin lies 5 to 7 mm below the lid crease. An increase in this distance suggests LDD ([Figures 14.16](#)

and 14.17). The lid excursion is normal, usually 9 mm or more. Trauma to the eyelid, as from contact lenses, may cause LDD in younger patients. Blepharochalasis (dermatochalasis) refers to age-related lax, baggy skin around the eyelids; it can also simulate ptosis but levator function is normal. Other nonneurologic conditions that may be confused with ptosis include blepharitis, lid edema, lid infiltration, and eyelid tumor. Patients with neurofibromatosis may have diffuse neurofibroma in the eyelid, causing a characteristic S-shaped lid. Chronic use of steroid eye drops can cause ptosis that has been attributed to a focal steroid myopathy.

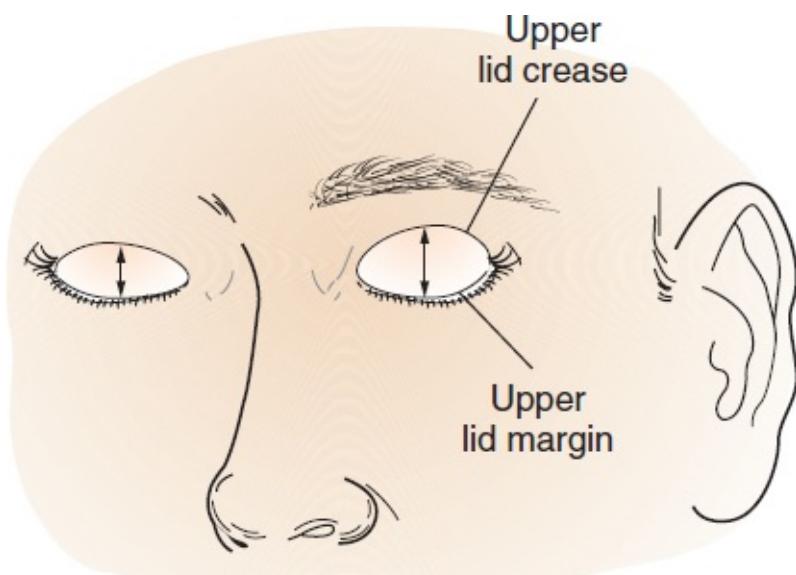


FIGURE 14.16 Levator dehiscence disinsertion on the left. The distance between the upper lid margin and the upper lid crease is increased compared to the normal right side.



FIGURE 14.17 Bilateral ptosis from dehiscence of the levator aponeurosis. Note the high, very defined upper eyelid crease. Levator function was 18 mm. (Reprinted from Penne RB. *Oculoplastics*. 2nd ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins Health, 2012, with permission.)

Congenital ptosis is common; because of levator fibrosis, it may be associated with lid lag in downgaze that is unusual in acquired ptosis. Jaw winking (Marcus Gunn phenomenon, for R. Marcus Gunn, Scottish ophthalmologist) occurs when there is congenital ptosis with abnormal communication between CN V and the levator palpebrae. The ptotic lid opens with jaw movement (see [Chapter 15](#)). Synkinesia between CN V and the levator more rarely causes ptosis on mouth opening (inverse Marcus Gunn phenomenon). Marin Amat syndrome is a facial nerve aberrant innervation syndrome with levator inhibition with mouth opening (see [Chapter 16](#)). Orbicularis oculi contraction causing eye closure on smiling is another common synkinesia. Eyelid myotonia may cause transient difficulty opening the eyes after a forceful contraction or transient lid retraction after looking up. Ptosis in Lambert-Eaton syndrome may temporarily improve after a brief period of upgaze. Blepharospasm is a focal dystonia causing involuntary eye closure; levator function is normal. In apraxia of lid opening, the patient has difficulty in voluntarily initiating lid elevation although there is no levator impairment or blepharospasm. A fine tremor of the lid (Rosenbach's sign) may occur in hyperthyroidism.

Pseudoptosis is the appearance of ptosis in the absence of levator abnormality. A narrow palpebral fissure can occur because of mechanical

limitation of levator excursion or enophthalmos. In vertical strabismus with the hypertropic eye fixing, the lid of the hypotropic eye may seem to be ptotic, but is not. In Duane's syndrome ([Box 14.9](#)), the palpebral fissure narrows on ocular adduction because of globe retraction causing dynamic enophthalmos (see *Type I Duane's syndrome* from Dr. Kathleen B. Digre, John A. Moran Eye Center, Neuro-ophthalmology Virtual Education Library [NOVEL], University of Utah, [Video Link 14.4](#)). The eyelids may also be intrinsically abnormal because of inflammation, trauma, or other factors, and these lid disorders may be mistaken for ptosis. Nonorganic ptosis is rare; it can occur because of voluntary unilateral blepharospasm. A telltale clue is that there is contraction of the orbicularis oculi or relaxation of the eyebrow elevators causing brow ptosis in addition to the appearance of lid ptosis.

Lid Retraction

Lid position is abnormal if there is a rim of sclera showing above the limbus, indicating either lid retraction or lid lag. TED is a common cause of lid abnormalities, including lid retraction in primary gaze (Dalrymple's sign), infrequent blinking (Stellwag's sign), and lid lag in downgaze (von Graefe's sign). Lid retraction in primary gaze also occurs with lesions involving the posterior commissure (Collier's sign, posterior fossa stare; see discussion of Parinaud's syndrome). Lid retraction with posterior commissure lesions is bilateral but may be asymmetric. With Collier's sign, the levators relax appropriately and the lids usually descend normally on downgaze without lagging behind as they do in TED. In addition, the lid retraction may worsen with attempted upgaze ([Figure 14.18](#)). Circumscribed midbrain lesions may cause eyelid retraction with minimal impairment of vertical gaze.

In Parkinson's disease, there is infrequent blinking and there may be some lid retraction. Topical instillation of sympathomimetic agents may cause lid retraction. Very weak sympathomimetics (e.g., tetrahydrozoline) may cause the lid with denervation supersensitivity, as in Horner's syndrome, to elevate. Apraclonidine may also improve the ptosis (see below). In vertical strabismus, the lid of the hypertropic eye may appear to be retracted when the hypotropic eye is fixing. Aberrant regeneration of CN III may cause lid retraction on adduction (the opposite of Duane's syndrome) or on downgaze. Lid retraction may also be mechanical, because of trauma or surgery. The plus minus lid syndrome is ptosis on one side and lid retraction on the other because of a

unilateral lesion of the third nerve nucleus extending rostrally to involve the region of the posterior commissure. Lid retraction may be confused with ipsilateral proptosis or contralateral ptosis.

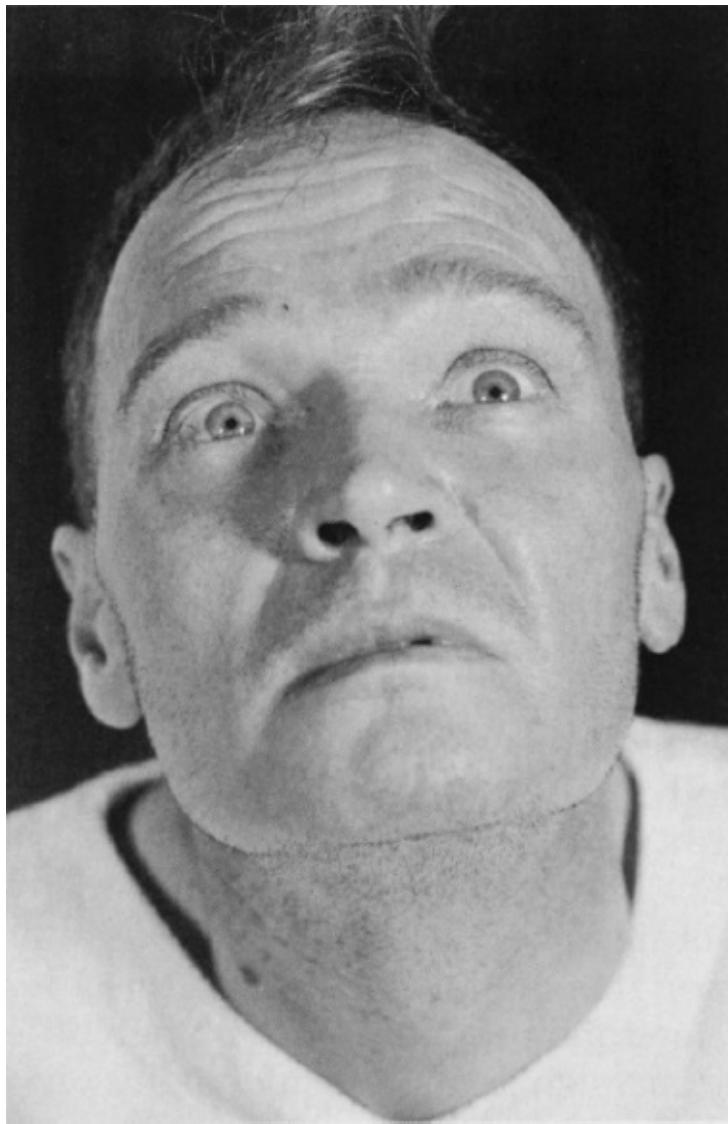


FIGURE 14.18 Paresis of upward gaze and lid retraction in a patient with a neoplasm of the posterior third ventricle.

The Pupils

The function of the pupil is to control the amount of light entering the eye, ensuring optimal vision for the lighting conditions. The pupils should be equal in size, round, regular, centered in the iris, and should exhibit specific reflex responses. Large, small, and abnormally reactive pupils are discussed in this

section. Normal pupils may display constant, small amplitude fluctuations in size under constant illumination (hippus, pupillary play). Hippus is of no clinical significance, even when pronounced, but can cause confusion in the evaluation of an afferent pupillary defect (APD) (see discussion of afferent pupillary defect).

Pupil examination should first assess pupillary size and equality. If they are unequal, determine whether the difference is greater in light or darkness. Compare the pupillary reactions to light and to near. Assess whether the pupils constrict and redilate with the same velocity. Finally, determine whether an APD is present.

Size

Pupillary size depends primarily on the balance between sympathetic and parasympathetic innervation and the level of ambient illumination. The most important determinants are the level of illumination and the point at which the eyes are focused. Accurate measurements are important. Measurements should be made with a pupil gauge or a millimeter ruler; estimates are surprisingly inaccurate. Special cameras can measure the pupil to within 0.1 mm. The size of the pupils should be determined at distance in ambient and dim light and at near. The normal pupil is 2 to 6 mm in diameter. In ordinary ambient light, the pupils are usually 3 to 4 mm in diameter. The pupils are small and poorly reactive at birth and in early infancy, becoming normal size around ages 7 to 8. They are normally larger in adolescents and young adults, about 4 mm in diameter and perfectly round. In middle age, they are typically 3.5 mm in diameter and regular, and in old age 3 mm or less and often slightly irregular.

Pupils less than 2 mm in diameter are miotic. Common causes of acquired miosis include old age, hyperopia, alcohol abuse, and drug effects. Neurologically significant causes of miosis include neurosyphilis, diabetes, levodopa therapy, and Horner's syndrome. Acute, severe brainstem lesions, such as pontine hematoma, may cause bilaterally tiny, "pinpoint" pupils that still react. Primary ophthalmologic conditions commonly cause miosis when there is external eye disease. Spastic or irritative miosis is due to spasm of the pupillary sphincter, often in association with corneal or intraocular foreign bodies or eye trauma. Other ophthalmologic disorders causing miosis include iridocyclitis, miotic drops, spasm of the near reflex, chronic anterior segment ischemia, and an old Adie's pupil. Synechia are adhesions that may develop in the eye, usually

after inflammation such as iritis. The scarring may bind the pupil down to the cornea (anterior synechia) or lens (posterior synechia) and cause miosis and pupillary irregularity. Paralytic miosis is due to paralysis of the pupillary dilator muscle (oculosympathetic paresis).

Pupils more than 6 mm in diameter are dilated. Common causes of bilateral mydriasis include anxiety, fear, pain, myopia, and drug effects—especially anticholinergics. Large pupils were once considered a sign of youth and beauty, and the anticholinergic belladonna (Ital. “fair lady”) alkaloids were named for their ability to produce this effect. Persons with light irises have larger pupils than those with dark irises. Only severe, bilateral lesions of the retina or anterior visual pathways, enough to cause near blindness, will affect the resting pupil size. Neurologically significant bilateral mydriasis occurs in midbrain lesions, in comatose patients following cardiac arrest, in cerebral anoxia, and as a terminal condition.

Shape

The normal pupil is round, with a smooth, regular outline. Gross abnormalities in shape are usually the result of ocular disease such as iritis or eye surgery. Synechia, a congenital coloboma (a gap in the iris), prior trauma, or iridectomy may all cause pupil irregularity. A slight change in shape, however, such as an oval pupil, slight irregularity in outline, serration of the border, or slight notching, may be significant in the diagnosis of neurologic disease.

Equality

The pupils are generally of equal size. A difference of 0.25 mm in pupil size is noticeable, and a difference of 2 mm is considered significant. Physiologic anisocoria (aniso, “unequal”; cor, “pupil”), mild degrees of inequality with less than 1 mm of difference between the two sides, occurs in 15% to 20% of normal individuals. With such physiologic anisocoria, the degree of inequality remains about the same in light and dark, and the pupils react normally to all stimuli and to instilled drugs ([Figures 14.19](#) and [14.20](#)). Slightly greater asymmetry in the dark sometimes occurs with physiologic anisocoria. Unequal pupils may be caused by primary eye disorders, such as iritis. Unilateral mydriasis is never due to isolated, unilateral visual loss. The reactivity of the normal eye and the consensual light reflex will ensure that pupil size remains equal. Anisocoria may

result from damage to the iris sphincter or pupillodilator muscles or to their nerve supply. Unilateral mydriasis can occur with local ocular trauma (traumatic iridoplegia).

Position

The pupil is normally situated in the center of the iris. An eccentric pupil (corectopia) usually signifies local eye disease, but it can occur with neurologic disease, especially disorders of the midbrain.

Etiologic Factor	Ambient Light	Strong Light	Dark	Conclusion	
Physiologic anisocoria	•	●	•	• ● ●	Same relative asymmetry under all conditions
Right Horner syndrome	•	●	•	• ● ●	More asymmetry in the dark; abnormal pupil cannot dilate
Left third cranial nerve palsy	•	●	•	● ● ●	More asymmetry in the light; abnormal pupil cannot constrict

FIGURE 14.19 Behavior of unequal pupils in light and dark conditions.

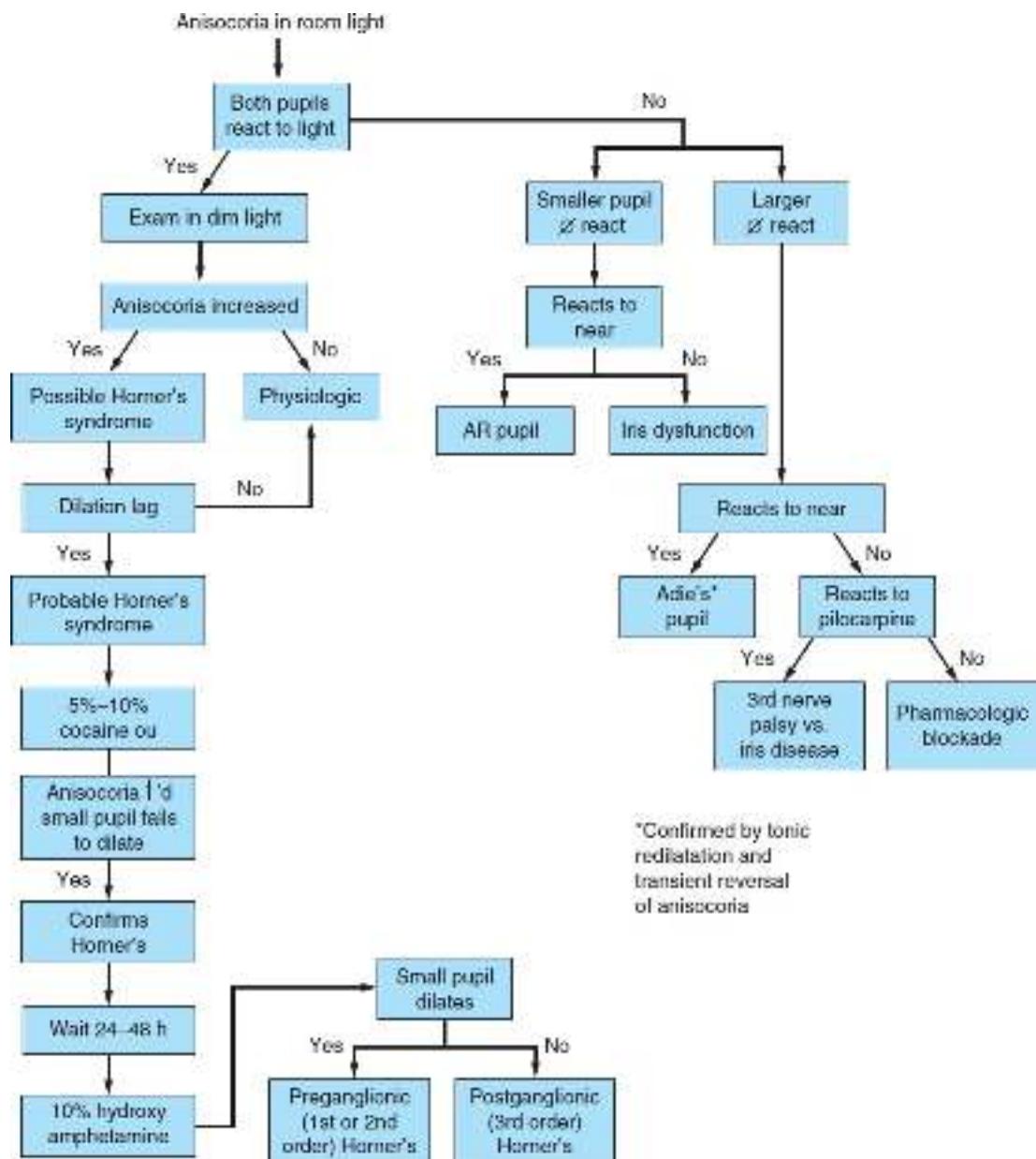


FIGURE 14.20 Flow diagram for the evaluation of anisocoria.

The Pupillary Reflexes

The principal pupillary reflex responses assessed on examination are the light response and the near response (“accommodation”). The normal pupil constricts promptly in response to light. Pupillary constriction also occurs as part of the near response, along with convergence and rounding up of the lens for efficient near vision. Normally, the light and near responses are of the same magnitude.

The Light Reflex

The pupillary light reaction is mediated by the macula, optic nerve, chiasm, and optic tract. Before reaching the lateral geniculate body, pupil afferents leave the optic tract to synapse in the pretectum. In addition to the decussation of nasal hemiretinal pupillary afferents, extensive crossing occurs through the posterior commissure with pupillary afferents synapsing both ipsilaterally and contralaterally. Because of the decussation in the chiasm and the decussation in the posterior commissure, pupillary fibers are extensively commingled and the reflex is bilateral, both direct and consensual (crossed) (Figure 13.9). Fibers project from the pretectum to the EW subnucleus of the oculomotor nuclear complex in the midbrain. Parasympathetic pupillary efferents from the EW subnucleus enter the third nerve and travel through the cavernous sinus and along the inferior branch of III in the orbit to innervate the pupilloconstrictor muscle of the iris. The pupillomotor fibers travel to the ciliary ganglion, then through the short posterior ciliary nerves between the sclera and the choroid to the pupillary sphincter. The sphincter is concentrically arranged; the pupillodilator muscle is radially arranged. Balancing parasympathetic input from the EW subnucleus is sympathetic input ascending from the superior cervical ganglion.

The light reflex should be tested in each eye individually. The examining light should be shone into the eye obliquely with the patient fixing at distance to avoid eliciting a confounding near response. A common error in pupil examination is to have the patient fixing at near, as by instructing her to look at the examiner's nose. This technique provides both a light stimulus and a near stimulus simultaneously, and the pupils may well constrict to the near target of the examiner's nose even when the reaction to light is impaired or absent. Using this technique, the examiner would invariably miss light-near dissociation. Always have the patient fix at a distance when checking the pupillary light reaction. Having the patient look up while directing the light forward to move the corneal light reflex away from the axis of the pupil may help to visualize the pupils in very dark irides. Another technique is to use ambient light by covering the eyes, then withdrawing the cover alternately, and looking for pupil constriction. The normal pupillary light reflex is brisk constriction followed by slight dilatation back to an intermediate state (pupillary escape). Escape may occur because of adaptation of the visual system to the level of illumination. The responses may be noted as prompt, sluggish, or absent, graded from 0 to 4+, or measured and

recorded numerically (e.g., 4 mm → 2 mm). In comatose patients, it is often important, but difficult, to see if the pupillary light reaction is preserved, especially if there is a question of brain death. A useful technique is to use the ophthalmoscope: focus on the pupil with high positive magnification, dim the ophthalmoscope, and then rapidly reilluminate. Even a small residual reaction may be seen. Obliquely illuminating the pupil by holding a dim light source to the side may help evaluate the consensual light reflex.

The Accommodation Reflex

The accommodation reflex (near response, near reflex) is elicited by having the patient relax accommodation by gazing into the distance, then shifting gaze to some near object. The best near object is the patient's own finger or thumb. The response consists of thickening of the lens (accommodation), convergence of the eyes, and miosis. The primary stimulus for accommodation is blurring. Without the near response, attempting to focus on a close object would result in blurred vision or frank diplopia. With special techniques, each component of the response can be tested separately. Routine bedside testing elicits all three components. Accommodation occurs because contraction of the ciliary muscle relaxes the zonular fibers, permitting the lens to become more convex because of its inherent elasticity. Accommodation is measured in diopters ([Box 14.1](#)).

The convergence movement of the near reflex is mediated by the vergence subcomponent of the supranuclear ocular motor control system. It consists of a long latency, slow dysconjugate eye movement to foveate the near object by contracting both medial rectus muscles. Convergence spasm causes excessive convergence for the distance of the object, and the patient cannot focus at distance. Convergence insufficiency causes inadequate convergence, and the patient cannot focus at near.

BOX 14.1

Myopia and Hyperopia

The near point of accommodation (NPA) is the closest point at which an object can be seen clearly. The NPA lengthens distressingly with advancing presbyopia. The far point of accommodation (FPA) is the distance at which a distant image is focused on the retina with no accommodative effort. An

emmetrope (person with a perfectly normal eye) has an FPA of infinity, and distant objects are properly focused on the fovea. In hyperopia (farsightedness, hypermetropia), the eyeball is too short, the FPA is behind the eye, accommodation can bring far objects into focus but may fail with near objects, and the correction is with positive lenses to add refractive power. In myopia (nearsightedness), the eyeball is too long or refractive power is excessive, the FPA falls in front of the fovea, relaxation of accommodation can bring near objects into focus but fails for distant objects, and the correction is with negative lenses to reduce refractive power. To quickly tell if a patient who uses correction has hyperopia or myopia, use the patient's glasses to look at some object about an arm's length away. Hyperopic glasses magnify, myopic lenses minify.

The pupils constrict at near to increase the depth of focus. The pathways are less certain than for the pupillary light reflex, but they involve the visual cortex with impulses probably descending through the corticotectal tract to near response cells in the pretectum. The midbrain mechanisms for pupillary constriction to near are separate from those for the light reflex; one response may be abnormal, whereas the other is preserved.

Other Pupillary Reflexes

The ciliospinal reflex consists of dilation of the pupil on painful stimulation of the skin of the ipsilateral neck. Local cutaneous stimulation (e.g., scratching the neck) activates sympathetics through connections with the ciliospinal center at C8-T2 that cause the ipsilateral pupil to dilate. An intact ciliospinal reflex is evidence of brainstem integrity when evaluating a comatose patient. The response is minimal and may be difficult to see even when normal. The oculosensory or oculopupillary reflex is pupil constriction in response to painful stimulation of the eye or its adnexa. The pupils normally constrict on attempted lid closure. Pupil dilation may occur in response to a loud noise (cochleopupillary reflex) or labyrinthine stimulation (vestibulopupillary reflex). The pupils may dilate in response to fear, anxiety, mental concentration, and sexual arousal because of sympathetic activity.

Effects of Drugs on the Pupil

Many systemically acting as well as locally acting drugs may influence pupil size and reactivity. An abnormal pupil may fail to respond appropriately or respond excessively because of denervation supersensitivity. Pupil pharmacology is complex. In brief, sympathomimetics and anticholinergics cause pupillary dilation, and parasympathomimetics or sympathetic blockers cause pupillary constriction. Agents that cause mydriasis include the anticholinergics atropine, homatropine, and scopolamine and the sympathomimetics epinephrine, norepinephrine, phenylephrine, hydroxyamphetamine, and cocaine. Agents that cause miosis include the cholinomimetics pilocarpine, methacholine, muscarine, and opiates, and the cholinesterase inhibitors physostigmine and neostigmine. Ergot derivatives block postganglionic adrenergic nerves and can cause pupil constriction. Pupillary pharmacology can be applied in the neurologic examination, primarily in the evaluation of Horner's syndrome and Adie's pupil (see [Table 14.1](#)).

**TABLE
14.1**

**Summary of Pharmacologic Pupillary Testing for
Horner's Syndrome**

	First Order	Second Order	Third Order
Cocaine	No response	No response	No response
Hydroxyamphetamine	Dilates	Dilates	No response

DISORDERS OF THE PUPIL

Pupils can be abnormal for numerous reasons. Common problems include pupils that are too large or too small, unilaterally or bilaterally, or pupils that fail to demonstrate normal reflex responses.

Large Pupils

The two conditions most commonly causing a unilaterally large pupil are third CN palsy and Adie's pupil. In CN III palsy, the large pupil has impaired reactions to light and to near; abnormalities of extraocular movement and eyelid position generally betray the origin of the abnormal pupil. With total CN III palsy, there is complete ptosis; lifting the eyelid reveals the eye resting in a down

and out position (Figure 14.12). Although CN III palsies often affect the pupil more than other functions, some ptosis and ophthalmoparesis is usually present. Because the pupillary parasympathetics occupy a position on the dorsomedial periphery of the nerve as it exits the brainstem, compressive lesions such as aneurysms generally affect the pupil prominently. Ischemic lesions tend to affect the interior of the nerve and spare the pupil, as in diabetic third nerve palsies, because the periphery of the nerve has a better vascular supply. This rule is not absolute: pupil-sparing third nerve palsies have been reported with aneurysms (in up to 10% of cases), as have diabetic palsies involving the pupil. In Keane's series of 1,400 patients, 53% of diabetic CN III palsies involved the pupil, but only 2% of aneurysms spared the pupil. In diabetics, pupil abnormalities were often bilateral, suggesting autonomic neuropathy. However, only rarely does a complete aneurysmal third nerve palsy spare the pupil. When the pupil is spared, some other functions are usually spared as well. Barton summarized the correct "pupil rule" as follows: complete pupil sparing with otherwise complete and isolated palsy of CN III is never due to an aneurysm. The pupil is usually involved early and prominently with third nerve compression because of uncal herniation (Hutchinson's pupil).

When the ocular sympathetics are involved along with CN III, the pupil may be midposition because the sympathetic denervation prevents the pupil from dilating fully. This occurs most often in cavernous sinus lesions when there is compression of both CN III and the pericarotid sympathetics, leaving the pupil midsize but unreactive. This should not be mistaken for pupil sparing. CN III palsies are sometimes complicated by aberrant reinnervation. This misdirection syndrome may cause abnormal pupil constriction in relation to eye movements that may mimic pupil sparing.

The patient presenting with Adie's pupil (tonic pupil, Holmes-Adie pupil) is typically a young woman who suddenly notes a unilaterally enlarged pupil, with no other symptoms. The pupillary reaction to light may appear absent, although prolonged illumination may provoke a slow constriction. The reaction to near, although slow, is better preserved. Once constricted, the tonic pupil redilates very slowly when illumination is removed or the patient looks back at distance, often causing a transient reversal of the anisocoria. The pathology in Adie's pupil lies in the ciliary ganglion or short ciliary nerves, or both; its precise nature remains unknown. The parasympathetic denervation eventually leads to denervation supersensitivity; the pupil may then constrict to solutions of pilocarpine or methacholine that are too dilute to affect a normal eye. About

20% of patients develop a tonic pupil in the other eye. Adie's syndrome is the association of the pupil abnormality with depressed or absent deep tendon reflexes, particularly in the lower extremities. With the passage of time, the pupil may become smaller. An old Adie's pupil can be a cause of unilateral miosis. The light reaction never recovers.

The term "tectal pupils" refers to the large pupils with light-near dissociation sometimes seen when lesions affect the upper midbrain. Such pupils may accompany the impaired upgaze and convergence/retraction nystagmus of Parinaud's syndrome. The variably dilated, fixed pupils reflecting midbrain dysfunction in a comatose patient carry a bleak prognosis. Glutethimide intoxication, infamous for causing fixed pupils in drug-induced coma, has fortunately become rare. Acute angle closure glaucoma can cause severe frontotemporal headache and a dilated, poorly reactive pupil. A cloudy cornea may provide the clue that the patient does not harbor an aneurysm and needs to quickly see an ophthalmologist rather than a neurologist or a neurosurgeon. Deliberately or accidentally instilled mydriatics will produce a dilated, fixed pupil. Such pharmacologic blockade can be distinguished by the failure to respond to full strength pilocarpine, which promptly constricts a large pupil of any other etiology.

Small Pupils

The pupils in the elderly are normally smaller. Many older patients use pilocarpine eye drops to manage chronic open angle glaucoma. Many systemic drugs, such as opiates, may symmetrically shrink the pupils. Important neurologic conditions causing an abnormally small pupil include Horner's syndrome and neurosyphilis.

HORNER'S SYNDROME

In Horner's syndrome, sympathetic dysfunction produces ptosis, miosis, and anhidrosis. Lack of sympathetic input to the accessory lid retractors results in ptosis and apparent enophthalmos. The ptosis of the upper lid due to denervation of Müller's muscle is only 1 to 3 mm, never as severe as with a complete CN III palsy, although it may simulate partial third nerve palsy. The ptosis can be subtle and is often missed. The lower lid is frequently elevated 1 to 2 mm because of

loss of the action of the lower lid accessory retractor that holds the lid down (inverse ptosis). The resulting narrowing of the palpebral fissure causes apparent enophthalmos. Because the fibers mediating facial sweating travel up the external carotid, lesions distal to the carotid bifurcation produce no facial anhidrosis except for perhaps a small area of medial forehead that is innervated by sympathetic fibers traveling with the internal carotid.

The small pupil dilates poorly in the dark. Pupillary asymmetry greater in the dark than in the light generally means Horner's syndrome. Recall that physiologic anisocoria produces about the same degree of pupillary asymmetry in the light and dark. In contrast, third nerve palsy and Adie's pupil cause greater asymmetry in the light because of the involved pupil's inability to constrict. Examining the eyes under light and dark conditions can help greatly in sorting out asymmetric pupils ([Figures 14.19](#) and [14.20](#)). Should the examiner err by having the patient fixate at near during testing, the pupillary constriction in the good eye may lessen the asymmetry and cause the abnormal pupil to be missed. The pupil in Horner's syndrome not only dilates less fully but also dilates less rapidly. In the first few seconds after dimming the lights, the slowness of dilation of the affected pupil may cause the anisocoria to be even more pronounced (dilation lag). There is more anisocoria at 4 to 5 seconds after lights out than at 10 to 12 seconds.

The causes of Horner's syndrome are legion and include the following: brainstem lesions (especially of the lateral medulla), cluster headache, internal carotid artery thrombosis or dissection, cavernous sinus disease, apical lung tumors, neck trauma, and other conditions ([Figure 14.21](#)). Horner's syndrome may be an isolated manifestation of syringomyelia. The tiny and minimally reactive pupils seen commonly in pontine hemorrhage may represent acute, severe, bilateral oculosympathetic paresis. The rare condition of reverse Horner's syndrome (Pourfour du Petit syndrome) is unilateral mydriasis, sometimes with facial flushing and hyperhidrosis, because of transient sympathetic overactivity in the early stages of a lesion involving the sympathetic pathways to one eye. In Harlequin syndrome, there is unilateral facial anhidrosis with contralateral flushing and sweating, induced by exercise, heat, and emotion. The condition is usually idiopathic but can occur as a manifestation of serious underlying disorders including brainstem infarction and carotid artery dissection. There are no eye findings.

Pharmacologic testing is occasionally done to help determine whether a miotic pupil is due to Horner's syndrome. In about half the patients with

Horner's syndrome, the etiology is apparent from other signs and the history. In the other half, clinical localization is uncertain; pharmacologic testing may help determine the level of the lesion and guide further investigations. Interruption of the sympathetic pathways between the hypothalamus and the spinal cord (e.g., Wallenberg syndrome) causes a first-order Horner's syndrome. The second-order neuron lies in the ciliospinal center at C8-T2. A lesion involving this portion of the pathway (e.g., syringomyelia, C8 root lesion) causes a second-order Horner's syndrome. The third-order neuron lies in the superior sympathetic ganglion; a lesion at or distal to here (e.g., carotid artery dissection) causes a third-order Horner's syndrome. With a third-order Horner's, the final neuron in the pathway dies and its peripheral processes atrophy and disappear. With first- and second-order Horner's syndrome, the third-order neuron is disconnected but intact, and its terminal connections sound and viable.



FIGURE 14.21 A patient with a right Horner's syndrome. (Reprinted from Campbell WW. *Clinical Signs in Neurology: A Compendium*. Philadelphia: Wolters Kluwer, 2016, with permission.)

Cocaine drops instilled into the eye can confirm the presence of Horner's syndrome, but cannot localize the lesion; hydroxyamphetamine can distinguish a third order from other types of Horner's syndrome. Cocaine blocks the reuptake of norepinephrine from the nerve terminals, increasing its effect. With Horner's syndrome of any type, there is less norepinephrine being released, less

accumulates at the pupillodilator, and cocaine will fail to dilate the affected pupil. Hydroxyamphetamine drops cause release of norepinephrine, but only from intact nerve endings. If the third-order neuron is intact, as with first- or second-order Horner's syndrome, the pupil will dilate in response to hydroxyamphetamine. In a third-order Horner's syndrome, there are no surviving nerve endings in the eye to release norepinephrine and the pupil will fail to dilate. [Table 14.1](#) summarizes pupil pharmacologic testing for Horner's syndrome. Apraclonidine, a new selective α_2 agonist used to reduce intraocular pressure, may also be used to demonstrate denervation hypersensitivity and is much more readily available than cocaine. It may also reverse the ptosis. Denervation hypersensitivity may occur as soon as 36 hours after development of the Horner's syndrome.

Other findings in Horner's syndrome include loss of the ciliospinal reflex, ocular hypotony, and increased amplitude of accommodation and vasodilation in the affected distribution. Congenital Horner's syndrome may cause sympathetic heterochromia iridis and other trophic changes of the head and face.

Thompson et al. described a group of patients with unilateral ptosis and miosis of unrelated origin simulating oculosympathetic paresis, which they called pseudo-Horner's syndrome. The majority of patients had simple, physiologic anisocoria accompanied by incidental ptosis because of LDD or blepharochalasis.

Argyll Robertson Pupil

Argyll Robertson pupils (AR pupil; for Argyll Robertson, Scottish ophthalmologist) are small (1 to 2 mm), irregular in outline, and have light-near dissociation. They react poorly or not at all to light, but very well to near. Anterior visual pathway function must be normal. Argyll Robertson pupils are generally bilateral and asymmetric, but may be symmetric and rarely unilateral. Argyll Robertson pupils are the classic eye finding of neurosyphilis and when present they mandate appropriate serologic testing. The lesion lies in the periaqueductal region, pretectal area, and rostral midbrain dorsal to the EW nuclei. Other conditions may cause an AR-like pupil. With the declining incidence of neurosyphilis, AR-like pupils with light-near dissociation are increasingly likely to be of some other etiology. Other causes of light-near dissociation are discussed in the following section.

Pupils with Abnormal Reactions

Disruption of the afferent or efferent limbs of the pupillary reflex arcs, or disease of the brainstem pupil control centers, may alter pupil reactivity to light or near, as may local disease of the iris sphincter (e.g., old trauma). Disease of the retina does not affect pupil reactivity unless there is involvement of the macula severe enough to cause near blindness. Cataracts and other diseases of the anterior segment do not impair light transmission enough to influence the pupil. Because of the extensive side-to-side crossing of pupillary control axons through the posterior commissure, light constricts not only the pupil stimulated (the direct response) but also its fellow (the consensual response). The eye with a severed optic nerve will show no direct response, but will have a normal consensual response to a light stimulus in the other eye, as well as constriction to attempted convergence (amaurotic pupil). Lesser degrees of optic nerve dysfunction can often be detected by checking for an APD (see below). The pupil frozen because of third nerve palsy will have no near response and no direct or consensual light response, but the other eye will exhibit an intact consensual response on stimulation of the abnormal side ([Table 14.2](#)).

Light-Near Dissociation

The pupillary reaction to light is normally equal to or greater than the reaction to near. Light-near dissociation refers to a disparity between the light and near reactions. The most common form is a poor light response but good constriction with the near response; it is relatively common, and there are a number of causes. The converse, better reaction to light than to near, is rare and most often because of lack of patient effort in attending to the near target. In the routine case, if the pupillary light reaction is normal, there is little to be gained by examining the near reaction.

TABLE 14.2

Direct and Consensual Light Reaction

Comparison of direct and consensual light reflex and pupillary constriction to the near reflex in the presence of a complete lesion of the right optic nerve versus the right oculomotor nerve. In both instances, the right pupil is frozen to direct light stimulation, and the distinction is made by the other reactions

	Complete Lesion CN II OD		Complete Lesion CN III OD	
	Response OD	Response OS	Response OD	Response OS
Light stimulus OD	No response	No response	No response	Normal
Light stimulus OS	Normal	Normal	No response	Normal
Near reflex	Normal	Normal	No response	Normal

OD, right eye; OS, left eye.

The fibers mediating the pupillary light reflex enter the dorsal brainstem, but the near response fibers ascend to the EW nucleus from the ventral aspect. Disorders that affect the dorsal rostral brainstem may affect the light reaction but leave the near reaction intact. This anatomical arrangement likely explains many instances of the phenomenon of light-near dissociation of the pupils. Pressure on the pupillary fibers in the region of the pretectum and posterior commissure (e.g., from pinealoma) impairs the light reaction. However, fibers mediating the near response, the EW nucleus, and the efferent pupil fibers are spared, which leaves the near response intact. Causes of light-near dissociation include neurosyphilis, other lesions involving the dorsal rostral midbrain, diabetic autonomic neuropathy (*tabes diabetica*), Lyme disease, chronic alcoholism, chiasmal lesions (*tabes pituitaria*), myotonic muscular dystrophy, amyloidosis, Adie's pupil, aberrant regeneration of CN III, sarcoidosis, multiple sclerosis (MS), and severe retinal or optic nerve disease.

Afferent Pupillary Defect

When testing the light reflex, the amplitude of the initial pupillary constriction and subsequent slight escape depend greatly on the specific circumstances of illumination. Therefore, the status of the light reflex must be judged by comparing the two eyes. The importance of the pupil light reflex as an indicator of optic nerve function has been recognized since antiquity; Hippocrates and Galen understood the basic concept. With mild to moderate optic nerve disease, it is difficult to detect any change in pupil reactivity to direct light stimulation. As provocatively pointed out by Landau, Marcus Gunn (in 1902) described pathologic pupillary escape, what he termed secondary dilatation under continued exposure (for 10 to 20 seconds), or the adapting pupillary response, due to optic nerve disease. In 1959, Levitan described looking for the Marcus

Gunn pupillary sign by swinging a light back and forth between the two eyes (swinging flashlight test, alternating light test). He thought that moving the light back and forth amplified the asymmetry of the pupillary escape. There seems to be general agreement that the swinging flashlight test is a very useful technique that can quickly and accurately compare the initial constriction and subsequent escape of the two pupils. It is a key clinical technique in the evaluation of suspected optic neuropathy, and it can often detect a side-to-side difference even when the lesion is mild and there is no detectable difference in the direct light reflex when testing each eye individually ([Figure 14.22](#)).

There are two techniques for the swinging flashlight test. In the first, the light is held about 1 in from the eye along and just below the visual axis; the light is rapidly alternated, pausing for about one full second on each side. The examiner attends only to the stimulated eye, comparing the amplitude and velocity of the initial constriction in the two eyes. The reaction is relatively weaker when the bad eye is illuminated. In the other technique, the light is allowed to linger a bit longer. With stimulation of the good eye, both pupils constrict smartly because of the direct reflex in the stimulated eye and the consensual reflex in the opposite eye. After 3 to 5 seconds to allow the pupil to stabilize, the light is quickly swung to the bad eye. With an optic nerve lesion, the brain detects a relative diminution in light intensity and the pupil may dilate a bit in response. The pupil in the other eye dilates as well because the consensual reflex constricting the pupil in the good eye is less active than its direct reflex, but this is not observed. On moving the light back to the good eye, the more active direct response causes the pupil to constrict. On moving back to the bad eye, the pupil dilates because the direct light reflex is weaker than the consensual reflex that had been holding it down. As the light passes back and forth, the pupil of the good eye constricts to direct light stimulation and the pupil of the bad eye dilates to direct light stimulation. It may require several swings to find the optimum speed to bring out the dynamic anisocoria. Over several cycles, it may be striking to see one pupil consistently dilate to the same light stimulus that causes the other to constrict. The weaker direct response or the paradoxical dilation of the light-stimulated pupil is termed an APD, or Marcus Gunn pupil. It is an extremely useful and important neurologic sign. Some modify the term with “relative” (RAPD) to emphasize that the finding depends on the difference between the two eyes—the state of the afferent system and activity of the light reflex in one eye relative to the other eye. The shorter form, APD, is currently in more widespread use. Active hippus may cause difficulty in interpretation. Hippus is random; a true

APD will be consistent over multiple trials. Pay attention to the first movement of the pupil; if it is consistently a dilation movement, the patient has an APD and not hippus.

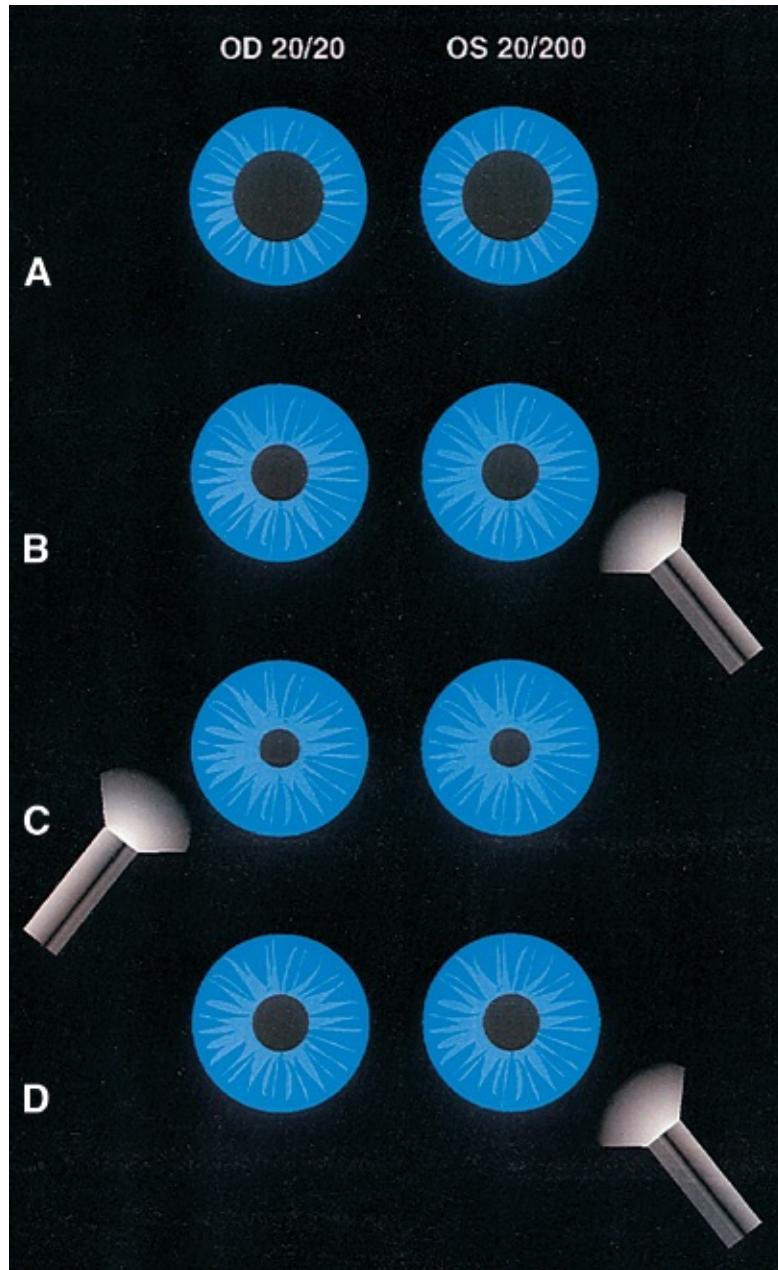


FIGURE 14.22 Relative afferent pupillary defect. Vision on the right 20/20; vision on the left 20/200 because of optic neuropathy. **A.** The pupils in dim light are equal. **B.** Light directed into the left eye results in a partial and sluggish contraction in each eye. **C.** Light directed into the right eye results in a brisk and normal reaction in each eye. **D.** The light quickly redirected into the left eye results in a dilatation of both pupils. Swinging the light back and forth will bring out the dynamic anisocoria. (From Tasman W, Jaeger E. *The Wills Eye Hospital Atlas of Clinical Ophthalmology*. 2nd ed. Baltimore: Lippincott Williams & Wilkins, 2001, with permission.)

The magnitude of an APD is often graded. In one scheme, a 1+ APD refers to initial constriction followed by escape, 2+ indicates no initial constriction, then dilation, 3+ indicates immediate redilation, and 4+ means an amaurotic pupil. More precise grading is done with neutral density filters. Asking the patient to compare the light intensity in the two eyes provides a subjective estimate of APD severity.

The presence of an APD depends on asymmetry in the afferent signal. A bilateral APD cannot occur, although a severe bilateral afferent defect may cause light-near dissociation or abnormal pupillary escape. An APD can occur with bilateral optic neuropathy only if there is significant asymmetry of involvement. An APD can also occur with asymmetric chiasmal disorders or an optic tract lesion. A pretectal lesion can cause a contralateral APD without visual field loss. Media opacities will not cause an APD. In fact, mature cataract may so scatter the incoming light as to actually increase the light reflex and cause a minor APD in the opposite eye. Only severe retinal or macular disease will cause an APD, and then it will be slight. Maculopathy with 20/200 vision might cause a 1+ APD, whereas optic neuropathy with 20/30 vision would cause a 3+ to 4+ APD. For a demonstration of the swinging flashlight test and a demonstration of an APD, see *RAPD Present* by Dr. Kathleen B. Digre, John A. Moran Eye Center, Neuro-ophthalmology Virtual Education Library [NOVEL], University of Utah, available at [Video Link 14.5](#).

BOX 14.2

Unusual Pupillary Abnormalities

Paradoxical pupils constrict in darkness. The phenomenon is seen in congenital retinal and optic nerve disorders; the mechanism is unknown. Springing pupil (benign, episodic pupillary dilation; mydriasis à bascule) is intermittent, sometimes alternating, dilation of one pupil lasting minutes to hours seen in young, healthy women, often followed by headache. Tadpole pupil is a benign condition in which a pupil intermittently and briefly becomes comma shaped because of spasm involving one sector of the pupillodilator; it may be a forme fruste of springing pupil. Periodic unilateral mydriasis has been reported in migraine and as an ictal phenomenon. Scalloped pupils occur in familial amyloidosis. Oval pupils usually portend

major intracranial pathology and may be a transient phase in evolving injury to the third nerve nuclear complex. Corectopia iridis (ectopia pupillae, Wilson's sign) is spontaneous, cyclic displacement of the pupil from the center of the iris; it is usually seen in severe midbrain disease.

Unusual Disorders of the Pupil

Some rare pupillary disorders include paradoxical pupils, springing pupil, tadpole pupil, oval pupils, and corectopia ([Box 14.2](#)).

OCULAR MOTILITY

The eyes move in the service of vision, bringing objects of regard into the field of vision and following them if they move. Eye movements are divided into ductions (movements of one eye), versions (binocular conjugate movements), and vergences (binocular dysconjugate movements). Vertical movements are sometimes divided into supraductions/versions and infraductions/versions. The different eye movement control systems (e.g., saccade, pursuit, vergence) normally function harmoniously to secure and maintain vision. The globe rotates around one or more of three primary axes that intersect at right angles at the center of rotation, 15.4 mm behind the cornea. Movement takes place perpendicular to the axis of rotation. Abduction and adduction are rotation in the horizontal plane about the vertical axis going from superior to inferior. Elevation and depression are up and down movements around the horizontal axis that runs from medial to lateral across the eye. The third axis runs from anterior to posterior; rotation about this axis is referred to as torsion. Intorsion (incyclotorsion) is movement of the upper pole of the eye toward the nose; extorsion (excyclotorsion) is movement away from the nose.

The eyes are said to be in primary position when gaze is straight ahead and the visual axes of the two eyes are parallel. Because the orbits diverge, primary position must be obtained by precisely adjusted contractions of the extraocular muscles, which are controlled by the cerebral cortex. It is a delicate system. When regarding an object, the extraocular muscles move the eyes so that the visual axes meet at the proper point to ensure that the object's image falls on corresponding points on each macula. The point where the visual axes meet is called the fixation point. Normal eye movements are usually conjugate in order

to maintain binocular vision and stereopsis. The MLF coordinates the contractions of the yoked muscles and the relaxation of their antagonists so that the two eyes move together.

During a monocular duction movement, the agonist contracts and the antagonist relaxes. When the medial rectus in one eye contracts, the lateral rectus in the same eye must relax. Sherrington's law describes the balance between the contraction of the agonist and the inhibition of the antagonist. In certain conditions (e.g., Duane's syndrome, Parinaud's syndrome), there is failure of antagonist inhibition resulting in co-contraction of muscles. Co-contraction causes the globe to retract into the orbit rather than moving in a normal manner.

During binocular version movements, the extraocular muscles work as yoked pairs (e.g., the lateral rectus in one eye contracts with the medial rectus in the other eye) ([Figure 14.3](#)). The yoke muscles are paired agonists for the binocular movement, and in each eye, their respective antagonists, per Sherrington's law, must be reciprocally inhibited. Hering's law, or the law of equal innervation, states that the same amount of innervation goes to an extraocular muscle and to its yoked fellow. The amount of innervation to the yoked pair is always determined by the fixating eye. Hering's law is important in understanding the topic of primary and secondary deviations.

Patients with diplopia become symptomatic because of visual confusion. The confusion results because of discordant retinal images—one real, one not. Diplopia is usually preceded by blurring of vision. Even when ocular malalignment is obvious, it is common for patients to have nonspecific complaints, such as blurry vision or dizziness, rather than complaining of frank “double vision.” Historical details are often helpful in deciphering the cause of diplopia. The first step should be to determine whether the diplopia is binocular or monocular. Surprisingly, few patients have been observant enough to cover one eye and thus answer this question. With binocular diplopia, covering one eye eliminates the visual confusion. Monocular diplopia persists when using the affected eye alone. Monocular diplopia is often considered a nonorganic symptom, but there are many organic causes, primarily ophthalmologic conditions such as cataract, corneal astigmatism, lens subluxation, retinal detachment, and macular disease. Rare patients with cortical lesions will develop polyopia, seeing multiple afterimages with either eye, which can be confused with monocular diplopia.

Observant patients may be able to state whether the diplopia is horizontal or vertical, worse at near or distance, or worse in a particular direction of gaze; all

are pertinent observations. Horizontal diplopia usually results from dysfunction of the medial or lateral rectus muscles. Vertical diplopia tends to result from disorders of the oblique muscles, less often of the vertically acting recti. Patients with sixth nerve palsy have difficulty diverging the eyes and tend to have more diplopia at distance. The lateral recti are not active when the eyes are converging for near vision, and patients have less diplopia at near (reading) as compared to distance (driving). Conversely, patients with medial rectus weakness have difficulty converging with more diplopia at near and less at distance. Diplopia is worse with gaze in the direction of the involved muscle. The patient with either a right sixth nerve palsy or a left third nerve palsy will have more diplopia on right gaze. Patients with fourth nerve palsy often describe an obliquity or tilt to the image. A patient with diplopia may keep one eye closed or may tilt or turn the head to minimize the visual confusion (ocular torticollis). An ocular cause of abnormal head position is common in children; the most common causes are congenital nystagmus, superior oblique paresis, dissociated vertical deviation, Brown's syndrome (see below), and refractive errors.

The diplopia of MG varies greatly with time of day and fatigue. Transient diplopia may occur with vertebrobasilar insufficiency. Persistent diplopia of sudden onset suggests a vascular event, with ischemia involving either a specific CN, as in diabetic third nerve palsy, or the brainstem. Ischemic CN palsy tends to resolve in 2 to 3 months. Progressive diplopia raises the possibility of a compressive lesion involving a CN. Trauma to the head or orbit frequently causes diplopia. Patients with a history of congenital strabismus may develop diplopia later in life because of decompensation of the squint and failure of fusion. A history of squint, "lazy eye," wearing glasses, patching one eye, or visits to the eye doctor as a child may all be relevant in the adult patient.

Associated symptoms may be important. Diplopia accompanied by ptosis may occur with third nerve palsy, as well as with MG and other neuromuscular disorders. Pain in the head or eye in association with diplopia suggests such conditions as diabetic third nerve palsy, posterior communicating aneurysm, ophthalmoplegic migraine, Tolosa-Hunt syndrome (painful ophthalmoplegia), and giant cell arteritis.

EXAMINATION OF EYE MOVEMENTS

Assessment of ocular movements should include an assessment of visual acuity.

When acuity is impaired, the patient may not be able to adequately fixate. This influences the results of various maneuvers used to assess motility, particularly the cover test. Note the position of the patient's head. Many patients with ocular malalignment will hold their head in an unusual position. Usually, there is a turn or tilt that minimizes the diplopia. Occasional patients will use a different strategy and hold the head in a position that maximizes diplopia in order to make the false image fainter and more easily ignored. Patients with congenital nystagmus typically turn the head to maintain the eyes in a null zone where the nystagmus is least. Note the lid position. Lid asymmetry may accompany vertical strabismus; the appearance depends on which eye is fixing.

Assuming reasonable visual acuity and normal head position, the motility examination begins with an assessment of fixation. A normal patient can fixate steadily on an object of regard, whether near or distant. Inability to maintain normal steady fixation may occur because of square wave jerks, macro square wave jerks, macrosaccadic oscillations, and other disorders. These conditions cause fixation instability, or saccadic intrusions, transient deviations away from fixation with a quick return. Saccadic intrusion may be more apparent when viewing the fundus. Saccadic intrusions may be mistaken for nystagmus. Although saccadic intrusions can occur in normals, especially the elderly, they are usually a sign of brainstem or cerebellar disease. The patient with nystagmus greater than first degree will also not have normal steady fixation.

In routine cases where there are no eye complaints and the likelihood of abnormality is low, the ocular motility examination is usually limited to assessing versional pursuit movements in the six cardinal positions of gaze, including full lateral gaze to each side, as well as upgaze and downgaze when looking to either side ([Figures 14.2](#) and [14.3](#)). The target should slowly trace a large letter "H" for the patient to follow. Some add primary gaze plus upgaze and downgaze in the center to make nine cardinal positions. Eye movements should remain smooth and conjugate throughout. The six cardinal positions are designed to search for dysfunction of individual muscles or nerves, as well as supranuclear abnormalities of horizontal gaze. Assessment of upgaze and downgaze in primary position assesses the supranuclear vertical gaze mechanisms.

Pursuit versions are done by asking the patient to follow a target held about 0.5 to 1.0 m away, such as an examining light, a pointer, a pen, or the examiner's finger. A linear target should be held perpendicular to the direction of gaze, vertical for testing horizontal gaze, and horizontal for vertical gaze. Use of an

examining light adds the ability to assess the corneal reflection, which gives objective evidence of ocular malalignment. The light reflection should be just medial to the center of the pupil and at corresponding points in each eye. The patient should indicate if she sees more than one target at any point. Pursuit movements are normally smooth. In certain disease states with abnormal pursuit, the tracking movements become disrupted by superimposed saccades, creating a ratchety or jerky movement termed saccadic pursuit (cogwheel eye movements). The finding is nonspecific and can occur bilaterally with fatigue, inattention, decreased consciousness, basal ganglia disorders, diffuse hemispheric disease, drug effects, or if the target velocity is too fast. Abnormal pursuit in one direction may indicate an ipsilateral deep occipitoparietal lobe lesion involving the pursuit pathways.

Normally, the eyes can move through a range of about 45 degrees to either side of primary position. In absolute terms, for the normal adult eye, the excursions are about 10 mm for adduction, abduction, and elevation, and about 7 mm for depression. The last 10 degrees of abduction is difficult to maintain and holding there may result in end-point nystagmus, a normal physiologic phenomenon. Patients can normally “bury the limbus” with both eyes in full lateral gaze in each direction, somewhat better on adduction than abduction. In full lateral gaze, the temporal limbus abuts the lateral canthus; in full medial gaze, about the inner third of the nasal limbus is buried. A small rim of sclera showing on extreme abduction is not abnormal. Normally, the amount of scleral show on abduction is symmetric in the two eyes. Greater scleral show on full abduction in one eye than the other may be a subtle sign of abduction impairment. Assessment of upgaze and downgaze is occasionally difficult. Normal aging causes impairment of upgaze, which varies from individual to individual. The best control for assessing normality of upgaze is usually the patient’s spouse.

The vergence system comes into play when an object moves toward or away from the observer. Dysconjugate eye movements, convergence or divergence, are required. Testing convergence is not always necessary. However, the central mechanisms subserving adduction of the eyes for convergence are different from the mechanisms for adduction during conjugate gaze. Testing convergence is helpful in some circumstances, such as when the pupillary light reflex is not crisply normal (in order to look for light-near dissociation of the pupils), or when there is anything to suggest an INO.

The saccadic system can be tested by having the patient rapidly refixate

between two targets. The patient is instructed to switch gaze between one target, such as the examiner's nose, and an eccentric target, such as the examiner's finger held to one side. The examiner assesses the velocity, magnitude, and accuracy of the saccades and compares adduction and abduction saccades in each eye and saccades in the two eyes. Saccadic velocity may be decreased globally in some conditions, such as MG, or selectively, such as slow adduction saccades in the involved eye in a unilateral INO. Saccades may be hypometric, falling short of target and requiring additional, smaller saccades to attain fixation, or hypermetric, overshooting the target and requiring saccades back in the opposite direction. In some conditions, reflex eye movements may be present when other movements are impaired. VOR movements can be examined by having the patient fix on a target, then passively moving the head from side to side, or up and down.

EVALUATION OF OCULAR MALALIGNMENT

Testing for diplopia and ocular malalignment may be subjective or objective. The subjective tests depend on the patient's observation of images, the objective tests on the examiner's observation of eye movements during certain maneuvers. Common subjective bedside evaluations include the red lens and Maddox rod tests; common bedside objective tests are the corneal light reflex tests and the cover tests (cover-uncover and alternate cover). The objective tests only require the patient to fixate; they do not require any subjective responses or interpretation of the color or separation of images.

Subjective Tests

Subjective tests for diplopia depend on the patient's description of the images seen. These are most helpful soon after the onset of an oculomotor disturbance. With the passage of time, there is compensation and precise delineation of the faulty nerve or muscle becomes more difficult. Testing should be done at a distance of 1 m to avoid any potentially confusing convergence. It may be useful to have the patient hold up both index fingers and demonstrate the separation of images in each position of gaze.

When a patient has diplopia because of extraocular muscle weakness, she sees two images. The real image falls on the macula of the normal eye. The false

image falls on the retina beside the macula of the paretic eye. The brain is accustomed to images falling off the macula coming from peripheral vision, so it projects the false image peripherally. The farther away from the macula that the image falls, the farther peripherally the misinterpretation of its origin. As the eye moves in the direction of the paretic muscle, the separation of images increases, and the false image appears to be more and more peripheral. The false image is also usually fainter than the true image because extramacular vision is not as acute. The clarity, however, depends on the visual acuity in the two eyes.

Consider a patient with right lateral rectus weakness gazing to the right. The left eye accurately tracks the target; the right eye does not pass midline. The true image falls on the left macula. The false image falls on the nasal hemiretina of the right eye. The brain interprets the light ray falling on the right nasal hemiretina as coming from the right side of space. The farther onto the right nasal hemiretina the light ray falls, the farther to the right side the brain thinks it came from. These considerations lead to three “diplopia rules” to identify the false object: (a) the separation of images is greatest in the direction of action of the weak muscle, (b) the false image is the more peripheral, and (c) the false image comes from the paretic eye.

The false image may be identified in different ways. The simplest is to move the patient’s eyes into the position with the greatest separation of images. Then cover one eye. If the more peripheral image disappears, the covered eye is the paretic eye. Consider a patient with maximal diplopia in right horizontal gaze. The candidate faulty muscles are the right lateral rectus and the left medial rectus. If the examiner then covers the patient’s left eye and the image on the patient’s left disappears, the diagnosis is right lateral rectus weakness. This is because the image that disappeared was less peripheral; therefore, the true image and the false image must have been arising from the right eye.

The red lens (red glass) and Maddox rod tests are attempts to be more precise. They may be especially useful when the diplopia is mild and the weak muscle or muscles not apparent from examination of ocular versions ([Box 14.3](#)). The theory of the red lens test is sound, but often the results of testing in clinical practice are less than clear. One reason is that the red lens breaks fusion just enough to bring out unrelated phorias, which muddy the findings. The results of the red lens test may be drawn to aid interpretation. There should be a notation as to whether the diplopia fields are drawn as seen by the patient or as seen by the examiner ([Figure 14.23](#)).

BOX 14.3

Red Lens and Maddox Rod Testing

The red lens is a simple translucent red glass that is placed, by convention, over the patient's right eye. When an examining light is shone into an orthophoric patient's eyes, the patient sees a single pink light in all positions of gaze. A Maddox rod is an array of cylinders in a plastic housing that creates a line, which may be vertical or horizontal depending upon how it is held. The vertical line is used for evaluating horizontal diplopia, the horizontal line for vertical diplopia. The Maddox rod is placed over the right eye. If the instrument is held so as to create a vertical line, the orthophoric patient sees a white light bisected by a red vertical line in all directions of gaze. The red line indicates which image is coming from the patient's right eye.

Consider again the patient with maximal diplopia in right horizontal gaze, with the red lens over the right eye. The patient sees a pink light in primary and left gaze, but a red light and a white light in right lateral gaze. If the red light is more peripheral, the patient has right lateral rectus weakness, because the more peripheral image is coming from the right eye. If the white light is more peripheral, the patient has left medial rectus weakness.

Diplopia may be divided into crossed (heteronymous) and uncrossed (homonymous). If the false image is on the same side as the eye that sees it, there is homonymous diplopia; if the image is on the opposite side, there is heteronymous diplopia. With the red-lens test, if the false image comes from the ipsilateral eye (e.g., red image to the right on right gaze), the diplopia is uncrossed (a line could be drawn directly from the false image to the paretic eye). If the false image comes from the contralateral eye (e.g., white image to the right on right gaze), a line from the false image to the paretic eye would cross a line drawn from the true image to the nonparetic eye and the diplopia is said to be crossed. For the patient with maximal separation of images on right horizontal gaze, uncrossed diplopia would imply right lateral weakness and crossed diplopia left medial rectus weakness. Of course, apparent weakness of any particular extraocular muscle could be simulated by any process that prevents relaxation of the antagonist—such as fibrosis, contracture, infiltrations, entrapment, or co-contraction.

Objective Tests

The corneal light reflex test (Hirschberg's test) depends on observing the reflection of an examining light on the cornea and estimating the amount of ocular deviation depending on the amount of displacement of the reflection from the center of the pupil. The test can only be done at near because distant reflections are too dim, so the confounding effects of the near reflex must be reckoned with. Each millimeter of light displacement from the center indicates 18 degrees of eye deviation.

Cover Tests

An elementary review of strabismus is useful to help understand the cover tests (Box 14.4). The cover tests are predicated on forcing one eye or the other to fixate by occluding its fellow, and determining the drift of the nonfixing eye while it is under cover. Varieties of cover testing include the cover-uncover test and the alternate cover test. The cover-uncover test is used primarily by ophthalmologists to evaluate patients with congenital strabismus where there is an obvious squint. When neurologic patients have an obvious malalignment, its nature is usually apparent. The alternate cover test is used to evaluate more subtle deviations.

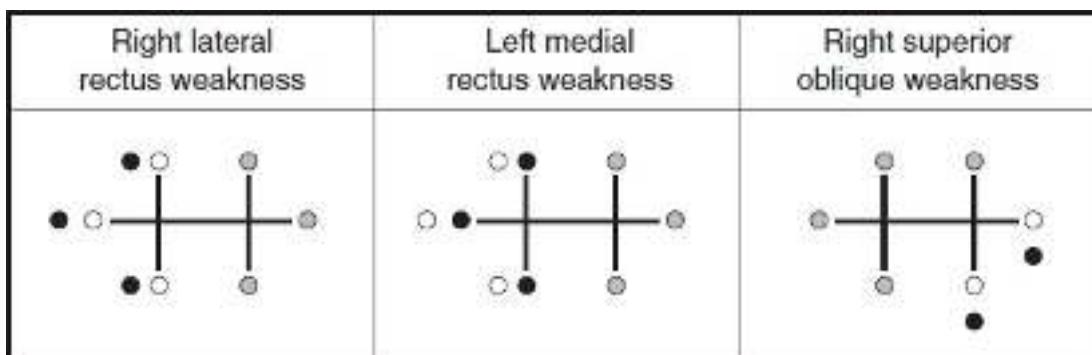


FIGURE 14.23 Red lens diplopia fields, drawn as seen by the examiner. The *red lens* is placed over the right eye, and the eyes move through the six cardinal positions of gaze with the patient looking at an examining light. *White circles* depict images coming from the left eye (*white light*); *dark circles*, images from the right eye (*red light*); and *intermediate circles*, images from both eyes (*pink light*).

BOX 14.4

Strabismus

Strabismus, or squint, means nonconcordance of the visual axes. Strabismus may be paralytic or nonparalytic. Ordinary strabismus, or congenital squint, occurs when the cerebral cortical mechanisms designed to maintain binocular vision fail for some reason, but the eyes are otherwise normal. This variety of strabismus is very common in children. Congenital strabismus is nonparalytic. In acquired strabismus, one or more eye muscles fail to function normally. Acquired strabismus is often paralytic (e.g., from third nerve palsy). There is an ocular malalignment, which is worse in the field of action of the affected muscle or muscles.

Perfect eyes are orthophoric (Gr. *orthos* “straight”) in all fields of gaze; the visual axes are precisely parallel during all versional eye movements, even without a stimulus to fusion. Any deviation from perfection is termed heterophoria or heterotropia, usually shortened to phoria and tropia, respectively. In heterotropia, the malalignment is evident at rest. Esotropia is a manifest medial deviation (convergent or internal strabismus; “cross eye”); exotropia is a manifest lateral deviation (divergent or external strabismus; “wall eye”). Hypertropia is elevation, and hypotropia is depression. Heterophoria is a latent tendency for deviation, which only becomes apparent when the stimulus to fusion fails under certain circumstances, such as fatigue or when binocular fusion is deliberately broken, as by covering one eye. Congenital exophoria is very common. Exophoria may occur with myopia, esophoria with hyperopia. When an eye with exophoria is not fixing, it tends to drift back to its anatomical position of slight abduction.

A phoria is a latent deviation held in check by fusion. Breaking fusion by covering one eye causes the covered eye to deviate nasally (esophoria) or temporally (exophoria). If the cover is switched to the other eye (alternate cover), the just uncovered eye is forced to move into position to take up fixation. If an adduction movement occurs, it means the eye had been deviated outward under cover (exophoria). An abduction movement means the eye had been deviated inward (esophoria). The magnitude of the deviation can be quantitated by placing base-in or base-out prisms of increasing diopter strength before the involved eye until the refixation movements no longer occur.

COMITANCE

A phoria or tropia may be comitant (concomitant) or incomitant (noncomitant, nonconcomitant). Comitance describes the consistency of the deviation in various fields of gaze (Box 14.5). In neurologic patients, strabismus is typically paralytic and incomitant. Primary and secondary deviations are related to which eye is abnormal and which eye is fixing. In paralytic strabismus, the secondary deviation is greater than the primary deviation.

OPTOKINETIC (OPTICOKINETIC, OPTOMOTOR) NYSTAGMUS

OKN is a normal, physiologic phenomenon sometimes affected by disease. OKN is conjugate nystagmus induced by a succession of moving visual stimuli. OKN occurs whenever the eyes must follow a series of rapidly passing objects, such as telephone poles zipping by a car or train window. Clinical testing entails moving a striped target, a rotating drum, or a cloth tape bearing stripes or squares in front of the patient and requesting that she “count” the stripes or squares. Several OKN applications are available for smartphones and similar devices. Although OKN is more complex, it can be viewed for clinical purposes as testing pursuit ipsilateral to the direction of target movement, and contralateral saccades. The ipsilateral PTOJ mediates pursuit of the acquired stripe via connections that run in the internal sagittal stratum, deep in the parietal lobe medial to the geniculocalcarine radiations and adjacent to the atrium of the lateral ventricle. When ready to break off, it communicates with the ipsilateral frontal lobe, which then generates a saccadic movement in the opposite direction to acquire the next target. In normal, alert individuals, an OKN stimulus induces brisk nystagmus with the fast phase in the direction opposite tape movement. The response is intensified if the subject looks in the direction of the quick phase. Responses in one direction are compared with responses in the other direction. A vertically moving stimulus can evaluate upgaze and downgaze. For an example of normal and of blunted OKN responses, see [Video Link 14.6](#).

BOX 14.5

Comitance and Primary and Secondary Deviation

A comitant strabismus shows the same degree of deviation in all directions of gaze. Congenital, nonparalytic strabismus is typically comitant. Paralytic strabismus, likely to be seen in neurologic patients, is characterized by incomitance; the ocular malalignment as revealed by cover testing varies with the direction of gaze and is greatest in the direction of action of the paretic muscle. A patient with right lateral rectus weakness will have no abnormality on alternate cover testing while looking to the left, because the right lateral rectus has no role to play in left gaze. In primary gaze, the affected eye might drift into esophoria under cover and changing the cover to the normal eye would reveal an abduction refixation movement of the right eye. In right lateral gaze, the right lateral rectus insufficiency would become more obvious. The right eye would drift even more to the left under cover than it did in primary gaze, and uncovering would reveal a larger abduction refixation saccade. The eye deviation thus varies with the direction of gaze, none in left gaze, mild in primary gaze, and moderate in right gaze. This variability is incomitance and is the hallmark of paralytic strabismus.

In paralytic strabismus, the affected eye will be deviated away from the field of action of the involved muscle. With a right cranial nerve (CN) VI palsy, the right eye will be slightly adducted. With equal vision in the two eyes, the noninvolved left eye will fixate so that in primary gaze the left eye is fixing and the right eye is deviated toward the nose. This deviation of the right eye is the primary deviation. If the target is moved into the field of action of the paretic muscle, to the right, and the left eye is covered so that the right eye is forced to fixate, the left medial rectus (the yoke muscle of the right lateral rectus) will receive equal and simultaneous innervation per Hering's law. Because the right lateral rectus is trying mightily to contract in an attempt to fixate, the left medial rectus is simultaneously contracting mightily and, under cover, the left eye is markedly adducting into right lateral gaze. Removal of the cover reveals deviation of the left eye, which is termed the secondary deviation. In summary, the primary deviation is the deviation of the bad eye with the good eye fixing; the secondary deviation is the deviation of the good eye with the bad eye fixing.

Patients with hemianopsias because of occipital lobe disease have a normal OKN response, despite their inability to see into the hemifield from which the tape originates. Because of interruption of the OKN pathways, patients with

hemianopsias because of disease of the optic radiations in the deep parietal lobe have abnormally blunted or absent OKN responses. The patient is unable to pursue normally toward the side of the lesion and is unable to generate contraversive saccades into the blind hemifield. The significance of OKN asymmetry lies in the vascular anatomy and the differing pathologies that affect the parietal and occipital lobes. Tumors are rare in the occipital lobe and much more common in the parietal lobe. Furthermore, the OKN pathways in the deep parietal lobe are outside the distribution of the posterior cerebral artery. Therefore, a patient with a hemianopsia and normal OKN responses is more likely to have an occipital lesion, and more likely to have had a stroke. With asymmetric OKNs, the lesion is more likely to reside in the parietal lobe, and more likely to be nonvascular, that is, a tumor (Cogan's rule). An asymmetric OKN response has a positive LR of 5.7 for detecting parietal lobe disease.

The primary clinical utility of OKN testing is investigation of patients with parietooccipital lesions, but the OKN tape has other uses. It may be used to crudely check visual acuity, especially in infants. OKN responses can be elicited beginning at 4 to 6 months of age. OKN may also be useful for estimating visual function in patients with depressed consciousness. It may provide a clue to the presence of psychogenic visual loss. OKN testing can demonstrate the slowed adducting saccades of a subtle INO, and sometimes accentuate the nystagmus in the abducting eye. OKN-forced upward saccades may induce convergence retraction nystagmus in patients with Parinaud's syndrome. OKN abnormalities may be seen early in PSP.

DISORDERED OCULAR MOTILITY

Abnormal eye movements can occur for many reasons. Disorders can be broadly divided into peripheral (intranuclear and nuclear) and central (internuclear and supranuclear). Peripheral disorders involve the extraocular muscles (e.g., MG or ocular myopathy) or the CNs (e.g., fourth nerve compression). Peripheral disorders include things that affect the CN nuclei, fascicles, or peripheral trunks. Although the nuclei and fascicles are "central," the clinical characteristics of conditions involving these structures is much more akin to other intranuclear conditions than to supranuclear disorders. Central disorders can be divided into supranuclear, involving the optomotor control centers; and internuclear, involving the pathways connecting and coordinating the activity of the ocular

motor nuclei, primarily the MLF. There are many primary ophthalmologic conditions that can cause abnormal eye movements that can be confused with neurologic disorders ([Table 14.3](#)).

PERIPHERAL DISORDERS OF OCULAR MOTILITY

Disturbances of ocular motility may result from processes involving the orbit causing mechanical limitation of eye movement, or from ocular myopathies, neuromuscular transmission disorders, or a palsy of an individual ocular motor nerve.

Orbital Disease

Masses within the orbit may mechanically inhibit movement of the globe, often causing telltale proptosis as well. Following trauma to the orbit, individual extraocular muscles may become caught in fracture fragments, such as entrapment of the inferior rectus by an orbital blowout fracture producing a mechanical limitation of upgaze and vertical diplopia. Other examples of orbital disease causing ocular dysmotility include orbital pseudotumor, lymphoma, and rhabdomyosarcoma. Mechanically limited eye excursions exist for passive as well as active movements. Forced ductions involve pushing or pulling on the anesthetized globe in order to passively move it through the impaired range. An eye affected by ocular muscle weakness, MG, or an ocular motor nerve palsy moves freely and easily through a full range. An eye affected by restrictive myopathy or an entrapped muscle cannot be moved passively any better than actively. Brown's tendon sheath syndrome is limitation of the free movement of the superior oblique tendon through the trochlea; it is most often congenital. The restriction of movement is analogous to trigger finger and causes an impairment of upgaze in adduction simulating inferior oblique palsy ([Video Link 14.7](#)).

TABLE 14.3 Disorders That May Cause Diplopia Mimicking Cranial Nerve Palsies

Disorder	Condition Mimicked	Distinguishing Feature
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Duane's syndrome	Cranial nerve (CN) VI palsy	Globe retraction and narrowing of palpebral fissure on adduction
Brown's tendon sheath syndrome	Inferior oblique palsy	Click on eye elevation
Myasthenia gravis	Any	Fluctuating findings
Thyroid eye disease	Any	Exophthalmos, lid abnormalities, chemosis, history of thyroid disease, abnormal forced ductions
Convergence spasm	CN VI palsy	Pupil constricts on lateral gaze
Medial rectus restriction	CN VI palsy	Abnormal forced ductions
Inferior rectus restriction	Elevator palsy	Abnormal forced ductions
Superior rectus restriction	CN IV palsy	Abnormal forced ductions
Möbius' syndrome	CN VI palsy	Congenital, often bilateral
Divergence insufficiency or paralysis	CN VI palsy	Full ductions, can't diverge
Orbital pseudotumor	Any	Proptosis, abnormal forced ductions
Decompensation of congenital squint	Any	Deviation is comitant

Muscle Disease

Primary ocular muscle disease may cause impaired motility because of weakness or because of restriction of movement. A number of myopathies and muscular dystrophies may affect eye muscles. Muscle disorders may be divided into myopathies and restrictive orbitopathies. The most common restrictive orbitopathy is TED, which is an autoimmune disorder that causes deposition of mucopolysaccharide and lymphocytic infiltration in eye muscles, making them bulky, stiff, and unable to relax during contraction of the antagonist. This sort of restrictive myopathy is easily confused with weakness of the antagonist (e.g., restrictive myopathy of the medial rectus simulating weakness of the lateral rectus). Extraocular muscles affected by TED also do not contract normally. Forced ductions are often done to clarify matters. The inferior rectus is the most commonly involved muscle in TED, producing impaired upgaze on the affected side. The possibility of TED must be constantly borne in mind when dealing with ocular motility disturbances.

Ocular myopathies cause weakness of the extraocular muscles, usually accompanied by ptosis and weakness of eye closure because of myopathic involvement of the facial muscles. Weakness of eye closure is strongly suggestive of ocular myopathy or neuromuscular transmission disorder as the cause of eye muscle weakness. Few other conditions affect both eye muscles and facial muscles. The common conditions causing ocular myopathy are chronic progressive external ophthalmoplegia (CPEO) and oculopharyngeal muscular dystrophy ([Box 14.6](#)).

Neuromuscular Transmission Disorders

MG, the most common neuromuscular transmission disorder, frequently involves the extraocular muscles, affecting any muscle or combination of muscles. Ocular involvement occurs early in 50% to 70% of patients, and it eventually develops in 90%. Patients typically present with ptosis or diplopia, or both. In some patients, the disease remains limited to the eyes (pure ocular myasthenia). Most patients present with ocular involvement and then later develop generalized MG, as the disease affects bulbar and limb muscles. Even in patients with generalized MG, the ocular component usually remains a prominent feature. The hallmark of

MG is fatigable weakness. The weakness gets worse with repetitive contraction of the muscle. The ptosis in MG is “fatigable”; it gets progressively worse with prolonged upgaze. The eyelid signs of MG are discussed above. Patients may develop diplopia with sustained eccentric gaze even when not present initially. Fluctuating ptosis and diplopia and worsening symptoms toward the end of the day are characteristic. The ptosis and ophthalmoparesis of MG are usually asymmetric and may vary from minute to minute. During the course of a neurologic examination, the ptosis may switch sides and the diplopia may vary. These features along with accompanying weakness of eye closure are virtually diagnostic. The earliest manifestation of ocular MG is slowing of saccadic movement on rapid refixation.

BOX 14.6

Ocular Myopathies

Chronic progressive external ophthalmoplegia (CPEO) is a syndrome that has numerous etiologies, but it is most often due to mitochondrial myopathy. It causes inexorably progressive ptosis and symmetric eye muscle weakness, eventually leaving the patient with marked ptosis and eyes that are essentially immobile. Patients do not typically have diplopia. Examination shows loss of both voluntary and reflex eye movements; Bell's phenomenon is absent. Muscle biopsy usually shows ragged red fibers. Kearns-Sayre syndrome is a type of CPEO that is associated with pigmentary retinopathy, cardiac abnormalities, particularly conduction block with an increased risk of sudden death, hearing loss, ataxia, mental retardation, endocrine dysfunction, short stature, and increased cerebrospinal fluid (CSF) protein; all with onset before age 20.

Most of the classical muscular dystrophies do not involve the eye muscles. An exception is oculopharyngeal dystrophy, which causes prominent, progressive bilateral ptosis and dysphagia that usually begin in the fifth or sixth decade. The signature of the disease is ocular myopathy accompanied by pharyngeal weakness. Congenital myopathies usually spare the eye muscles. An exception is myotubular myopathy, where there may be early and prominent involvement. Myotonic dystrophy causes prominent ptosis. It can affect the extraocular muscles causing slowed saccades, but major involvement is not a typical feature of the disease. Eyelid myotonia is

common but can occur with most of the myotonic disorders, and it is not specific for myotonic dystrophy. Rarely, the extraocular muscles may be affected by inflammatory myositis.

BOX 14.7

Myasthenia Gravis

Having the patient rest with eyes closed for 30 minutes may produce temporary improvement of the ophthalmoparesis (sleep test). Applying a cold pack to the eye may relieve, and a hot pack exacerbate, both the ptosis and ophthalmoparesis. A convenient way to warm the eye is with an electric hair dryer on low setting. Warming just one eye can produce dramatic asymmetries. The edrophonium (Tensilon) or neostigmine (Prostigmin) test can be very helpful when there is a muscle with clear-cut weakness to evaluate before and after the injection. Myasthenia gravis (MG) may induce central adaptive effects to compensate for the extraocular muscle weakness. Because of fatigue during a saccade, the central nervous system may begin to generate an increased signal for a saccadic movement in order for the eye to find the target. Administration of edrophonium may cause the weakness to temporarily resolve, but the central adaption effect persists and saccades suddenly become hypermetric, overshooting the target. The development of hypermetric saccades or macrosaccadic oscillations after edrophonium is highly suggestive, some say diagnostic, of MG. Other useful tests include assay for antiacetylcholine receptor antibodies, repetitive nerve stimulation, and single-fiber electromyography.

MG can cause weakness of any muscle or combination of muscles. It is rare but not unheard of to have ophthalmoparesis without ptosis. MG can cause weakness of any isolated muscle and should be considered in the differential diagnosis whenever ophthalmoparesis does not fit any particular pattern. MG can also produce ophthalmoparesis that simulates other conditions. Selective involvement of one medial rectus may produce a “myasthenic pseudo-INO,” complete with nystagmus of the abducting eye ([Figure 14.15](#), also see [Video Link 14.8](#)). Involvement of one lateral rectus can simulate sixth nerve palsy. MG can mimic gaze palsy or the pattern of any individual nerve. It should be

considered in the differential diagnosis of virtually any patient with external ophthalmoplegia, but involvement of the pupil excludes MG. Ability to manipulate the myasthenic eye signs helps greatly in diagnosis ([Box 14.7](#)).

Except for mild ptosis, Lambert-Eaton syndrome does not usually involve the eyes. Botulism can cause severe ophthalmoparesis, often but not invariably with pupillary involvement. Other unusual neuromuscular disorders, such as marine toxins and congenital myasthenic syndromes, can also produce ophthalmoparesis.

INDIVIDUAL NERVE PALSIES

The same basic processes cause third, fourth, and sixth nerve palsies, but with different frequencies. As many as 25% of cases are idiopathic, and of these, 50% recover spontaneously. Some processes may affect more than one ocular motor nerve. Trauma is the most common cause of fourth nerve palsy and the second most common cause of third and sixth nerve palsy. Microangiopathic vascular disease because of diabetes or hypertension is the most common etiology of nontraumatic third and sixth nerve palsies. Aneurysms are an important etiology of third nerve disease. Increased intracranial pressure may cause third nerve palsies because of uncal herniation and sixth nerve palsies as a nonspecific and nonlocalizing effect. Neoplasms may affect any of these nerves. A third nerve palsy developing after trivial head trauma suggests the possibility of subclinical stretch because of an underlying mass. Basilar meningitis, migraine, viral infection, immunizations, cavernous sinus disease, sarcoid, vasculitis, and Guillain-Barré syndrome are occasional etiologies; the list of rare etiologies is long.

The Oculomotor Nerve

CN III palsy produces varying degrees and combinations of extraocular muscle weakness, ptosis, and pupil involvement. Internal ophthalmoplegia means involvement limited to the pupillary sphincter and ciliary muscle; external ophthalmoplegia means involvement of only the extraocular muscles; complete ophthalmoplegia is both. The most common identifiable etiologies are ischemia, aneurysm, tumor, and trauma; some 20% remain unexplained. Differentiating benign ischemic palsies from those due to aneurysms is a challenge, especially

because both can present with painful diplopia; delay in diagnosis increases mortality. Third nerve dysfunction is frequently an ominous sign, especially in the setting of any alteration of consciousness. Uncal herniation from mass effect of any sort may result in compression as the temporal tip crowds through the tentorial hiatus and traps CN III against the sharp edge of the tentorium. Posterior communicating or distal internal carotid aneurysms commonly cause third nerve palsy ([Figure 14.5](#)). With third nerve palsy, processes affecting the nucleus or fascicles within the brainstem generally produce accompanying neighborhood signs permitting localization (e.g., Weber's or Benedikt's syndrome). In its long course along the base of the brain, CN III may be affected in isolation. In the cavernous sinus or orbit, accompanying deficits related to involvement of other structures usually permit localization.

Complete paralysis of the third nerve causes severe ptosis of the upper lid; impairment of medial, upward, and downward gaze; and loss of accommodation, with a dilated pupil that does not react to light, directly or consensually, or to near ([Figure 14.12](#)). There may be no complaint of diplopia if the lid completely covers the eye. When there is diplopia, the images are often oblique because of the combination of weak muscles. The eye rests in a down and out position because of preservation of the lateral rectus and superior oblique functions.

In a large series, third nerve palsies were complete in only 33%. Incomplete CN III lesions, causing paresis rather than paralysis and affecting certain functions more than others, are more common than complete ones. Ischemic lesions usually spare pupillary function. Lesions involving the midbrain or the course of the nerve after it has split into its superior and inferior divisions are more likely to involve only certain functions (see “Large Pupils,” below). Lesions between the interpeduncular fossa and the point of division tend to cause paralysis of all functions, but divisional palsy may occur from a lesion anywhere along the course of the nerve. Very rarely, the only manifestation of a third nerve palsy may be an abnormal pupil. Depending on the etiology, a CN III palsy may show fluctuations, even over a short period of time, especially when there is nerve compression. A third nerve palsy because of uncal herniation may promptly resolve if the herniation can be reversed.

In addition to pupil sparing, the most helpful clinical feature distinguishing ischemic from mechanical, compressive lesions is aberrant reinnervation (misdirection syndrome, oculomotor synkinesis). Aberrant reinnervation is very common after facial nerve lesions (see [Chapter 16](#)), and a similar process may involve CN III ([Box 14.8](#)). Conditions that mechanically disrupt the nerve may

result in regenerating sprouts growing into the wrong tubes and eventually innervating some structure other than the one originally intended. For instance, fibers that originally innervated the medial rectus may reinnervate the levator palpebrae. The common causes are aneurysm and head trauma, less common causes are tumor and neurosyphilis; the condition can occur congenitally. The misdirection syndrome typically emerges about 3 months after the inciting event. Aberrant reinnervation does not occur after ischemic or idiopathic third nerve palsy. For a dramatic example of bilateral third nerve synkinesias because of a midbrain injury, see [Video Link 14.9](#) (From Taieb et al). The lid changes are the reverse of those seen in Duane syndrome (see [Box 14.9](#)).

Localization of Oculomotor Nerve Lesions

CN III palsy can occur because of lesions anywhere along its course from the oculomotor nucleus in the midbrain to the orbit. Common causes are trauma, tumor, diabetes, aneurysm, surgery, and stroke. Midbrain lesions are discussed further in [Chapter 21](#); they are usually accompanied by neighborhood signs that permit localization. Processes involving the third nerve nucleus may cause characteristic patterns of weakness not seen with lesions at other locations. Because of the contralateral innervation of the superior rectus, a nuclear lesion may cause weakness of the contralateral superior rectus. Involvement of the caudal central subnucleus may cause bilateral ptosis with an otherwise unilateral CN III palsy, or isolated bilateral ptosis. Conversely, patients with midbrain disease may have a lid-sparing third nerve palsy if the central caudal nucleus is not involved. Incomplete lesions involving the third nerve fascicles in the midbrain may cause partial CN III palsies. The pattern of involvement may mimic divisional palsy and suggest disease in the cavernous sinus or orbit (pseudodivisional palsy).

BOX 14.8

Aberrant Regeneration of CN III

The third nerve misdirection syndrome has certain characteristic features. The dual innervation of muscles causes a failure of normal reciprocal relaxation of the antagonist, violating Sherrington's law and causing co-contraction and retraction of the globe on certain movements. The clinical

picture is stereotyped but may vary in degree. Attempted upgaze causes adduction and retraction because of misdirection of superior rectus fibers to the medial and inferior recti with co-contraction. The upper lid may retract on downgaze (pseudo-Graefe sign) because of inferior rectus fibers aberrantly innervating the levator. The lid retracts on adduction because of synkinesis between the medial rectus and the levator. The lid may droop on abduction because the reciprocal inhibition of the medial rectus causes the levator to relax.

Misdirection may also involve the pupil. The pupillary light reaction typically remains poor to absent, but the pupil constricts on ocular adduction with either convergence or horizontal gaze. The constriction on convergence with an impaired light reaction mimics light-near dissociation (pseudo-Argyll Robertson pupil). The ciliary muscle is about 30 times larger than the iris sphincter; most of the neurons in the ciliary ganglion are devoted to accommodation rather than pupillary function. The great preponderance of ciliary muscle over pupillary sphincter axons make it likely that misdirection will result in accommodation fibers aberrantly innervating the pupil, which causes pupil constriction with any attempt to focus.

Processes involving the subarachnoid course of the nerve usually produce isolated unilateral CN III palsy with few associated findings to assist in localization. Incomplete involvement mimicking divisional palsy can occur. The most pressing diagnostic consideration in an isolated third nerve palsy is posterior communicating artery or basilar artery aneurysm. Aneurysmal third nerve palsies are typically acute, painful, and involve the pupil.

Ischemic third nerve palsies most often occur because of microvasculopathy related to diabetes and hypertension. Patients with ischemic palsies are typically older than those with aneurysms. Microvascular third nerve palsies are of sudden onset, painful, may spare the pupil, begin to resolve by about 2 months, and do not result in aberrant regeneration.

BOX 14.9

Duane's Syndrome

There are three recognized subtypes of Duane's syndrome; type I accounts for about 80% of cases. The core feature of type I Duane's syndrome is a

limitation of abduction with otherwise normal eye movements. It is caused by aplasia or hypoplasia of the sixth nerve nucleus, as occurs in Möbius' syndrome, but accompanied by anomalous innervation of the lateral rectus by CN III. The patient is unable to abduct the eye, and adduction induces co-contraction of the lateral rectus, causing retraction of the globe into the orbit. Dynamic enophthalmos caused by co-contraction makes the palpebral fissure narrow on adduction (pseudoptosis). Aberrant reinnervation of the third nerve causes the palpebral fissure to widen on adduction; Duane's syndrome causes it to narrow.

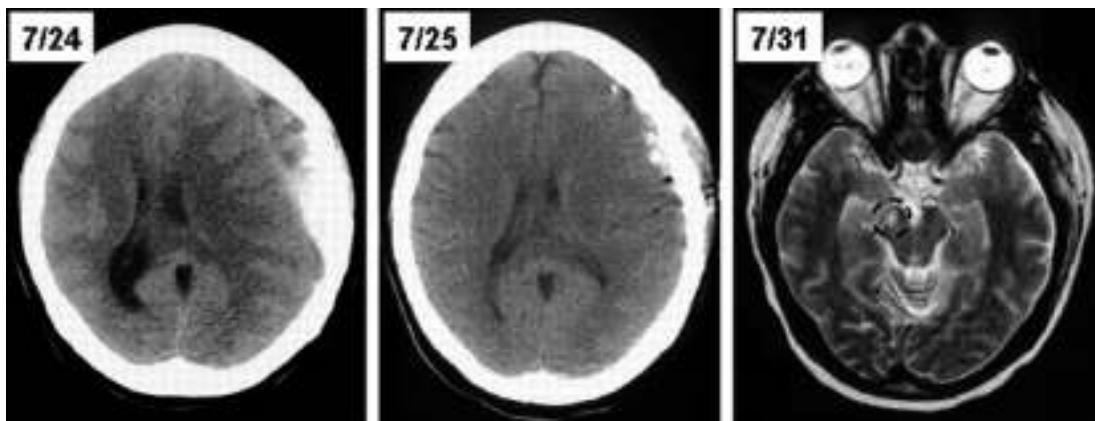


FIGURE 14.24 CT brain scan showed a left subdural hematoma with 1.5 cm midline shift (panel 7/24). After emergency platelet transfusion, the subdural hematoma was evacuated. Brain CT the next day showed resolution of the shift (panel 7/25). Brain MRI a week later showed a cerebral peduncle lesion in the T2-weighted sequence (panel 7/31). There was no history of head trauma.

Traumatic CN III palsy usually occurs only with major head injuries, severe enough to cause loss of consciousness or skull fracture. Increased intracranial pressure with uncal herniation most often compresses the ipsilateral nerve; the earliest sign is usually an abnormal pupil. Compression of the contralateral cerebral peduncle causing a false localizing hemiparesis ipsilateral to the lesion is not uncommon (Kernohan's notch syndrome, [Figure 14.24](#)). CN III can be affected bilaterally with lesions in the region of the rostral midbrain, such as central transtentorial herniation with Duret hemorrhages, ischemic top of the basilar syndrome, and basilar tip aneurysm.

Cavernous sinus disease usually affects other structures in addition to CN III, but mononeuropathy can occur. It is important in the evaluation of a complete third nerve palsy to be sure that CN IV is intact by having the patient attempt to

look down and medially; look for a slight intorsion movement (best appreciated by observing the conjunctival blood vessels). For an example of a pupil-sparing ischemic CN III palsy with preserved CN IV function, see *3rd nerve palsy with preserved 4th nerve function* from Dr. Daniel R. Gold, Neuro-ophthalmology Virtual Education Library [NOVEL], University of Utah, available at [Video Link 14.10](#). If the third nerve palsy is accompanied by involvement of CN IV, the likelihood of cavernous sinus disease is high. Cavernous sinus syndromes are discussed in [Chapter 21](#). Lesions in the anterior cavernous sinus or orbit may selectively involve one of the divisions. A superior division third nerve palsy causes ptosis and impairment of upgaze. An inferior division palsy causes medial and inferior rectus weakness and pupillary dysfunction but with no accompanying ptosis or superior rectus weakness. Lesions involving CN III in the apex of the orbit often involve CN II as well and may cause proptosis.

Other causes of isolated third nerve palsy include nerve sheath tumors, Lyme disease, sarcoidosis, dolichoectatic basilar arteries, ophthalmoplegic migraine, dural arteriovenous malformations, postinfectious syndromes, sphenoid sinusitis or mucocele, nasopharyngeal carcinoma, herpes zoster, and meningeal inflammation or infiltration.

The Trochlear Nerve

CN IV is slender and has a long intracranial course; these two factors increase its vulnerability to injury. The most common etiology of acquired CN IV palsy is head trauma. Nontraumatic cases are usually microvascular, idiopathic, or congenital. A patient with a congenital fourth nerve palsy may decompensate as an adult and present as an apparently new onset condition. Other causes of fourth nerve palsy include meningioma, cavernous sinus syndrome, herpes zoster, Lyme disease, ophthalmoplegic migraine, sarcoidosis, Guillain-Barré syndrome, meningeal disease, and Tolosa-Hunt syndrome.

Patients with fourth nerve palsies may not complain of diplopia, but rather blurry vision or some vague problem when looking down—as when reading a book or descending stairs. The diplopia is vertical or diagonal and maximal in downgaze. Patients may tilt the head to the opposite side to eliminate diplopia, tucking the chin so the affected eye may ride up and into extorsion, out of the field of action of the weak superior oblique. Some fourth nerve palsies, particularly in children, present with head tilt rather than diplopia. On examination, there is extorsion and impairment of depression of the adducted

eye ([Figure 14.25](#)). The involved eye has incomitant hypertropia or hyperphoria; with the patient looking down and in, alternate cover testing shows corrective downward refixations indicating upward drift of the affected eye under cover. The Bielschowsky head tilt test consists of tilting the head to each side, localizing the fourth nerve palsy by the changes in diplopia that result. If diplopia improves with head tilt to the left and worsens with tilt to the right, the patient has a right fourth nerve palsy. Forcing the involved eye to intort worsens the diplopia. For an excellent discussion of the bedside evaluation of vertical diplopia, see Prasad and Volpe. For a demonstration of the head tilt test in a patient with a CN IV palsy, see *Fourth Nerve Palsy* from Dr. Shirley Wray, Neuro-ophthalmology Virtual Education Library [NOVEL], University of Utah, available at [Video Link 14.11](#).



FIGURE 14.25 Right fourth nerve palsy. The patient is unable to depress the adducted eye on attempted downgaze.

Except that a nuclear lesion causes the fourth nerve palsy on the contralateral side, lesions at the nuclear and fascicular level in the midbrain cause the same clinical appearance as lesions involving the nerve proper in the subarachnoid space, cavernous sinus, or orbit. CNs III and IV can be involved together in processes affecting either the midbrain or cavernous sinus.

Superior oblique myokymia (microtremor) is a spasmotic, intermittent contraction of the superior oblique muscle that may cause transient vertical diplopia or monocular oscillopsia. The etiology is unknown but likely related to other conditions that cause focal myokymia. In rare instances, patients may go on to develop weakness of the superior oblique.

The Abducens Nerve

Sixth nerve palsies are common, and many resolve with no explanation. With a complete CN VI palsy, the eye cannot be abducted and often rests in a position of adduction ([Figure 14.26](#)). Patients present with horizontal diplopia worse at distance. There may be esotropia in primary position. Examination shows paralytic (noncomitant) strabismus, worse in the direction of action of the involved muscle. Incomplete palsies are common, and mild weakness may show only esophoria on alternate cover testing when the patient looks toward the side of the involved muscle. Neoplasms, trauma, demyelinating disease, and microvascular neuropathy are the most common etiologies. Many cases remain unexplained.

Neighborhood signs usually permit localization when the nerve is involved in the brainstem, cavernous sinus, or orbit. Pontine syndromes are discussed in [Chapter 21](#). Brainstem lesions do not necessarily produce other signs and can cause an apparently isolated sixth nerve palsy. The CN VI nucleus contains both lateral rectus motor neurons and interneurons that project up the MLF, so a lesion involving the nucleus causes an ipsilateral gaze palsy rather than a sixth nerve palsy.

Sixth nerve palsies occur with increased intracranial pressure, after head injury, with structural disease in the middle or posterior fossa, with nasopharyngeal tumors, and for numerous other reasons. CN VI palsies are the most common and classic of all false localizing signs: they are nonspecific and bear no necessary anatomical relationship to the CNS pathology producing them. Elevated intracranial pressure often produces CN VI dysfunction because of stretching of the nerve over the petrous tip as the increased pressure forces the brainstem attachments inferiorly. Sixth nerve palsy is common in pseudotumor cerebri, see *Bilateral 6th nerve palsies due to idiopathic intracranial hypertension* from Dr. Daniel R. Gold, Neuro-ophthalmology Virtual Education Library [NOVEL], University of Utah, available at [Video Link 14.12](#).

Gradenigo's syndrome is sixth nerve palsy, facial pain, and V₁ sensory loss because of lesions at the petrous apex (usually neoplastic, traumatic, or inflammatory). Any process in the cavernous sinus can involve CN VI, usually along with other structures. Iatrogenic CN VI palsy may occur after lumbar puncture, myelography, and certain neurosurgical procedures. Other etiologies for CN VI palsy include Möbius' syndrome, herpes zoster, ophthalmoplegic migraine, viral infection, and postviral syndromes. Bilateral sixth nerve palsies are not uncommon. They may occur because of tumors along the clivus, where the two nerves lie close together, with meningeal processes such as subarachnoid

hemorrhage and meningitis and with increased intracranial pressure.

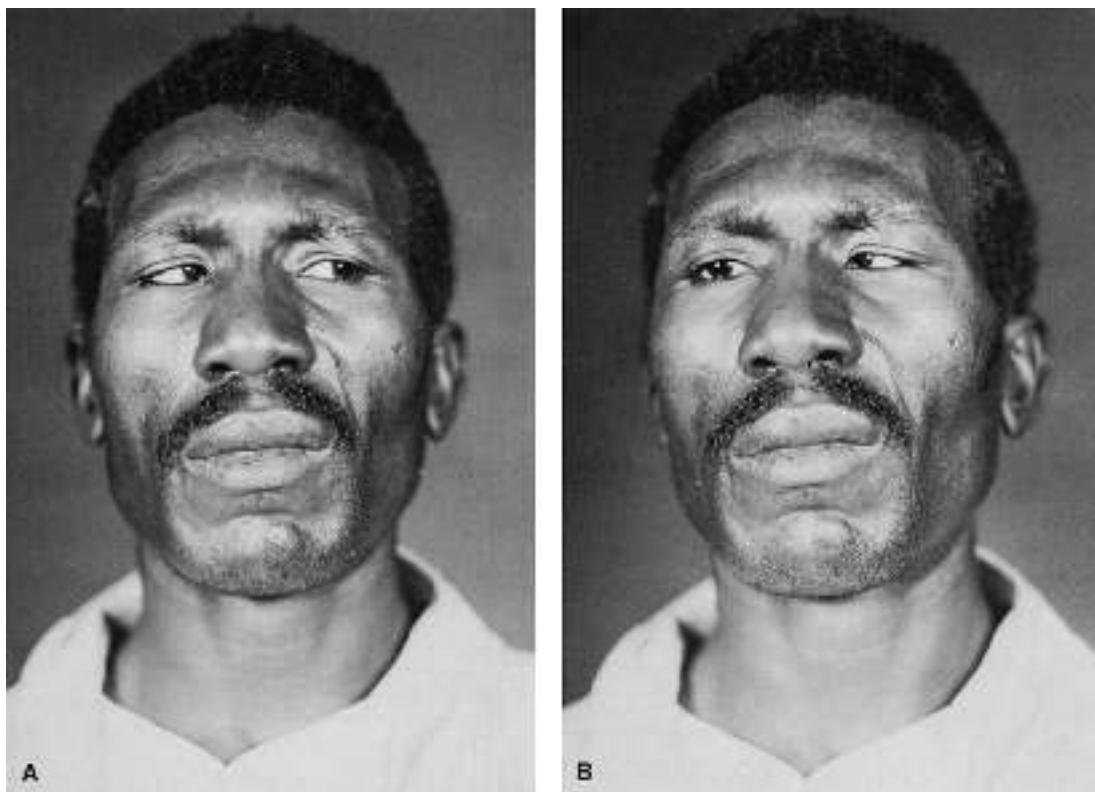


FIGURE 14.26 Paralysis of the right abducens nerve in a patient with a posterior fossa neoplasm. **A.** Patient looking to left. **B.** Patient attempting to look in the direction of action of the paralyzed muscle.

Other Causes of Abduction Impairment

Not all abduction failure is due to CN VI palsy. Some of the other causes include entrapment of the medial rectus by a medial orbital fracture, TED, MG, convergence spasm, divergence insufficiency, Duane's syndrome, orbital pseudotumor, and Möbius syndrome (Table 14.3).

Duane's retraction syndrome is a common cause of congenital strabismus that can mimic sixth nerve palsy (Box 14.9). Divergence insufficiency and divergence paralysis are conditions in which there is impaired abduction with esotropia when looking at distance, but full abduction on testing ductions. Patients have horizontal, comitant, uncrossed diplopia at far with no abnormality at near. Divergence insufficiency may develop as an isolated, benign, often self-limited abnormality in an otherwise healthy individual, or in patients who have other neurologic findings and underlying disease of the kind that more typically

causes sixth nerve palsy.

Convergence spasm causes esotropia on lateral gaze that can mimic a CN VI palsy. The disorder is usually functional and caused by voluntary convergence interrupting normal lateral gaze. As the patient looks laterally, the sudden convergence halts the abducting eye in midflight and simulates weakness of the lateral rectus. The mechanism is betrayed by pupillary constriction accompanying the eye movement that indicates the patient is converging. There is a report of convergence spasm as an isolated finding in a patient with midbrain compression.

CENTRAL DISORDERS OF OCULAR MOTILITY

Central disorders can be divided into supranuclear and internuclear. Supranuclear disorders include those that affect the supranuclear gaze centers in the hemispheres and brainstem, as well as other areas that influence eye movements, such as the basal ganglia and cerebellum. Internuclear disorders affect the connections between the ocular motor nerve nuclei in the brainstem.

Internuclear Ophthalmoplegia

Lesions of the MLF cause an INO ([Figure 14.27](#)). The contralateral medial rectus receives no signal to contract when the PPRF and sixth nerve nucleus act to initiate lateral gaze. As a result, gaze to one side results in abduction of the ipsilateral eye, but no adduction of its fellow. Typically, the abducting eye has nystagmus as well, sustained or only a few beats ([Video Link 14.13](#)). Failure of the medial rectus to adduct is an isolated abnormality in the affected eye; normality of the lid and pupil distinguish an INO from a third nerve palsy. Some patients have total adduction failure, and some may have exotropia in primary gaze. Patients with bilateral INO and exotropia have been said to have the wall-eyed bilateral INO (WEBINO) syndrome. An INO is commonly accompanied by vertical nystagmus, most commonly gaze-evoked upbeat.

The earliest detectable sign of an INO is often slowness of adducting saccades compared to abducting saccades, demonstrated by rapid refixations or OKNs. By convention, the INO is labeled by the side of the adduction failure; a right INO produces adduction failure of the right eye. Many brainstem lesions can cause an INO, but the common conditions are MS and brainstem stroke.

INOs due to MS are usually bilateral and seen in young patients; those due to brainstem vascular disease are more often unilateral and seen in older patients. Conditions such as MG, Wernicke's encephalopathy, TED, or partial third nerve palsy can cause a "pseudo-INO." Wernicke's encephalopathy can occur without mental status changes.

Despite impaired adduction on horizontal gaze, some patients with INO are still able to converge. INOs have been divided into those with and without preservation of convergence. The convergence centers are in the midbrain, and when adduction on convergence is impaired, the INO may be classified as rostral (anterior). When convergence is preserved, the INO may be classified as caudal (posterior). However, many normal individuals have impaired convergence, and the localizing value of convergence ability has not been borne out.

Gaze Palsies and Gaze Deviations

The FEFs move the eyes into contralateral conjugate horizontal gaze. The eyes normally remain straight ahead because of a balance of input from the FEFs in each hemisphere. Seizure activity in one frontal lobe drives the eyes contralaterally. In an adversive seizure, the eyes and then the head deviate to one side, after which the seizure may generalize. Sustained eye deviation can be a manifestation (rarely the only manifestation) of seizure activity, even of status epilepticus. With destructive frontal lobe lesions, most often ischemic stroke, the patient is unable to move the eyes contralaterally—a gaze palsy, or, if less severe, a gaze paresis. The intact, normal hemisphere maintains its tonic input, the imbalance causing the eyes to move contralaterally, toward the diseased side—a gaze deviation. Patients may have gaze palsy without gaze deviation. The presence of gaze deviation usually means gaze palsy to the opposite side, but it may occasionally signal seizure activity.

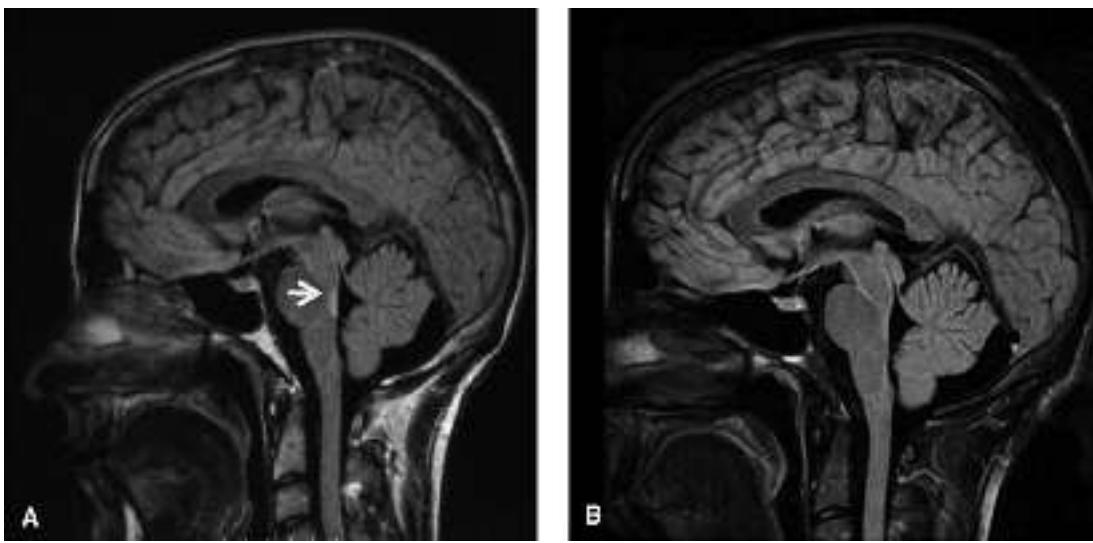


FIGURE 14.27 Sagittal MRI demonstrating a focus of high FLAIR signal change in the medial longitudinal fasciculus within the posterior pons (*white arrows*) in a patient with internuclear ophthalmoplegia, acutely (**A**) and with resolution (**B**). (Reproduced from Auce P, Rajakulendran S, Nesbitt A, et al. Neurological picture. Internuclear ophthalmoplegia following African tick bite fever. *J Neurol Neurosurg Psychiatry* 2011;82[6]:681, with permission from BMJ Publishing Group Ltd.)

Similar considerations apply to disease of the pons. The PPRF governs ipsilateral, conjugate horizontal gaze. The PPRF draws the eyes ipsilaterally, in contrast to the FEFs, which force the eyes contralaterally. Destructive lesions of the PPRF impair the ability to gaze ipsilaterally, resulting in a gaze deviation toward the intact side as the normal PPRF pulls the eyes over (see *Unilateral Horizontal Gaze Palsy* from Dr. Shirley Wray, Neuro-ophthalmology Virtual Education Library [NOVEL], University of Utah, available at [Video Link 14.14](#)). The PPRF is the final common pathway for horizontal gaze, and pontine gaze palsies that involve the PPRF affect all functions, voluntary and reflex. Even ice water calorics will not move the eyes. Large, bilateral lesions may cause bilateral gaze palsy, and the only preserved eye movements are vertical.

When faced with a patient whose eyes rest eccentrically to one side, the possibilities are (a) frontal lobe seizure activity, (b) frontal lobe destructive lesion, and (c) pontine destructive lesion. Patients with destructive frontal lesions gaze away from the side of the hemiparesis; patients with pontine strokes gaze toward the hemiparesis. Frontal lobe gaze deviations are generally large amplitude, pronounced, and clinically obvious, whereas pontine gaze deviations tend to be subtle and easily missed. Frontal gaze deviations tend to resolve in a few days, pontine deviations persist much longer, sometimes permanently. Epileptogenic gaze deviations are usually betrayed by a component of jerky eye

movement and subtle twitches elsewhere.

One-and-a-Half Syndrome

The MLF fibers arising from the CN VI nucleus decussate just after their origin and run in close proximity to the PPRF and sixth nerve nucleus on the opposite side. A medial pontine lesion can affect both the PPRF on one side and the MLF crossing from the contralateral side. Because of the ipsilateral lesion, the patient has a gaze palsy to the same side. Because of the MLF lesion, the patient has an INO on the same side. A lesion of the right pons can then cause a right gaze palsy with a superimposed right INO, which results in complete horizontal gaze palsy to the right and inability to adduct the right eye on left gaze (“half a gaze palsy” to the left). The only eye movement possible is abduction of the left eye, see *One and Half Syndrome* from Dr. Robert Daroff, Neuro-ophthalmology Virtual Education Library [NOVEL], University of Utah, [Video Link 14.15](#). Fisher named this constellation of findings the “one-and-a-half syndrome.” The most common causes are infarction and demyelinating disease. Paralytic pontine exotropia refers to such patients in the acute phase who have exotropia in primary position because of the preserved abduction in the contralateral eye.

Vertical Gaze Abnormalities

Two common disorders affecting vertical gaze are Parinaud’s syndrome and PSP.

Parinaud’s Syndrome

The core feature of Parinaud’s syndrome (for Henri Parinaud, French neurologist, considered the father of neuro-ophthalmology) is impaired upgaze ([Figure 14.18](#)). Patients are unable to look up, and when they attempt it, the eyes may spasmically converge and retract backward into the orbits (convergence-retraction nystagmus). The convergence-retraction movements readily appear during forced upward saccades in response to a down-moving OKN tape. The retraction movement is best seen from the side. Parinaud’s syndrome usually results from a mass lesion involving the region of the posterior third ventricle and upper dorsal midbrain, such as a pinealoma; it is also known as the sylvian aqueduct, dorsal midbrain or pretectal syndrome, or the syndrome of the posterior commissure. Other frequent signs include eyelid retraction (Collier’s

sign) and abnormal pupils. The pupils in Parinaud's syndrome have a poor, rarely absent, light response, and much better near response (tectal pupils). The pupils tend to be large, partly because young people have larger pupils and lesions in this region tend to occur in younger patients. Sometimes, upgaze paresis is severe enough that the eyes are forced into sustained downgaze with retracted eyelids—the “setting sun sign,” seen in children with obstructive hydrocephalus ballooning the posterior third ventricle and rostral aqueduct. Leading causes of the pretectal syndrome in Keane's series were hydrocephalus, stroke, and tumor. For a video showing all the features of Parinaud's syndrome, see [Video Link 14.16](#).

Progressive Supranuclear Palsy

In PSP, degenerative changes in the rostral brainstem and thalamus result in impairment first of downgaze, then of upgaze, and eventually in global gaze paresis. Reflex eye movements are preserved until late in the disease. The gaze abnormalities are accompanied by parkinsonian signs and a pronounced tendency to extensor axial rigidity. Patients may have particular difficulty with the antisaccade task.

Other Disorders of Vertical Gaze

Skew deviation is a small, vertical misalignment of the eyes that usually results from a prenuclear lesion involving the brainstem or cerebellum. The deviation is usually comitant, remaining about the same in all directions of gaze, and the lesion is usually on the side of the hypotropic eye. Skew deviation is sometimes associated with an INO, with the lesion on the side of the hypertropic eye. The ocular tilt reaction (OTR) consists of skew deviation with torsion of the eyes and a head tilt; the head and the upper poles of both eyes tilt toward the hypotropic eye ([Figure 14.28](#)). It occurs primarily with peripheral vestibular disease, but can be seen in lateral medullary infarction. The OTR can simulate fourth nerve palsy because both cause an unusual head tilt. The pathway responsible for the OTR crosses the midline just above the sixth nerve nucleus and ascends in the contralateral MLF; lesions in the lower pons cause an ipsilateral OTR; and more rostral lesions cause a contralateral OTR. Cerebellar lesions may cause either an ipsilateral or contralateral OTR depending on the structures involved. Isolated downgaze palsy is rare, but it can occur with small strategically placed lesions in

the rostral midbrain. Double elevator palsy is a monocular paresis of elevation involving both the superior rectus and inferior oblique; it may occur with pretectal lesions. A vertical one-and-a-half-syndrome has been described.



FIGURE 14.28 The ocular tilt reaction refers to the head tilt, ocular torsion, and skew deviation that are ascribed to asymmetry in the otolithic pathway from the utricle. The head tilt and ocular torsion occur toward the hypotropic eye. (Reprinted with permission from Huh YE, Kim JS. Bedside evaluation of dizzy patients. *J Clin Neurol* 2013;9[4]:203–213. Copyright © 2013 Korean Neurological Association.)

Nystagmus and Other Ocular Oscillations

Nystagmus is a rhythmic, biphasic, involuntary movement of the eyes. When faced with a patient with nystagmus or similar-appearing movements, the usual clinical exercises include the following two steps: (a) deciding if the nystagmus indicates neurologic pathology and (b) if so, whether the pathology is central or peripheral. There are normal, physiologic forms of nystagmus. A few beats of nystagmus at the extremes of lateral gaze occur commonly in normals and have no pathologic significance. A whole host of conditions can cause nystagmus, including ocular disease, drug effects, peripheral vestibular disease, and CNS disease. Nystagmus may also be congenital. Schemes have classified nystagmus in many different ways. This discussion focuses on the types of nystagmus commonly encountered in neurologic practice and on the differentiation between nystagmus that likely signifies neurologic disease (neuropathologic) and the kind that does not (nonneuropathologic).

Nystagmus is classified in multiple ways: pendular (both phases of equal amplitude and velocity) versus jerk (a fast phase and a slow phase); central versus peripheral; induced versus spontaneous; and physiologic versus pathologic. Further characterizations include rapid/slow, coarse/fine, manifest/latent, sensory/motor, and horizontal/vertical. Pendular nystagmus is classified by its plane of movement, usually horizontal. Pendular nystagmus only rarely signifies neurologic disease, and this discussion is focused primarily on jerk nystagmus. Jerk nystagmus is classified by the direction of the fast phase. Alexander's law states that jerk nystagmus increases with gaze in the direction of the fast phase. First-degree nystagmus is present only with eccentric gaze (e.g., right-beating nystagmus on right gaze). Second-degree nystagmus is present in primary gaze and increases in intensity with gaze in the direction of the fast component (e.g., right-beating nystagmus in primary gaze increasing with gaze to the right). With third-degree nystagmus, the fast component continues to beat even with gaze in the direction of the slow component (e.g., right-beating nystagmus persisting even with gaze to the left). Dissociated nystagmus is different in the two eyes (e.g., the nystagmus in the abducting eye in INO).

Nonneuropathologic Nystagmus

Nystagmus that does not signify neurologic disease may be physiologic, or because of ocular disease (e.g., poor vision), or other conditions.

Physiologic Nystagmus

Types of physiologic nystagmus include end point, OKN, and induced vestibular. Although these types of nystagmus are normal, they may be altered when disease is present in such a way as to assist in localization.

End-point nystagmus is fine, variably sustained nystagmus at the extremes of lateral gaze, especially with gaze eccentric enough to eliminate fixation by the adducting eye. In some normals, physiologic end-point nystagmus appears with as little as 30 degrees of deviation from primary position, often with greater amplitude in the abducting eye. End-point nystagmus is typically low amplitude and irregular. Symmetry on right and left gaze, abolition by moving the eyes a few degrees toward primary position, and the absence of other neurologic abnormalities generally serve to distinguish end-point from pathologic nystagmus. End-point nystagmus is the most common form of nystagmus seen in routine clinical practice.

Although OKN is a normal response, its characteristics may be altered in disease. Changes in OKN occur primarily with deep parietal lobe lesions. OKN abnormalities are discussed above (see section on OKN).

Vestibular nystagmus can be induced by rotation (e.g., Barany chair) or by irrigation of the ear with hot or cold water. This complex subject is discussed in more detail in [Chapter 17](#).

Other Forms of Nonneuropathologic Nystagmus

These types of nystagmus are not physiologic, but they do not result from neurologic disease.

Voluntary Nystagmus

Some normal individuals have the ability to saccade very rapidly back and forth horizontally, producing a high frequency, low amplitude, pendular eye movement that is startling but of no consequence (see *Voluntary Nystagmus* from Dr. Robert Daroff, Neuro-ophthalmology Virtual Education Library [NOVEL], University of Utah, available at [Video Link 14.17](#)). Voluntary nystagmus may alarm the physician who has not previously seen these impressive oscillations. The movements cannot be sustained for long, generally less than 30 seconds.

Drug-Induced Nystagmus

Alcohol, sedative hypnotics, anticonvulsants, and other drugs commonly produce nystagmus. Such drug-induced nystagmus is typically symmetric and gaze evoked horizontally and vertically, especially in upgaze, only rarely in downgaze. Nystagmus more prominent than the commonly seen, few unsustained end-point jerks will usually prove to be a drug effect.

Congenital Nystagmus

A patient with a clear history of nystagmus present because infancy presents no neurologic diagnostic problem. However, occasionally, patients with congenital nystagmus are unaware of its presence; when they present later in life with neurologic complaints, sorting out the significance of the nystagmus may prove difficult. In distinguishing congenital from other types of nystagmus, the following features are helpful. Congenital nystagmus is most often horizontal jerk and remains horizontal even in upgaze and downgaze (i.e., it is not gaze evoked). This pattern is unusual in other forms of nystagmus. Patients often have a null point of least nystagmus intensity and best vision in slightly eccentric gaze. They may adopt a head turn or tilt to maintain gaze in this null zone. The nystagmus typically damps with convergence. The patient with congenital nystagmus characteristically holds reading material extremely close and regards it with a peculiar head tilt and may still have mediocre vision. For video, see *Congenital Nystagmus* from Dr. Shirley Wray, Neuro-ophthalmology Virtual Education Library [NOVEL], University of Utah, available at [Video Link 14.18](#). A virtually pathognomonic feature of congenital nystagmus is “inversion” of OKNs. Moving an OKN tape so as to cause an expected summation with the fast phase of the congenital nystagmus produces instead a diminution or a paradoxical reversal of nystagmus direction. Patients with congenital nystagmus are not immune to acquired visual system abnormalities. Eye movement recordings help differentiate it from other nystagmus types. Confirmation that it is long-standing supports the diagnosis.

A form of congenital nystagmus, latent nystagmus occurs only when one eye is covered. This may happen when the examiner blocks the patient’s vision during ophthalmoscopic examination, causing jerk nystagmus with the fast component toward the uncovered eye. The nystagmus disappears with binocular fixation. Latent nystagmus may exist in isolation or as a manifestation of typical

congenital nystagmus.

Ocular Disease

Patients with very poor vision may develop continuous pendular nystagmus, and nystagmus can occur in otherwise normal individuals who work in perpetually dark environments. Visual-loss–induced nystagmus usually damps with convergence. Pendular nystagmus can develop monocularly in an eye with visual loss. Spasmus nutans is a disorder usually seen in infants between 6 and 12 months of age, but onset can be later. The classic triad is nystagmus, head nodding, and torticollis, but not all patients have all three. Head nodding and nystagmus are the most common manifestations, with head turn in a third. The nystagmus is low amplitude, high frequency, and dysconjugate. The nystagmus may be monocular. The etiology is uncertain, possibly related to sensory deprivation, but the condition is benign and disappears before age 4.

Neuropathologic Nystagmus

Nystagmus is a frequent manifestation of disease of the nervous system. Common types include vestibular, positional, gaze evoked, and gaze paretic nystagmus. [Table 14.4](#) summarizes important but less often encountered types of nystagmus and related movements. Vestibular and positional nystagmus are discussed in [Chapter 17](#). There are many online sources for videos of different types of nystagmus, especially the Neuro-ophthalmology Virtual Education Library at the University of Utah (<https://novel.utah.edu>) and the Canadian Neuro-Ophthalmology Group (<http://www.neuroophthalmology.ca>).

Symmetric, equal activity of the vestibular systems on each side normally maintains the eyes in straight-ahead, primary position. Vestibular imbalance causes the eyes to deviate toward the less active side as the normal side overcomes the weakened tonic activity from the hypoactive side. In an alert patient, the FEFs generate a saccade to bring the eyes back toward primary position, creating the fast phase of vestibular nystagmus. When the cortex does not generate a correcting saccade, as in coma, only the tonic deviation develops; the eyes deviate toward the ice-water–irrigated ear.

TABLE 14.4 Nystagmus and Other Abnormal Ocular Movements

Nystagmus Type	Characteristics	Location of Pathology	Possible Disease or Condition
Upbeat nystagmus	Upbeating nystagmus in primary gaze	Cerebellar vermis (if nystagmus increases), or medulla (if it decreases) in upgaze	Cerebellar or medullary lesion; meningitis; WE; rarely, drug intoxication
Downbeat nystagmus	Downbeating nystagmus in primary gaze, maximal in eccentric downgaze gaze ("downbeat in the corners")	Cervicomедullary junction	Arnold-Chiari malformation; basilar invagination; MS; foramen magnum tumor; spinocerebellar degeneration; WE; vascular disease; rarely, drug intoxication
Convergence-retraction nystagmus	Convergence motions and/or simultaneous retraction of globes back into the orbits	Rstral midbrain, pretectum, posterior commissure, posterior third ventricle	Mass lesions, especially pinealoma; vascular disease; upward transtentorial herniation
Rebound nystagmus	Horizontal nystagmus that briefly beats in opposite direction on return to primary position	Cerebellum or cerebellar connections	MS; cerebellar or posterior fossa lesion
Periodic alternating nystagmus	Horizontal nystagmus that beats in one direction for 1–3 min, pauses, then beats in the other direction, cycling continuously	Brainstem or cerebellum	Craniocervical junction abnormality; MS, spinocerebellar degeneration; tumor; cryptococciosis; neurosyphilis; congenital; phenytoin intoxication
Seesaw nystagmus	Pendular nystagmus; one eye rises and intorts, the other falls and extorts; sometimes associated with bitemporal hemianopsia	Anterior third ventricle; parasellar or optic chiasm region	Tumor, especially craniopharyngioma; head trauma; septo-optic dysplasia; congenital
Bruns' nystagmus	Large and coarse in one direction, fine in the opposite direction	Cerebellopontine angle	Tumor
Ocular bobbing	Downward jerk with slow drift back to primary position	Pons (lesion usually massive and patient comatose)	Pontine hemorrhage or infarct; atypical forms occur
Ocular flutter	Intermittent, rapid, back-to-back horizontal saccades causing a quivering or shimmering movement	Cerebellum or brainstem cerebellar connections; dentate nucleus	Same as for opsoclonus (see next page); flutter and opsoclonus are a continuum
Opsoclonus	Continuous, involuntary, random, chaotic saccades in any direction (saccadomania, dancing eyes, lightning eye movements)	Cerebellum or brainstem cerebellar connections; dentate nucleus	In children: occult neuroblastoma (dancing eyes-dancing feet; opsoclonus-myoclonus syndrome, Kimbourne's syndrome); in adults: occult lung or breast carcinoma; encephalitis; cerebellar disease

Nystagmus is jerk unless otherwise noted.
MS, multiple sclerosis; WE, Wernicke's encephalopathy.

Degenerative changes in the otoliths frequently produce the syndrome of positional vertigo and nystagmus. Nystagmus occurs after a latency of up to 30 seconds, beats with the fast phase toward the down ear, quickly fatigues despite holding the position, and adapts with repeated attempts to elicit it. Positional nystagmus is a very common condition. Although generally peripheral, it may occur with central disease (tumor, stroke, MS, degenerative disease). See Chapter 17 for further discussion.

Any nystagmus not present in primary gaze but appearing with gaze in any direction with the fast phase in the direction of gaze is referred to as gaze-evoked nystagmus. Normal physiologic end-point nystagmus is gaze evoked, but only present horizontally and at extremes of gaze. Abnormal gaze-evoked nystagmus occurs short of extreme gaze and is more sustained than end point. Drug-induced

nystagmus is gaze evoked, usually horizontally and in upgaze. Nystagmus with the same appearance in the absence of drug effects is nonspecific but usually indicates disease of the cerebellum or cerebellar connections. Gaze paretic nystagmus is a form of gaze-evoked nystagmus seen in patients with incomplete gaze palsies. Rather than having an absolute inability to gaze in a particular direction, the patient achieves full lateral gaze transiently but is not able to maintain it. The eyes drift back toward neutral and then spasmodically jerk back in the desired gaze direction.

Other Disorders of Ocular Motility

Other types of abnormal eye movements include ocular bobbing, ocular flutter, and opsoclonus ([Table 14.4](#)). Ocular flutter and opsoclonus are types of saccadic intrusions, spontaneous saccades away from fixation; they may be confused with nystagmus. Patients with ocular motor apraxia are unable to generate saccades to look horizontally and develop compensatory blinking or head-thrusting movements to shift gaze. The blinks or head movements help to trigger a saccade. Ataxia telangiectasia may cause similar gaze difficulties. Parkinson's disease can produce a variety of ocular motility disturbances, including hypometric saccades, impaired smooth pursuit, square wave jerks, and lid retraction. Oculogyric crisis refers to attacks of involuntary conjugate upward deviation of the eyes, which may be transient or last for hours. Occasionally, there is also some deviation to one side, or the eyes may be turned downward. Classically associated with postencephalitic parkinsonism, these episodes are now seen as a dystonic reaction from phenothiazines and related drugs. Oculogyric crises from neuroleptic drugs may also occur as a tardive syndrome. In absence seizures, there may be brief spasms of upward gaze. Ocular dysmetria is an over- or undershooting of the eyes on rapid refixation of gaze toward either side or on returning to the primary position that requires corrective saccades; there may also be overshooting in following movements when the object of regard is suddenly stopped.

Video Links

Video Link 14.1. Cogan's lid twitch sign and eyelid hopping.

http://neurosigns.org/wiki/Cogan%27s_lid_twitch_and_eyelid_hop

Video Link 14.2. Curtain sign in myasthenia gravis.

[http://neurosigns.org/wiki/Curtain_sign_\(enhanced_ptosis\)](http://neurosigns.org/wiki/Curtain_sign_(enhanced_ptosis))

Video Link 14.3. Positive edrophonium test in myasthenia gravis.

https://collections.lib.utah.edu/details?id=188589&q=sort_type_t%3A%2AMovingImage%2A+AND+ec

Video Link 14.4. Duane's syndrome. <https://collections.lib.utah.edu/details?id=180331>

Video Link 14.5. Demonstration of APD by swinging flashlight test.

https://collections.lib.utah.edu/details?id=180307&q=sort_type_t%3A%2AMovingImage%2A+AND+re

Video Link 14.6. Optokinetic nystagmus.

http://neurosigns.org/wiki/Optokinetic_nystagmus

Video Link 14.7. Brown's tendon sheath syndrome.

<http://www.youtube.com/watch?v=lBdEZU7Vkrs&NR=1>

Video Link 14.8. Myasthenic pseudo-INO.

<http://www.neuroophthalmology.ca/case-of-the-month/eye-movements/intermittent-diplopia-and-trouble-sucking-on-a-straw>

[Video Link 14.9. Bilateral third nerve synkinesias.](#)

<http://archneur.jamanetwork.com/multimediaPlayer.aspx?mediaid=2522009>

Video Link 14.10. Pupil-sparing ischemic CN III palsy with preserved CN IV function. <https://collections.lib.utah.edu/details?>

[Video Link 14.11. Head tilt test in CN IV palsy.](#)

<https://collections.lib.utah.edu/de>

[id=188602&q=sort_type_t%3A%2AM](#)

.12. Bilateral 6th nerve palsies due to idiopathic intracranial

hypertension. <https://collections.lib.utah.edu/details?>

[id=1256233&q=creator%3A%22gold%22+AND+e](#)

[Video Link 14.13. Internuclear ophthalmoplegia](#)

http://neurosigns.org/wiki/Internuclear_ophthalmoplegia

[http://www.youtube.com/watch?v=IwJLmIuHnA](#)

<https://collections.lib.utah.edu/details?>

http://www.collections.lib.utah.edu/details/?id=188642&page=2&q=sort_type_t%3A%2AMovingImage%2A

[Video Link 14](#) [15](#) One-and-a-half syndrome

<https://collections.lib.utah.edu/details?>

https://collections.mfa.tulane.edu/details/id/188473&q=sort_type%3A%2AMovingImage%2A+AND+or

Video Link 14.16. Parinaud's syndrome. <http://www.youtube.com/watch?v=u7D1-zj98l8>

Video Link 14.17. Voluntary nystagmus. https://collections.lib.utah.edu/details?id=188469&q=sort_type_t%3A%2AMovingImage%2A+AND+%

Video Link 14.18. Congenital nystagmus. https://collections.lib.utah.edu/details?id=188527&q=sort_type_t%3A%2AMovingImage%2A+AND+%

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CHAPTER 15

The Trigeminal Nerve

ANATOMY AND PHYSIOLOGY

The trigeminal, or fifth cranial, nerve (CN V) is the largest and one of the most complex CNs. It has a large sensory part (portio major; 170,000 fibers) and a much smaller motor part (portio minor; 7,700 fibers). The sensory component has three divisions: the first or ophthalmic division (CN V₁), the second or maxillary division (CN V₂), and the third or mandibular division (CN V₃). The motor and principal sensory nuclei are located in the mid-pons ([Figure 15.1](#)). The spinal tract and nucleus, which subserve pain and temperature, extend from the pons down into the upper cervical spinal cord. The mesencephalic root receives proprioceptive fibers. Trigeminal nuclear structures thus extend from the rostral midbrain to the rostral spinal cord. The sensory portion innervates the face, teeth, oral and nasal cavities, the scalp back to the vertex, the intracranial dura, and the cerebral vasculature, and provides proprioceptive information for muscles of mastication. The motor portion innervates the muscles of mastication. CN V has extensive connections with other CNs. There is a small input to both the mossy and climbing fiber systems of the cerebellum (trigeminocerebellar fibers). Functional magnetic resonance imaging (MRI) using specific sensory stimuli or motor tasks has been used to localize the brainstem nuclei.

The Motor Portion

Upper motor neuron control of trigeminal motor functions arises primarily from the lower third of the contralateral motor cortex, although each trigeminal motor nucleus receives projections from both cerebral hemispheres. Fibers descend in the corticobulbar tract to the pons, where they decussate ([Figure 15.2](#)). There is extrapyramidal innervation from the premotor cortex and basal ganglia. The

muscles supplied by the trigeminal are derived from the first branchial arch, and the system is special visceral efferent (SVE) or branchial motor. The fibers exit laterally, typical for SVE fibers, but do not form an internal loop as other branchial motor fibers do.

The motor root exits the lateral pons anteromedial to the sensory root. It passes beneath the gasserian ganglion, leaves the skull through the foramen ovale, and then joins the mandibular sensory division briefly before separating to supply the muscles of mastication and associated muscles.

The principal function of the motor root is to innervate the muscles of mastication: masseter, temporalis, and medial and lateral pterygoids. The masseter muscles close the jaw and protrude it slightly; the masseter may be the most powerful muscle in the body. The temporalis muscles close the jaw and retract it slightly. The medial pterygoids acting synchronously close the jaw and protrude it. The lateral pterygoids acting synchronously open the jaw and protrude it. The medial and lateral pterygoids originate from the skull base and extend laterally to insert on the inner aspect of the mandible. When they contract on one side, they pull the mandible contralaterally. When there is unilateral pterygoid weakness, the jaw deviates toward the side of the weak muscles.

Mastication is a complex opening, closing, forward, backward, and lateral movement of the jaw. The motor root of CN V is responsible for all of these intricate motions. CN V also supplies the mylohyoid, anterior belly of the digastric, tensor veli palatini, and tensor tympani muscles. The mylohyoid pulls the hyoid bone upward and forward, raising the floor of the mouth and pressing the base of the tongue against the palate. The anterior belly of the digastric raises and advances the hyoid bone if the jaw is fixed. The tensor veli palatini tenses the soft palate and helps prevent food from escaping from the oro- to the nasopharynx; it also dilates the eustachian tube. The tensor tympani, through interaction with CN VIII, tenses the tympanic membrane and helps dampen its excursions in response to sound intensity.

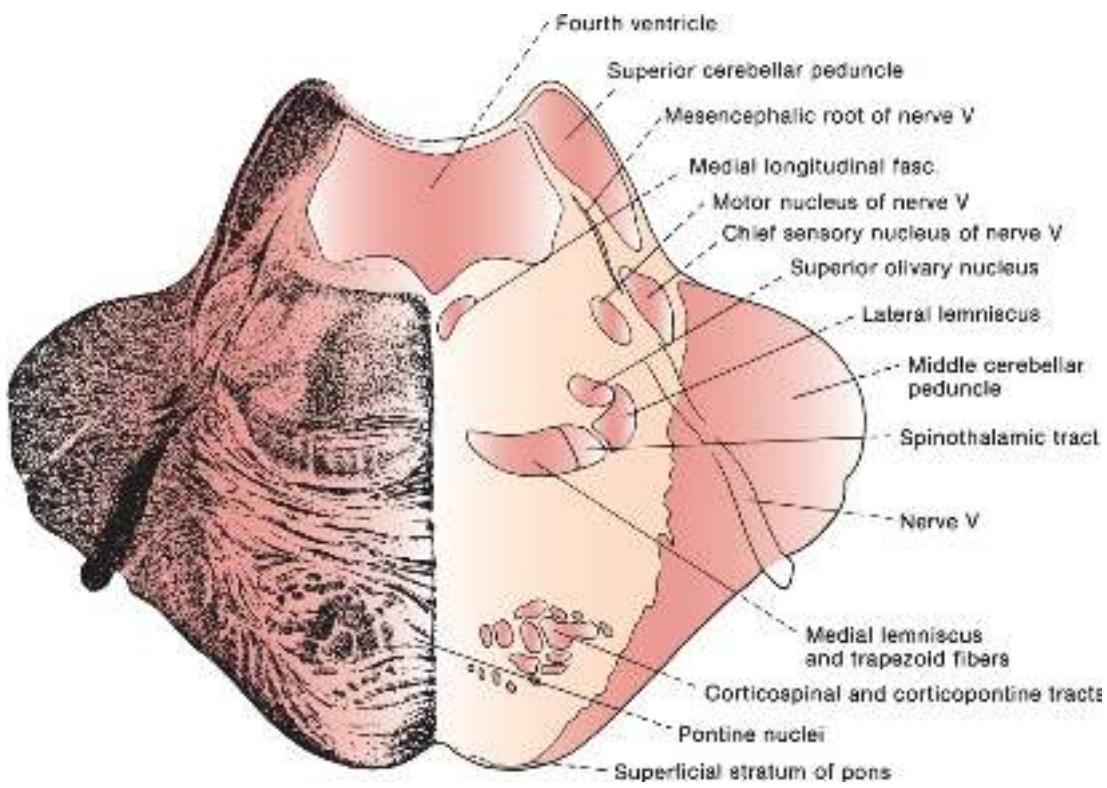


FIGURE 15.1 Section through the pons at the level of the trigeminal nuclei.

The Sensory Portion

The trigeminal, or gasserian (for J. L. Gasser), ganglion, the largest ganglion in the peripheral nervous system, lies just beside the pons in a shallow depression in the petrous apex called Meckel's cave. The ganglion is crescent shaped, convex anterolaterally, and is also known as the semilunar ganglion. It lies just lateral to the internal carotid artery and the posterior part of the cavernous sinus. The ganglion is analogous to a dorsal root ganglion; it contains unipolar sensory neurons, whose central processes enter the lateral pons through the large sensory root that passes beneath the tentorium to connect the concave side of the ganglion to the brainstem. The sensory root can be compressed by vascular loops, causing trigeminal neuralgia (TN). The peripheral processes subserve sensation to the face and head. There are two types of sensory neurons in the gasserian ganglion. One mediates fine discriminative touch; the other mediates primarily pain and temperature.

Afferent fibers conveying light touch and pressure enter the principal sensory nucleus, which lies in the tegmentum just lateral and posterior to the motor nucleus; most fibers synapse there and give rise to second-order neurons that

cross the midline and ascend in the ventral trigeminothalamic tract en route to the ventral posterior medial (VPM) thalamic nucleus ([Figure 15.2](#)). Some fibers ascend ipsilaterally in the small dorsal trigeminothalamic tract to VPM. The two sets of trigeminothalamic fibers, both of which run near the medial lemniscus, are sometimes referred to as the trigeminal lemniscus.

Fibers subserving pain and temperature take a much more circuitous route to the thalamus. The spinal tract, or the descending root, of the trigeminal extends from the principal sensory nucleus down through the lower pons and medulla, into the spinal cord as far as C3, or even C4 ([Figure 15.2](#)). There the spinal tract becomes continuous with Lissauer's tract. The nucleus of the spinal tract is a cell column that lies just medial to the fiber tract throughout its course. In the cervical cord, the nucleus of the spinal tract becomes continuous with the substantia gelatinosa of the posterior horn. Fibers conveying pain and temperature enter the spinal tract of the trigeminal and descend to various levels depending on their somatotopic origin, then synapse in the adjacent nucleus of the spinal tract. The axons of second-order neurons cross the midline, aggregate in the ventral trigeminothalamic tract, and ascend to VPM alongside the medial lemniscus and spinothalamic tracts. Fibers arising from the pars caudalis send collaterals to the intralaminar and posterior thalamic nuclei. From VPM, fibers project through the thalamic radiations to the sensory cortex in the postcentral gyrus, where facial sensation occupies the lower third. Some projections from VPM terminate in the precentral gyrus. Fibers from the intralaminar nuclei project well outside the primary sensory cortex. Sensory fibers from CNs VII, IX, and X provide sensation to the region of the external ear canal; these fibers join the trigeminal system centrally.

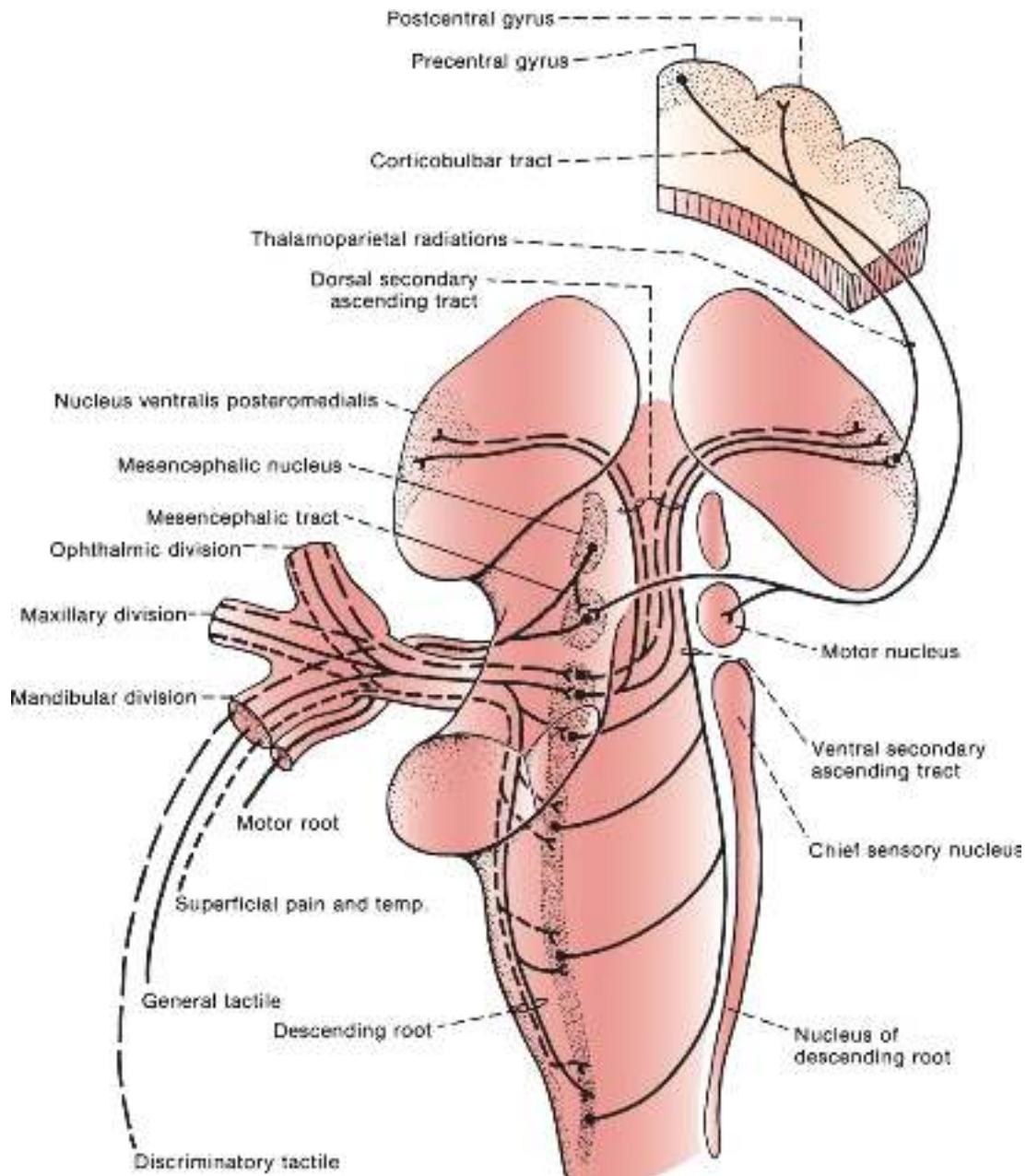


FIGURE 15.2 The trigeminal nerve and its connections.

The somatotopic organization of the nucleus and spinal tract is complex. There are three subnuclei, from above to below—the nuclei (or pars) oralis, interpolaris, and caudalis. The pars oralis extends from mid-pons to the level of the inferior olive, the pars interpolaris from the inferior olive to the obex, and the pars caudalis from there to the upper cervical cord. At one time, it was thought that different divisions of the trigeminal descended to different levels in the spinal tract. This concept was based in part on the alterations in corneal

sensation after surgical tractomy of the cervical cord, which is done to treat chronic pain. Current thinking is that all three divisions are represented at all levels of the nucleus, although V₁ may not project as far caudally as V₂ and V₃. Somatotopically, V₁ is represented most anteriorly, and V₂ and V₃ more posteriorly (resembling a small inverted face with the forehead anterior on a typical cross section).

Dejerine, using clinical and pathologic material, demonstrated an “onion skin” somatotopic organization ([Figure 15.3](#)). The face is represented as concentric rings from the perioral region to the preauricular region. Fibers from the foreface (upper lip, mouth, and tip of the nose) synapse most rostrally in the nucleus of the spinal tract; those from the hindface synapse more caudally, adjacent to the sensory input from C2 and C3. Because of this organization, there is occasionally sparing, less frequently selective involvement of the perioral region compared to the posterior face (balaclava helmet distribution). The onionskin distribution is important in understanding the patterns of facial sensory loss that may occur with intrinsic brainstem and cervical spinal cord lesions, especially syringomyelia and syringobulbia. Chang reported a clinical demonstration of the onionskin organization in a case of central cord syndrome where facial dysesthesias retreated from the center toward the periphery. Onionskin sensory loss was apparently common in neurosyphilis.

The third sensory component, the mesencephalic root of the trigeminal nerve, runs with the motor root and then extends posteriorly and cephalad from the level of the motor nucleus into the mesencephalon. It carries proprioceptive impulses from the muscles supplied by the trigeminal nerve and probably for the extraocular muscles and the muscles of facial expression as well. Neurons subserving proprioception are unipolar neurons, but they reside inside the brainstem in the mesencephalic nucleus of CN V, making it in essence an ectopic dorsal root ganglion within the central nervous system (CNS). Proprioceptive fibers pass through the gasserian ganglion without synapsing and terminate in the mesencephalic nucleus. The mesencephalic nucleus mediates the jaw jerk reflex. Projections join the trigeminothalamic tracts and ascend to VPM.

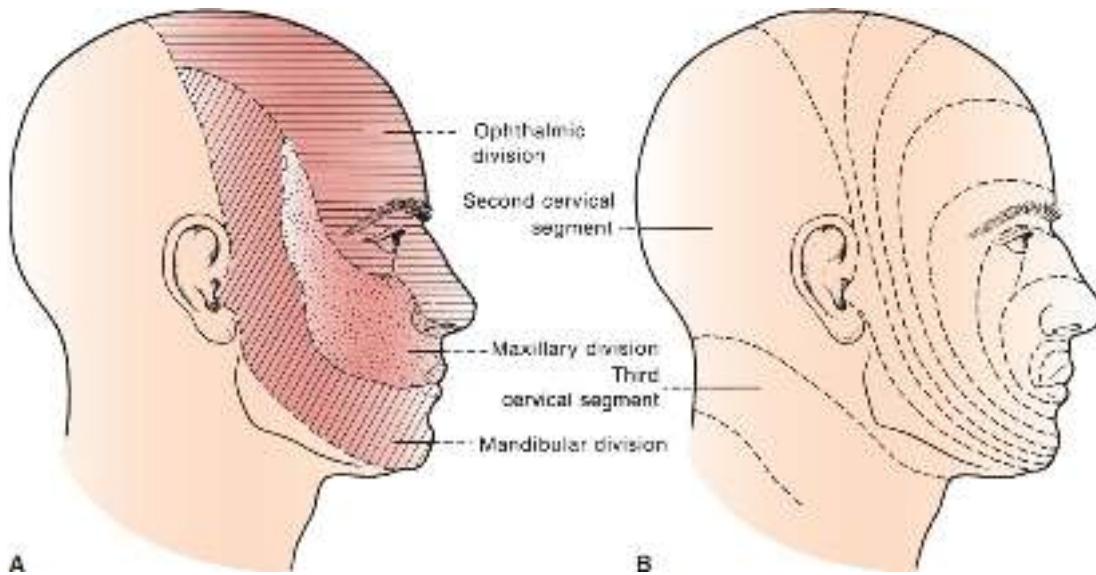


FIGURE 15.3 Cutaneous distribution of the trigeminal nerve. **A.** Peripheral distribution. **B.** Segmental distribution.

The Trigeminal Divisions

The three divisions of CN V arise from the trigeminal ganglion. Each division has a meningeal branch. Disregarding these, the ophthalmic division has three major terminal branches; the other two divisions have four each. The terminal branches of V_1 are the frontal, lacrimal, and nasociliary nerves. The terminal branches of the maxillary division are the infraorbital, zygomatic, superior alveolar, and pterygopalatine. The terminal branches of the mandibular division are the buccal, lingual, inferior alveolar, and auriculotemporal. The cutaneous distribution of the divisions is summarized in [Table 15.1](#).

From the gasserian ganglion, V_1 —the smallest of the three divisions—runs forward and enters the cavernous sinus; it lies laterally in the wall of the sinus between the folds of dura ([Figure 14.6](#)). A branch is given off to the meninges of the tentorium cerebelli just after leaving the ganglion. CN V_1 runs forward through the superior orbital fissure and divides into its terminal branches. The sensory innervation of V_1 is shown in [Figure 15.3](#). Note that V_1 supplies most of the nose. Sensory loss along the nose because of a lesion of the distal branches of V_2 is shown in [Figure 15.5](#). The sensory fibers to the eye pass through the ciliary ganglion without synapsing and continue as the short ciliary nerves; these convey sensation from the globe and carry postganglionic sympathetic fibers to the pupilloconstrictor muscle. The long ciliary nerves carry sensation from the

ciliary body and cornea, as well as sympathetic fibers to the pupillodilator muscle. Proprioceptive fibers from the extraocular muscles travel initially with their respective CNs but join V₁ and proceed to the mesencephalic nucleus.

The maxillary branch gives off the middle, or recurrent, meningeal nerve to the dura of the middle fossa, passes through the lateral wall of the cavernous sinus, and then exits through the foramen rotundum. It crosses the pterygopalatine (sphenopalatine) fossa, where the sensory branches to the palate are given off, after which the nerve splits into the zygomatic and posterior superior alveolar branches. The palatine nerves traverse the sphenopalatine ganglion without synapsing to innervate the hard and soft palate. The nerve enters the orbit via the inferior orbital fissure and transits the infraorbital canal. The middle and anterior alveolar branches arise in the infraorbital canal. The anterior alveolar branch exits through the infraorbital foramen and becomes the infraorbital nerve. Lesions of the infraorbital nerve cause the numb cheek syndrome (see below).

The mandibular division, the largest of the branches, gives off a small meningeal branch, and then exits through the foramen ovale. It runs for a short distance with the motor root, forming a large trunk. This trunk gives off the nervus spinosus and the branch to the medial pterygoid muscle. The nervus spinosus is a recurrent twig that re-enters the skull through the foramen spinosum and runs alongside the middle meningeal artery to innervate the meninges of the anterior and middle fossa. The trunk then divides into a small, anterior, chiefly motor branch and a large, posterior, chiefly sensory branch. The sensory filaments of the anterior branch form the buccal nerve. The posterior branch divides into three large terminal nerves. Two, the lingual and auriculotemporal, are purely sensory. The third, the inferior alveolar, also carries motor fibers to the mylohyoid and anterior belly of the digastric. The lingual nerve carries somatic sensation from the anterior two-thirds of the tongue. Taste sensation from the same region is carried by the chorda tympani and CN VII. After the origin of the lingual nerve, the nerve enters the mandibular foramen, traverses the mandibular canal, and emerges through the mental foramen as the mental nerve to supply sensation to the chin. Lesions of the mental nerve produce the numb chin syndrome (see below).

**TABLE
15.1**

The Divisions of the Trigeminal Nerve, the Foramina Through Which They Pass, Their Terminal Branches, and Fields of Cutaneous Innervation

Division	Skull Foramen	Terminal Branches	Cutaneous Innervation of Division
Ophthalmic	Superior orbital fissure	Frontal Lacrimal Nasociliary Meningeal	Bridge and side of nose; upper eyelid, forehead, scalp back to vertex, eyeball, lacrimal gland, nasal septum, lateral wall of nasal cavity, ethmoid sinus, tentorium cerebelli
Maxillary	Foramen rotundum	Infraorbital Zygomatic Superior alveolar Pterygopalatine Meningeal	Cheek, lateral forehead, side of nose, upper lip, upper teeth and gums, palate, nasopharynx, posterior nasal cavity, meninges of anterior and middle cranial fossa
Mandibular	Foramen ovale	Buccal Lingual Inferior alveolar Auriculotemporal Meningeal	Inner cheek, temple, lateral scalp, external auditory meatus, tympanic membrane, temporomandibular joint, mandible, lower teeth and gums, anterior two-thirds of tongue, lower lip, chin, meninges of anterior and middle cranial fossa

Some specifics about the trigeminal sensory innervation are clinically noteworthy. The innervation of the cornea is generally said to be CN V₁, although there is some evidence that the upper cornea may be CN V₁ and the lower cornea CN V₂, at least in some patients. CN V₁ innervates most of the nose, including the nasal septum. CN V₁ territory extends back to the scalp vertex; it does not stop at the hairline. [Figure 15.4](#) demonstrates the territory of the ophthalmic division outlined by post-zoster scarring. CN V₂ innervates the inferior lateral aspect of the nose and the cheek. The cutaneous distribution of CN V₂ is nearly identical to the infraorbital nerve ([Figure 15.5](#)). Changes in sensation involving the upper teeth and gums can be helpful in distinguishing a CN V₂ lesion from an infraorbital nerve lesion in patients with the numb cheek syndrome. The major terminal branch of CN V₃ is the mental nerve, which provides sensation to the chin and lower lip. The distribution of CN V₃ does not extend to the jaw line; there is a large “notch” at the angle of the jaw innervated by the greater auricular nerve (C2-C3). This notch of C2-C3 innervation can be surprisingly large ([Figure 15.6](#)).



FIGURE 15.4 A remote case of ophthalmic division zoster has left severe postinflammatory scarring, which outlines the cranial nerve (CN) V₁ distribution. Note the scarring extends back to the interaural line and involves much of the nose.



FIGURE 15.5 Patient with infraorbital neuropathy from carcinomatous infiltration. Note that the maxillary division innervates only the side of the nose distally. This patient had numbness of only the anterior teeth and gums, which proved the lesion was at the infraorbital foramen and not intracranial. (Reprinted from Campbell WW. The numb cheek syndrome: a sign of infraorbital neuropathy. *Neurology* 1986;36[3]:421–423, with permission.)

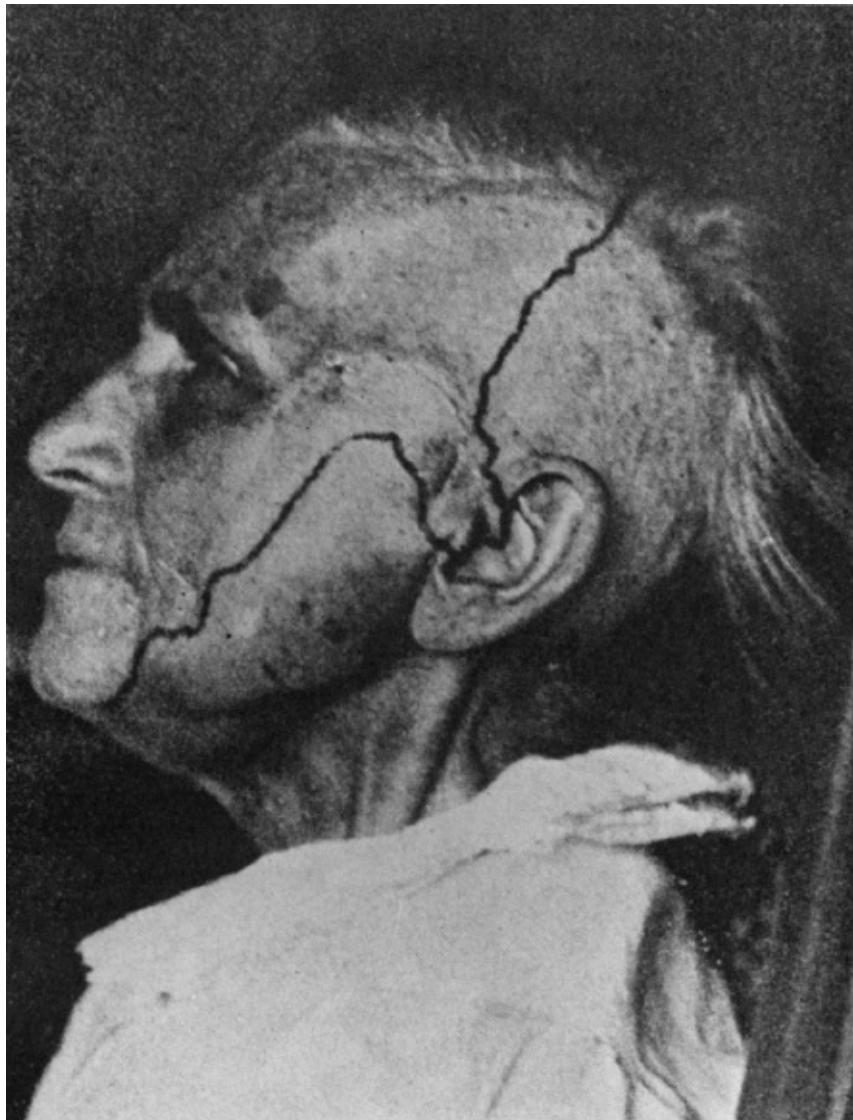


FIGURE 15.6 The distribution of sensory loss following complete section of the trigeminal root. Note the large area at the angle of the jaw that is innervated by C2 through the greater auricular nerve, and the inclusion of the tragus of the ear in the trigeminal distribution.

CN V supplies filaments to four ganglia in the head: the ciliary, sphenopalatine, otic, and submaxillary (Box 15.1).

CLINICAL EXAMINATION

Examination of the Motor Functions

Assessment of trigeminal motor function is accomplished by examining the

muscles of mastication. Bulk and power of the masseters and pterygoids can be gauged by palpating these muscles as the patient clinches the jaw. An effective technique is to place the examining fingers along the anterior, not lateral, border of the masseters bilaterally. When the jaw is clenched, the fingers will move forward; this movement should be symmetric on the two sides. Unilateral trigeminal motor weakness causes deviation of the jaw toward the weak side on opening, because of the unopposed action of the contralateral lateral pterygoid. The tongue also deviates toward the side of the weakness with CN XII lesions. So, both the tongue and the jaw deviate toward the weakness. Whether this is toward or away from the lesion depends on the specifics of the lesion. [Figure 15.7](#) shows a patient with both tongue and jaw deviation. For a video of a patient with jaw deviation, see [Video Link 15.1](#).

BOX 15.1

The Ciliary, Sphenopalatine, Otic, and Submaxillary Ganglia

The ciliary ganglion, located in the posterior orbit, receives sensory fibers from the nasociliary branch of cranial nerve (CN) V₁ (the long root of the ciliary ganglion), parasympathetic fibers from the Edinger-Westphal nucleus through the inferior division of CN III (the short root), and sympathetic fibers from the cavernous sympathetic plexus, running through the long ciliary nerves. Its branches, the short ciliary nerves, supply the ciliary muscle, sphincter and dilator of the pupil, and cornea.

The sphenopalatine ganglion, located in the pterygopalatine fossa, receives sensory fibers from the sphenopalatine branches of CN V₂, parasympathetic fibers from the nervus intermedius via the greater superficial petrosal nerve, and sympathetic fibers from the pericarotid plexus through the deep petrosal nerve. The deep and greater superficial petrosal nerves join to form the vidian nerve, or nerve of the pterygoid canal, before entering the ganglion. The sphenopalatine ganglion sends branches to the posterior ethmoidal and sphenoidal sinuses, the hard and soft palates, tonsils, uvula, nasal mucosa, and nasopharynx. Lacrimal fibers pass along the zygomaticotemporal branch of CN V₂ to the lacrimal branch of CN V₁, then to the lacrimal gland.

The otic ganglion, located in the infratemporal fossa just below the foramen ovale, receives a motor and possibly a sensory branch from CN V₃,

parasympathetic and sensory fibers from CN IX through the lesser superficial petrosal nerve, and sympathetic fibers from the plexus surrounding the middle meningeal artery. It sends motor branches to the tensor tympani and tensor veli palatini muscles and secretory fibers to the parotid gland through the auriculotemporal nerve.

The submaxillary ganglion, located near the submaxillary gland, receives sensory fibers from the lingual branch of CN V₃, parasympathetic fibers from the superior salivatory nucleus of CN VII through the chorda tympani, and sympathetic fibers from a plexus around the external maxillary artery. It sends secretory fibers to the submaxillary and sublingual glands and the mucous membrane of the mouth and tongue.

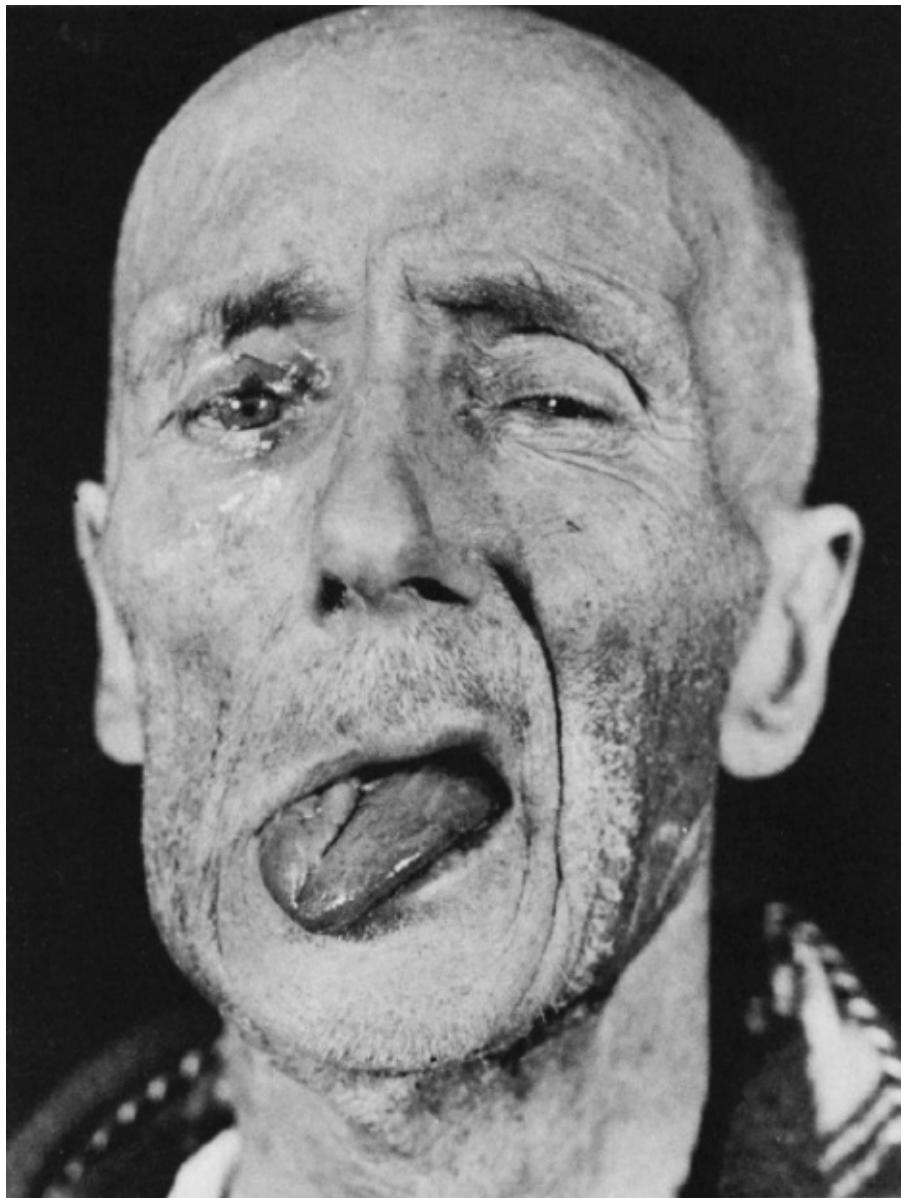


FIGURE 15.7 Infranuclear paralysis of the right trigeminal, facial, and hypoglossal nerves in a patient with metastatic carcinoma, showing deviation of the tongue and mandible to the right.

Careful observation of jaw opening is often the earliest clue to the presence of an abnormality. It is occasionally difficult to be certain whether the jaw is deviating or not. Note the relationship of the midline notch between the upper and lower incisor teeth; it is a more reliable indicator than lip movement. The tip of the nose and the interincisural notches should line up. A straightedge against the lips can help detect deviation. Another useful technique is to draw a vertical line across the midline upper and lower lips using a felt-tip marker. Failure of the

two vertical marks to match when the jaw is opened indicates deviation. If there is any suggestion of a problem, have the patient move the jaw from side to side. With unilateral weakness, the patient is unable to move the jaw contralaterally. To review, weakness of the right pterygoids causes deviation of the jaw to the right on spontaneous opening and inability to move the jaw to the left on command. With facial weakness, there may be apparent deviation of the jaw, and of the tongue, because of the facial asymmetry. Holding up the weak side manually will sometimes eliminate the pseudo-deviation.

Other techniques for examining trigeminal motor function include having the patient protrude and retract the jaw, noting any tendency toward deviation, and having the patient bite on tongue depressors with the molar teeth, comparing the impressions on the two sides and comparing the difficulty of extracting a tongue depressor held by the molar teeth on each side.

Unilateral weakness of CN V–innervated muscles generally signifies a lesion involving the brainstem, gasserian ganglion, or the motor root of CN V at the base of the skull. Severe bilateral weakness of the muscles of mastication with inability to close the mouth (dangling jaw) suggests motor neuron disease, a neuromuscular transmission disorder, or a myopathy. With significant atrophy of one masseter, a flattening of the jowl on the involved side may be apparent ([Figure 15.8](#)). With temporalis atrophy, there may be a hollowing of the temple. Rarely, fasciculations or other abnormal involuntary movements occur. There is no reliable or realistic method for examination of the other muscles supplied by CN V. Paralysis of the tensor tympani may cause difficulty hearing high notes. Because of bilateral innervation, unilateral upper motor neuron lesions rarely cause significant impairment of trigeminal motor function. There may be mild, transitory unilateral weakness. The amount of involvement depends on the extent of decussation. In bilateral supranuclear lesions, there may be marked paresis.

Examination of the Sensory Functions

In testing facial sensation, touch, pain, and occasionally temperature are examined in the same manner as elsewhere on the body ([Chapter 32](#)), searching for areas of altered sensation. It is better to ask the patient if the stimuli feel the same on the two sides, rather than suggesting they might feel different. Sensation should be compared in each trigeminal division, and the perioral region compared to the posterior face to exclude an onionskin pattern. Pain or

temperature should be compared with touch to exclude dissociated sensory loss (a common finding in lateral medullary syndrome). Sometimes it is useful to examine the nostrils, gums, tongue, and insides of the cheeks. Proprioception cannot be adequately tested, but one can test for extinction and the ability to identify figures written on the skin.

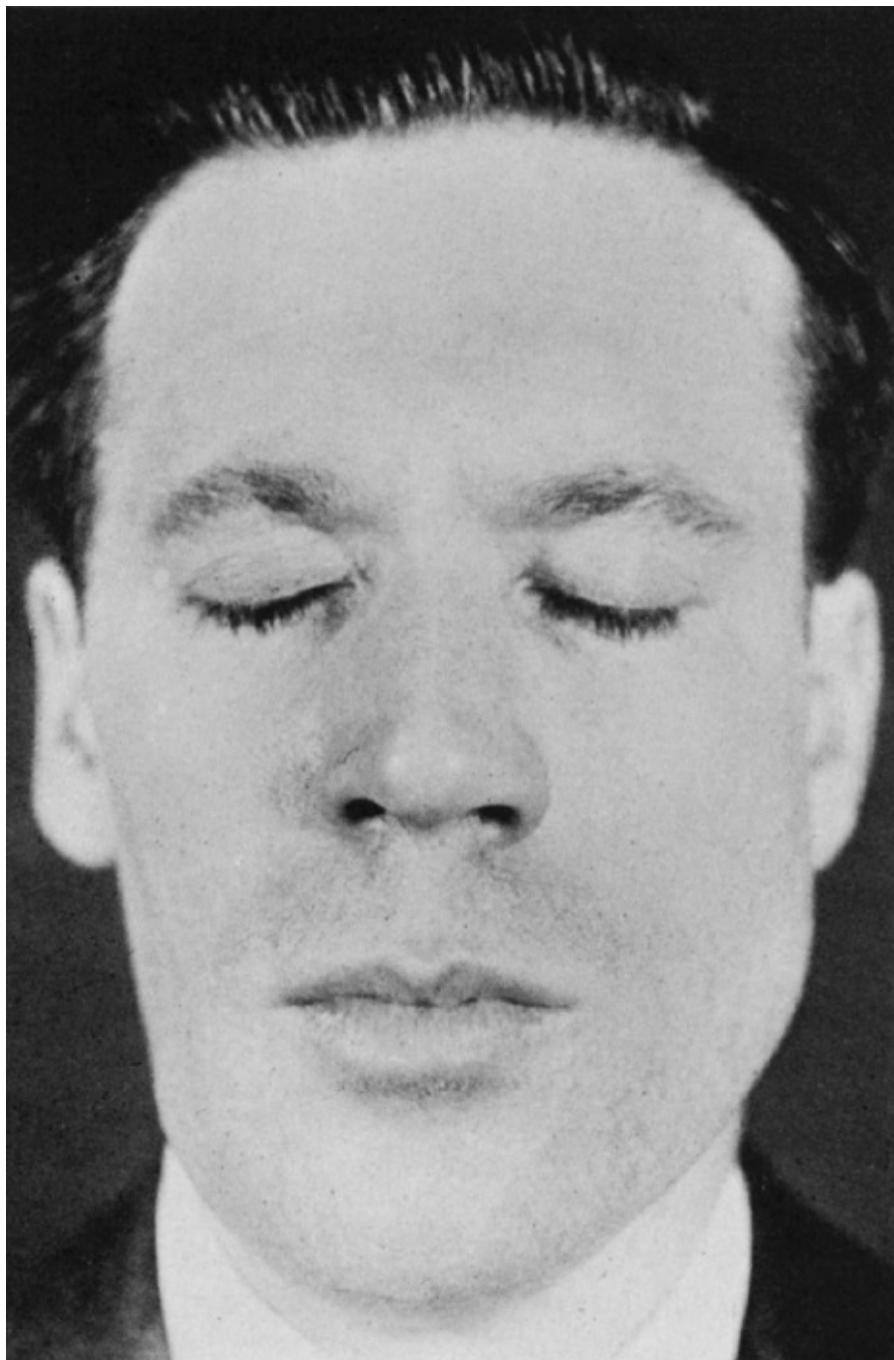


FIGURE 15.8 Infranuclear paralysis of the right trigeminal nerve with atrophy of the muscles of mastication.

There are three common exercises in evaluating facial sensation: (a) determining whether sensory loss is organic or nonorganic, (b) determining which modalities are involved, and (c) defining the distribution. Complaints of facial numbness are common, and not all are organic. However, real facial sensory loss can be a serious finding, occasionally signifying underlying malignancy. The various methods and tricks for detecting nonorganic sensory loss are not entirely reliable, and this diagnosis should be made with caution. Patients with nonorganic sensory loss may have a demarcation of the abnormal area at the hairline rather than the scalp vertex. On the lower face, functional sensory loss tends to follow the jaw line and involve the notch over the masseter muscle, which is not trigeminal innervated ([Figure 15.6](#)). However, patients with intramedullary lesions may have involvement of the angle of the jaw. On the trunk, organic sensory loss typically stops short of midline because of the overlap from the opposite side, and splitting of the midline suggests nonorganicity. This finding is not reliable on the face because there is less midline overlap, so organic facial sensory loss may extend to the midline. The corneal and sternutatory reflexes (see below) should be normal in nonorganic sensory loss. Splitting of vibration along the midline is reputedly a nonorganic sign. Because the frontal bone and mandible are single bones, there should be no difference in vibratory sensibility on either side of midline. Patients who report a difference in vibratory sensibility on testing just to either side of midline may have nonorganic sensory loss. The reliability of this sign has not been validated; it can be misleading. Other signs suggestive of nonorganicity include dissociation between pinprick and temperature, variability from trial to trial, history of hypochondriasis, secondary gain, la belle indifference, nonanatomical sensory loss, and changing boundaries of hypalgesia. Gould et al. have appropriately cautioned about the validity of hysterical signs and symptoms.

Examination of the Reflexes

The corneal, sternutatory, and jaw reflexes are the reflexes most often assessed in evaluating the trigeminal nerve.

The Jaw, Masseter, or Mandibular Reflex

To elicit the jaw (or jaw muscle) reflex, the examiner places an index finger or thumb over the middle of the patient's chin, holding the mouth open about

midway with the jaw relaxed, then taps the finger with the reflex hammer. The response is an upward jerk of the mandible. Other methods to elicit the reflex include tapping the chin directly and placing a tongue blade over the tongue or the lower incisor teeth and tapping the protruding end. All of these cause a bilateral response. A unilateral response may sometimes be elicited by tapping the angle of the jaw or by placing a tongue blade over the lower molar teeth along one side and tapping the protruding end.

The afferent impulses of this reflex are carried through the sensory portion of the trigeminal nerve to the mesencephalic nucleus, with the efferent impulses through its motor portion. In normal individuals, the jaw jerk is minimally active or absent. Its greatest use is in distinguishing limb hyperreflexia because of a cervical spine lesion (where the jaw jerk is normal) from a state of generalized hyperreflexia (where the jaw jerk is increased along with all of the other reflexes). The jaw reflex is exaggerated with lesions affecting the corticobulbar pathways above the motor nucleus, especially if bilateral, as in pseudobulbar palsy or amyotrophic lateral sclerosis (ALS). It is sometimes possible to elicit extra beats or jaw clonus. For a video of a hyperactive jaw reflex see Osama et al. The reflex may be unilaterally depressed in lesions involving the reflex arc.

The Corneal Reflex

The corneal reflex is elicited by lightly touching the cornea with a wisp of cotton or tissue. It is used to assess CN V₁ function. The stimuli should ideally be delivered to the upper cornea, because the lower cornea may be CN V₂ innervated in some individuals. The stimuli should be brought in from below or from the side so the patient cannot see it ([Figure 15.9](#)). The stimulus must be delivered to the cornea, not the sclera. If there is any evidence of eye infection, different pieces of cotton or tissue should be used for the two eyes. Crude stimuli, such as a large blunt object or fingertip, should never be used, even in comatose patients.



FIGURE 15.9 Eliciting the corneal reflex. The stimulating object should be brought in outside the patient's vision. The patient should look upward as the object is brought in from below, or laterally as the object is brought in from the other side. The stimulus must be applied to the cornea, not the sclera.

In response to the corneal stimulus, there should be blinking of the ipsilateral (direct reflex) and contralateral (consensual reflex) eyes. The afferent limb of the reflex is mediated by CN V₁, the efferent limb by CN VII. The blink reflex is an electrophysiologic test in which an electrical stimulus is delivered to the trigeminal nerve, and a response is recorded from facial muscles. It can provide further information about CN V, CN VII, and the connections between them. For brainstem lesions, electrophysiologic lesion localization corresponds well with imaging findings.

With a unilateral trigeminal lesion both the direct and consensual responses may be absent; neither eye blinks. Stimulation of the opposite eye produces normal direct and consensual responses. With a unilateral CN VII lesion, the direct response may be impaired, but the consensual reflex should be normal. Stimulation of the opposite side produces a normal direct response but an

impaired consensual response. These patterns are summarized in [Table 15.2](#). Lesions involving the brainstem polysynaptic trigeminofacial connections may produce impairment of both direct and consensual responses. The corneal reflex may be depressed with lesions of the contralateral hemisphere, especially if there is thalamic involvement. Because of the descent of the spinal tract and nucleus of CN V into the upper cervical cord, lesions there sometimes affect the corneal reflex. Corneal anesthesia can be a complication of cervical tractotomy done for chronic pain. Corneal sensation may be impaired in contact lens wearers, even when the lenses are out.

The Sternutatory (Nasal, Sneeze) Reflex

Stimulation of the nasal mucous membrane with cotton, a spear of tissue, or similar objects causes wrinkling of the nose, eye closure, and often a forceful exhalation resembling a feeble sneeze, as the nose tries to rid itself of the foreign object. The ophthalmic, not the maxillary, division of the trigeminal innervates the nasal septum and the anterior nasal passages. The afferent limb of the reflex arc is carried over CN V₁, the efferent limb over CNs V, VII, IX, X, and the motor nerves of the cervical and thoracic spinal cord. The reflex center is in the brainstem and upper spinal cord. The nasal mucosa may also be stimulated by irritating inhalants; this is a nasal reflex that should not be confused with olfaction ([Chapter 12](#)). The primary clinical use of the sternutatory reflex is as a cross-check on the corneal reflex. The ordinary sneeze reflex can obviously be elicited in many ways. An interesting phenomenon is the photic sneeze, photosternutatory, or “ACHOO” (autosomal dominant compelling helio-ophthalmic outburst) reflex—sneezing in response to looking at a bright light, which is seen in many normal individuals. Pryse-Phillips commented, “The acronym is slightly forced, but remains... the best of the decade.”

TABLE 15.2 Patterns of Direct and Consensual Corneal Reflex Abnormality with Trigeminal and Facial Nerve Lesions

		Direct Corneal Reflex	Censensual Corneal Reflex
Complete Trigeminal Nerve Lesion	Stimulate involved eye	Absent	Absent
	Stimulate opposite eye	Normal	Normal
Complete Facial Nerve Lesion	Stimulate involved eye	Absent	Normal
	Stimulate opposite eye	Normal	Absent

Other Trigeminal Mediated Reflexes

Other reflexes mediated in part by CN V include the nonfocal orbicularis oculi reflex and other trigeminofacial responses (Chapter 16), corneomandibular reflex (Chapter 40), and the snout reflex (Chapter 40). Many other reflexes have been described, but they are of limited value and are seldom used. The afferent limbs of these reflexes are trigeminal mediated. In some, the efferent limb is also trigeminal (e.g., the jaw jerk); in others, the efferent limb is executed through connections with CN III, CN VII, or other pathways.

Disorders of Function

Trigeminal nerve lesions may cause weakness, abnormal involuntary movements, sensory loss or other sensory abnormalities, facial pain, trophic abnormalities, autonomic dysfunction, or abnormalities of the reflexes mediated by the trigeminal nerve. The conditions most commonly seen are facial pain, particularly TN, and facial numbness.

Motor Dysfunction

Because of the bilateral hemispheric innervation, weakness in the trigeminal distribution does not often occur with upper motor neuron lesions, although slight weakness of the contralateral muscles with an exaggerated jaw reflex can occur. Bilateral supranuclear lesions, as in pseudobulbar palsy or ALS, can cause marked weakness, often with a grossly exaggerated jaw reflex. In supranuclear lesions, no atrophy or fasciculations occur.

Significant weakness in the trigeminal motor distribution is most often the result of a neuromuscular transmission disorder or ALS. Patients with myasthenia gravis (MG) may have chewing difficulties with masticatory fatigue, especially when eating difficult-to-chew things such as tough meat. When

severe, MG may cause an inability to close the mouth (jaw drop). Patients with severe polymyositis, rarely with other myopathies, may also have difficulty with jaw power. Patients with giant cell arteritis commonly have jaw claudication with focal pain in the masseter when chewing, which can be confused with weakness. ALS commonly causes a jaw drop, often with dysphagia and difficulty swallowing saliva, requiring the patients to constantly keep absorbent materials in their mouth. Jaw drop may also occur in Kennedy's disease. Needle electromyography of trigeminal innervated muscles may demonstrate subclinical involvement. Lesions anywhere along the course of the lower motor neuron can cause weakness accompanied by atrophy, sometimes marked; fasciculations; and a decreased jaw jerk ([Figure 15.7](#)).

Abnormal involuntary movements commonly affect the jaw. Oromandibular dystonia produces a variety of abnormal movements: jaw opening, jaw closing, lateral movements, bruxism, and combinations of these (see [Video Link 15.2](#)). Jaw dystonia may occur as part of an extrapyramidal syndrome due to psychoactive drugs, and abnormal jaw movements are a common manifestation of tardive dyskinesias. Meige's syndrome is oromandibular dystonia and blepharospasm. Chewing movements and grinding of the teeth are sometimes present in psychoses, and chewing or tasting movements in complex partial seizures. Bruxism may occur as a side effect of levodopa. Rarely, a focal seizure limited to the muscles of mastication may cause clenching of the jaws with biting of the tongue or cheeks. Trismus is marked spasm of the muscles of mastication: The teeth are tightly clenched, the muscles hard and firm, and the patient is unable to open his jaws. It is a classical manifestation of tetanus, and sometimes occurs in encephalitis, rabies, acute dystonic reactions due to neuroleptic medications, and tetany. Trismus may occur in Foix-Chavany-Marie syndrome ([Chapter 9](#)). Some myopathies, especially polymyositis, may result in fibrosis of the masseters, which causes painless trismus. Trismus may be psychogenic. Patients with Parkinson's disease may have jaw tremor. Hemimasticatory spasm is a syndrome of brief, sometimes painful, involuntary contractions or spasms of the jaw-closing muscles unilaterally. It may eventually result in masseter hypertrophy. Hemimasticatory spasm may be associated with other conditions, including scleroderma and facial hemiatrophy. Neuromyotonia of the jaw muscles may follow cranial irradiation.

Sensory Dysfunction

Supranuclear lesions, particularly of the parietal lobe or sensory radiations, may raise the sensory threshold of the contralateral face; a thalamic lesion may cause facial hypesthesia with hyperpathia or allodynia. Lesions of the principal sensory nucleus in the pons may cause diminished tactile sensation involving both skin and mucous membranes on the involved side, and loss of reflexes in which the afferent arc is mediated by the trigeminal nerve. Lesions of the spinal tract or nucleus cause a disturbance of the pain and temperature modalities, and, possibly to a lesser extent, of tactile sense.

Dissociation of sensation, with different degrees of involvement of light touch as compared to pain and temperature, suggests a lesion in the substance of the brainstem (intramedullary), where the different sensory pathways are running in widely separate locations. Extramedullary lesions are characterized by loss or diminution of all types of exteroceptive sensation, dysesthesias or paresthesias, or spontaneous pain. A lesion central to or at the gasserian ganglion will affect all three divisions; a lesion peripheral to the ganglion, will involve only isolated divisions or branches. There may also be reflex changes, such as absence of the corneal or sternutatory.

Trigeminal nerve lesions may also cause trophic changes. With CN V₁ lesions impaired, corneal sensation may result in corneal ulcerations and other ocular complications. The eye must be scrupulously protected when the cornea is anesthetic. Interaction between the trigeminal and olfactory systems has a powerful influence on the perception of odors, and trophic changes in the nasal mucosa because of a trigeminal lesion may cause a secondary anosmia. Nasal anesthesia may result in disfiguring erosion of the ala nasi. Because of the many connections of CN V with other CNs, particularly CNs VII and IX, a decrease or increase in lacrimal, salivary, and mucous secretion can follow a trigeminal lesion, particularly when the functions are trigeminal-mediated reflex responses. Even taste, not a trigeminal function, may be affected because of taste fibers carried through the lingual nerve to the chorda tympani.

The most common disorder to involve trigeminal sensory function is TN, or tic douloureux. TN causes paroxysms of fleeting but excruciating unilateral facial pain. It usually involves the second or third division, rarely the first (the inverse of herpes zoster [HZ]). Occasional patients have involvement of both CN V₂ and CN V₃. The lancinating pain usually lasts only seconds, occasionally up to 2 minutes, but may occur many times a day. The patient may wince, hence the designation “tic.” Stimulation of some specific area, a trigger zone, in the involved nerve distribution will often provoke a paroxysm of pain. Pain may be

brought on by activities such as talking, chewing, brushing teeth, exposure to cold, or by wind on the face. Men may present with the trigger zone unshaven, women with it not made up. The patient may be reluctant to allow neurologic examination of the involved area for fear of triggering a paroxysm of pain. Trigger zones are small, sometimes punctate. Stimulus-evoked pain is one of the most striking features of TN and has high diagnostic value. A refractory period lasting seconds or minutes following a provoked paroxysm may occur. TN enters into periods of complete remission in up to 63% of patients.

The most common cause of TN is compression of the sensory root by an ectatic arterial loop off the basilar artery, usually the anterior inferior cerebellar or superior cerebellar. However, advanced imaging studies have shown that some contact between the trigeminal nerve and nearby vessels occurs in asymptomatic individuals. A meta-analysis showed neurovascular contact in 89% of symptomatic nerves, but also in 36% of asymptomatic nerves, indicating high sensitivity but poor specificity. Displacement, distortion, flattening, or atrophy of the nerve roots are sensitive signs of clinically relevant neurovascular compression. MRI in TN is rarely abnormal except for vascular loops or abnormalities related to vascular compression.

Rarely, structural lesions may cause facial pain resembling TN, referred to as secondary or symptomatic TN. These lesions may cause sensory loss in the involved distribution, motor dysfunction, or involve neighboring structures. Examples include multiple sclerosis (MS), tumors involving the gasserian ganglion or its branches, and other tumors in the cerebellopontine angle. Among patients with TN-like symptoms, 6% to 16% are variously reported to harbor an intracranial tumor, such as an acoustic neuroma. The presence of a complaint of numbness, impaired sensation on examination, other neurologic abnormalities, history of symptom progression, and duration of symptoms of less than 1 year increase the likelihood of an abnormal imaging study. Other central processes involving the trigeminal pathways in the brainstem, such as syringobulbia and infarction, may cause pain resembling TN. Facial pain is not uncommon in Wallenberg's lateral medullary syndrome and may rarely resemble TN.

Patients with idiopathic or classical TN have no clinical motor or sensory deficit in the distribution of the involved nerve. Absence of a sensory deficit is one criterion for the diagnosis of classical TN. Subtle sensory changes may be detected with quantitative sensory testing. Reports indicate that about one-third of patients with TN because of tumor or MS have a demonstrable sensory deficit, but the absence of a sensory deficit does not exclude secondary TN.

Occasional patients develop persistent, non-paroxysmal, pain in the involved distribution, frequently described as dull, burning, or tingling. This has been referred to as atypical TN or TN2. The term atypical TN is problematic because of potential confusion with the entity of atypical facial pain. Some have used the term TN2, or atypical TN, in referring to what others would cause atypical facial pain.

TN occurs in MS patients much more commonly than in the general population; it is usually caused by a demyelinating lesion involving the trigeminal root entry zone in the pons, although vascular compression at the root entry zone can occur even in MS patients. TN occurs in 2% to 5% of patients with MS, and MS is found in 2% to 14% of patients presenting with TN. Bilateral TN is especially suggestive of MS. Most TN patients are in the fifth decade or beyond; onset in a young person should prompt consideration of symptomatic TN, especially due to demyelinating disease.

Some published diagnostic guidelines have inadvertently made the classification of TN more difficult. The most recent version of the International Classification of Headache Disorders no longer includes symptomatic or secondary TN as a diagnostic category. Cruccu et al. proposed a new classification and diagnostic grading scheme for practice and research. In this scheme, classical TN is defined as a specific category in which MRI demonstrates vascular compression with morphologic changes of the trigeminal nerve root. Secondary TN is that due to a major underlying neurologic disease, such as tumor or MS. The category of idiopathic TN is reserved for the small proportion of patients in which imaging studies are completely normal except for incidental vascular contact. TN with continuous pain refers to those patients who experience nonparoxysmal pain between attacks.

The operative technique of microvascular decompression insulates the nerve from a compressing vessel. Microvascular decompression is widely performed and quite effective. In the past, ablative involvement procedures such as retrogasserian rhizotomy were often performed on the gasserian ganglion or sensory root. These would leave the patient's face numb to various degrees. Sometimes the operation would cause facial numbness but fail to relieve the pain, leaving the patient with a numb but painful face, a condition called anesthesia dolorosa or deafferentation pain. Ablative procedures used currently in resistant cases can also cause anesthesia dolorosa.

Many other craniofacial neuralgias have been described, but most of these syndromes have not withstood the test of time and their existence as real entities

remains in doubt. These include Sluder's, or sphenopalatine, neuralgia, vidian neuralgia, Costen's syndrome, and Eagle's syndrome. The term persistent idiopathic facial pain, formerly called atypical facial pain, is used to refer to a syndrome of facial pain that does not have the characteristics of TN. The pain in atypical facial pain is typically constant and not paroxysmal, described as deep and poorly localized, not restricted to a single trigeminal division, not lancinating, and not associated with any trigger zone. No identifiable etiology is usually apparent, and the pain is often attributed to depression or other emotional factors. There is increasing evidence that in some cases it is a neuropathic pain syndrome with objective abnormalities on neurophysiologic testing. Forssell et al. found that 75% of a series of 20 patients with atypical facial pain had either an abnormal electrodiagnostic blink reflex or abnormal thermal quantitative thermal sensory testing. Aching pain in the face may precede the development of TN (preTN).

Unusual facial pain may occur in Gradenigo's syndrome because of gasserian ganglion involvement in lesions at the petrous apex. Affected patients may have pain and sensory disturbances in the V₁ distribution, accompanied by CN VI palsy ([Chapter 14](#)). In Raeder's paratrigeminal syndrome (paratrigeminal oculosympathetic syndrome), there is headache, facial pain in the distribution of V₁ and an oculosympathetic paresis. There is no anhidrosis as in Horner's syndrome because those fibers travel via the external carotid artery. There may or may not be demonstrable trigeminal sensory loss. Other CNs may be involved. The responsible lesion lies in the middle cranial fossa near the petrous apex. Headache and oculosympathetic paresis (or Horner's syndrome) may also occur with cluster headache and carotid dissecting aneurysms. CN V₁ or V₂, or both, may be involved in lesions of the cavernous sinus ([Chapter 21](#)). In the superior orbital fissure syndrome, there is involvement of V₁ and other structures passing through the fissure ([Chapter 21](#)). Only when V₂ is affected can lesions of the cavernous sinus and superior orbital fissure be clinically differentiated. Nurmikko stressed the value of a semi-structured interview, posing a series of specific questions, in the differential diagnosis of facial pain syndromes.

Acute HZ of the trigeminal nerve is extremely painful. It is usually seen in elderly or immunocompromised patients, and affects CN V₁ in 80% of cases, causing pain and vesicles over the forehead, eyelid, and cornea (herpes ophthalmicus). The inflammation causes neuronal loss in the affected ganglion, and a reduction of both axons and myelin in the affected nerve. Cutaneous

scarring is common ([Figure 15.4](#)). Ophthalmic involvement may lead to keratitis, corneal ulcerations, residual corneal scarring, and sometimes result in blindness. In some patients, only the eye, mainly the cornea, is involved. Zoster may affect any of the trigeminal divisions, and there may be motor involvement ([Figure 15.10](#)). Rarely, trigeminal HZ may be complicated by encephalitis or a syndrome of delayed contralateral hemiparesis due to arteritis. Pain without a cutaneous eruption is referred to as zoster sine zoster or zoster sine herpete.

Postherpetic Neuralgia

In some patients with trigeminal HZ, the pain of the acute phase evolves into a dreadful, persistent neuralgic pain syndrome called postherpetic neuralgia (PHN). Pain persisting for more than 3 months after the acute eruption is appropriately labeled as PHN. The pain is probably related to deafferentation and mediated centrally. It is typically dysesthetic with a burning component, constant but with superimposed paroxysms of lancinating pain that may be provoked by touching certain spots within the affected area. There may be hypesthesia or hyperesthesia in the affected area. Age is an important factor in predisposing to PHN; it develops in only 10% of those less than age 60, but in 40% of those over 60 years.

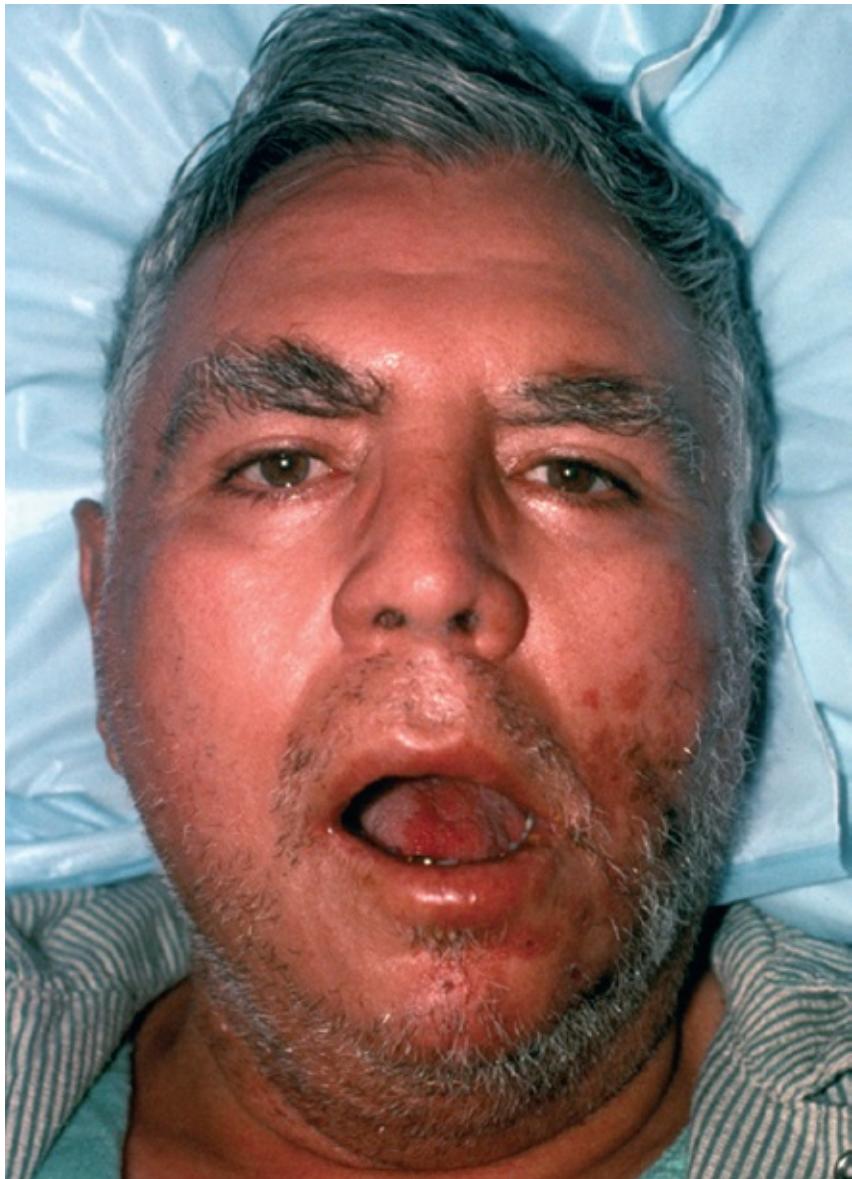


FIGURE 15.10 A patient with herpes zoster of the mandibular division on the left involving the motor root, producing weakness of the pterygoids, and causing deviation of the jaw to the left. The herpetic rash is in the distribution of CN V₃.

Facial Numbness

Isolated facial numbness is a common problem. Facial sensory loss may occur with lesions involving the main trigeminal divisions or their distal branches. A number of processes, some ominous, may be responsible. The numb chin syndrome refers to hypesthesia and sometimes paresthesias involving the lower lip and chin, approximately in the distribution of the mental nerve (chin neuropathy, Roger's sign). The numb chin syndrome is often due to a neoplastic

process, with metastasis either to the mental foramen of the mandible or to the intracranial meninges or skull base, often from carcinoma of the breast or lung. Lesions of the inferior alveolar nerve may also be responsible. The predilection for involvement of the CN V₃ distribution may reflect the relatively protected position of the other trigeminal divisions in the cavernous sinus, with greater exposure of the third division to neoplastic processes involving the meninges and base of the skull. Possible clues to a skull base or meningeal origin of a numb chin include sensory disturbance extending beyond the chin or involvement of other CNs. Loss of sensation of the anterior teeth and gums suggests a distal process involving the inferior alveolar nerve. Sparing of oral sensation or dissociation of modalities suggests an intraparenchymal CNS lesion. In a series of 42 numb chin patients with cancer, 50% had metastases to the mandible, 22% had neoplastic meningitis and 14% had metastases to the skull base. Non-neoplastic causes include dental procedures, tooth abscess, connective tissue disease, sickle cell disease, tumors or cysts of the mandible, erosion of the mental foramen in edentulous patients, and trauma. In one series, the most common etiology of the numb chin syndrome was dental.

The numb cheek syndrome is similar but usually because of a lesion involving the infraorbital nerve with perineural spread of a tumor ([Figure 15.5](#)). When hypesthesia also involves the medial and lateral upper incisors and canine teeth (distribution of the anterior superior alveolar branch), and adjacent gingiva, sparing the more posterior teeth and gums, the pathologic process localizes to the infraorbital foramen and makes involvement of the maxillary division more proximally unlikely. Perineural spread of skin cancer is the most common etiology. The molar and premolar teeth and gums are innervated by the posterior and middle superior alveolar nerves. The numb cheek-limp lower lid syndrome includes weakness involving the distal branches of the facial nerve because of carcinoma infiltrating the infraorbital and facial nerves.

The numb chin or cheek syndrome can be the presenting manifestation of cancer, more often it is due to progression or relapse of a known malignancy. Unusual causes of trigeminal sensory dysfunction include pontine hemorrhage, Wegener's granulomatosis, localized hypertrophic mononeuropathy, and a midbrain lesion affecting the trigeminothalamic fibers. Trauma may involve the distal trigeminal branches. Trumpet player's neuropathy affects musicians, causing pain and numbness of the upper lip because of injury to the anterior superior alveolar nerve.

Trigeminal sensory neuropathy (TSN) refers to a syndrome of isolated facial

numbness, usually gradual in onset, which may involve a single division or the entire face; it is occasionally bilateral. Some patients have paresthesias and dysesthesias. The pathology probably involves the ganglion. Some cases are idiopathic, but many underlying diseases, particularly connective tissue disorders, can cause TSN (Table 15.3). Occasionally, TSN is part of a multiple cranial neuropathy syndrome, especially in patients with scleroderma. Some patients with idiopathic TSN have shown gadolinium enhancement in the cisternal segment suggesting a similarity to Bell's palsy.

TABLE 15.3 Some Causes of Trigeminal Sensory Neuropathy

Idiopathic
Connective tissue disorder
Sjögren's syndrome
Scleroderma
Mixed connective tissue disorder
Other
Sarcoidosis
Wegener's granulomatosis
Giant cell arteritis
Multiple sclerosis
Tumor
Diabetes
Syringobulbia
Toxins
Trichlorethylene
Stilbamidine
Mefloquine

Facial sensory loss is common in brainstem lesions; most are vascular. A frequent cause is the lateral medullary syndrome (Wallenberg's), which classically causes loss of pain and temperature sensation over the ipsilateral face and contralateral body. Variations on this pattern have been well reported, including sensory loss of only V_{1,2} or only V_{2,3}. In a series of 50 patients, only

13 (26%) had the classic pattern. Others had bilateral facial sensory loss, contralateral facial sensory loss, only body and limb loss, only facial loss not involving the body, or no sensory signs. When facial sensory loss occurred, it was most often in an onionskin distribution. Intraoral sensation may be spared.

Other Trigeminal Nerve Disorders

Pathology involving the trigeminal nerve and its connections may result in misdirection of nerve fibers, producing unusual and interesting effects. Congenital ocular aberrant innervation syndromes are a complex group of disorders involving abnormal miswiring of the extraocular muscles ([Chapter 14](#)). The Marcus Gunn phenomenon, or jaw-winking, occurs in patients with congenital ptosis; opening the mouth, chewing, or lateral jaw movements causes an exaggerated reflex elevation of the ptotic lid, see [Video Link 15.3](#). The phenomenon may be the result of proprioceptive impulses from the pterygoid muscles being misdirected to the oculomotor nucleus. Trigemino-abducens synkinesis is due to abnormal communications between CN V and CN VI. Involuntary closure of one eye on mouth opening (reversed Gunn phenomenon, inverse jaw winking, or Marin Amat sign) is a synkinesia because of aberrant regeneration of the facial nerve; it occurs most often following Bell's palsy ([Chapter 16](#)). The auriculotemporal (Frey) syndrome produces flushing, warmth, and excessive perspiration over the cheek and pinna on one side following ingestion of spicy food (gustatory sweating). This syndrome is due to misdirection of the secretory fibers to the parotid gland to the sweat glands and vasodilator endings in the auriculotemporal nerve distribution; it usually follows trauma or infection of the parotid gland or local nerve injury.

Migraine may be a neurovascular syndrome related to abnormalities in the trigeminovascular system with serotonin playing an important role. Other trigeminal autonomic cephalgias involve pain in the V₁ distribution and autonomic symptoms. These include cluster headache; paroxysmal hemicrania; and the short-lasting, unilateral, neuralgiform headache with conjunctival injection, and tearing syndrome. In encephalotrigeminal angiomyomatosis (Sturge-Weber syndrome, or Weber-Dimitri disease), there are congenital nevi or angiomas over one side of the face in the trigeminal distribution with associated ipsilateral leptomeningeal angiomas and intracortical calcifications with attendant neurologic complications ([Figure 15.11](#)). Neck-tongue syndrome is a rare disorder involving the trigeminal and upper cervical nerves. Pain and

numbness in the distribution of the lingual nerve and C2 root are provoked by sudden head turning. Afferent fibers from the lingual nerve are thought to join the hypoglossal nerve and send filaments to the upper cervical nerves. The symptoms are allegedly caused by minor subluxation of the C2 articulatory process tweaking these nearby structures.

Localization of Trigeminal Nerve Lesions

In reviews of the regional pathology of the trigeminal nerve from an imaging perspective, the common brainstem lesions were neoplasms, vascular disease, and demyelinating processes.

The most common causes in the segment from the brainstem to the skull base—including the cisternal, Meckel cave, and cavernous sinus segments—were neurovascular compression, followed by acoustic or trigeminal schwannoma, meningioma, lymphoma, epidermoid cyst, lipoma, pituitary adenoma, metastasis, and aneurysm. Skull base abnormalities included chordoma, chondrosarcoma, metastasis, bone dysplasias, and Paget's disease. The peripheral divisions of the trigeminal nerve were commonly involved by adjacent inflammatory disease in the sinuses, perineural spread of malignancy, and schwannoma. Trauma is a common cause of impaired trigeminal sensory dysfunction, because of dental and other surgical procedures, dental anesthetic injections and facial fractures.



FIGURE 15.11 Child with the Sturge-Weber syndrome, causing the typical port-wine

hemangioma of the skin along the distribution of the left trigeminal nerve. (Reprinted from Allingham RR, Damji KF, Shields MB. *Shields' Textbook of Glaucoma*. 6th ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins, 2011, with permission).

Video Links

Video Link 15.1. Jaw deviation. <https://www.youtube.com/watch?v=cbW6ki4g0JE>

Video Link 15.2. Oromandibular dystonia.
http://neurosigns.org/wiki/Oromandibular_dystonia

Video Link 15.3. Marcus Gunn phenomenon (jaw-winking).
http://neurosigns.org/wiki/Jaw_winking

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CHAPTER 16

The Facial Nerve

ANATOMY AND PHYSIOLOGY

The facial, or seventh, cranial nerve (CN VII) is a predominantly motor nerve that innervates the muscles of facial expression and the muscles of the scalp and ear, as well as the buccinator, platysma, stapedius, stylohyoid, and posterior belly of the digastric. In addition, it carries parasympathetic secretory fibers to the submandibular and sublingual salivary glands, the lacrimal gland, and to the mucous membranes of the oral and nasal cavities. It has some sensory functions; the most important is to mediate taste from the anterior two-thirds of the tongue. It also conveys exteroceptive sensation from the eardrum and external auditory canal, proprioceptive sensation from the muscles it supplies, and general visceral sensation from the salivary glands and mucosa of the nose and pharynx. Anatomically, the motor division of the nerve is separate from the sensory and parasympathetic portions. In its course from its exit from the pons until its terminal arborizations, several important branches are given off in the following order: the greater (superficial) petrosal nerve, the nerve to the stapedius, and the chorda tympani.

The nerve may be understood as a series of segments: a brainstem or intramedullary segment (from the brainstem nuclei to the exit point), a segment from the exit point to the entrance into the internal auditory canal (IAC) or cisternal segment, a meatal or canal segment (course through the IAC) to the entrance to the facial canal, a labyrinthine segment (from there to the geniculate ganglion), a short horizontal segment (from the geniculate ganglion to the pyramidal eminence of the posterior wall of the tympanic cavity), a mastoid segment (from the pyramidal eminence to the stylomastoid foramen), and an extratemporal or peripheral segment (from the stylomastoid foramen to the pes anserinus). These segments are discussed in more detail below. The associated

findings in CN VII palsy often allow identification of the involved segment.

The Motor Portion

The supranuclear innervation to the muscles of facial expression arises from the lower third of the contralateral precentral gyrus in the facial area of the motor homunculus. Fibers descend in the corticobulbar tract through the corona radiata, genu of the internal capsule, medial portion of the cerebral peduncles and into the pons, and then decussate to converge on the facial nuclei. The portion of the nucleus that innervates the lower half to two-thirds of the face has predominantly contralateral supranuclear control; the portion that innervates the upper third to half has bilateral control. The muscles of the lower face may also receive more abundant cortical innervation than the muscles of the upper face and forehead. This scheme applies to voluntary facial movements. Unconscious, emotional, involuntary supranuclear control follows a different pathway. Patients with lesions in certain parts of the nervous system may have different degrees of involvement of the voluntary and involuntary systems (see below).

Studies in humans and nonhuman primates show distributed motor control of facial expression with at least five cortical regions involved: the primary motor cortex, the ventral lateral premotor cortex, the supplementary motor area, and the cingulate cortex. Recent investigations confirm the long established paradigm of bilateral control of the upper face and mainly contralateral control of the lower face. The primary motor cortex, the ventral lateral premotor cortex, and the supplementary motor area are essential for voluntary control of facial expressions. The cingulate cortical areas receive input from different structures of the limbic system and are important for emotional facial expression.

Although most corticobulbar fibers to the facial nuclei decussate in or rostral to the pons, some descend in the aberrant pyramidal tract to medullary levels, decussate there, and ascend contralaterally in the dorsolateral medulla to reach the facial nucleus. The aberrant pyramidal tract is a normal descending fiber tract that leaves the pyramidal tract in the crus cerebri and travels in the medial lemniscus to the upper medulla. Involvement of the aberrant pyramidal tract explains the occurrence of ipsilateral upper motor neuron facial palsy in the lateral medullary syndrome.

A study using transcranial magnetic stimulation to investigate the corticofacial projections found that in the majority of patients, the corticofacial fibers traveled in the base of the pons and crossed at the level of the facial

nucleus. But in some individuals, corticofacial fibers formed an “aberrant bundle” in a paralemniscal position at the dorsal edge of the pontine base. In other patients, the corticofacial fibers looped down into the ventral upper medulla, crossed the midline, and ascended in the dorsolateral medullary region ipsilateral to the facial nucleus. The findings suggest that facial paresis because of a brainstem lesion may present as contralateral supranuclear facial paresis by a lesion of the cerebral peduncle, pontine base, the aberrant bundle, and the ventral medulla. Supranuclear facial paresis ipsilateral to the lesion side may result from a lesion in the lateral medulla, and facial paresis of the supranuclear type may be imitated by a lesion of the peripheral facial nerve in the dorsolateral medulla with involvement of the lower pons. The facial nuclei also receive bilateral extrapyramidal, basal ganglia, and hypothalamic innervations that are concerned with maintaining facial muscle tone and with automatic and emotional movements.

The facial nucleus is special visceral efferent, or branchiomotor; it innervates the muscles of the second branchial arch. It lies deep in the tegmentum of the caudal pons, anteromedial to the nucleus of the spinal tract of CN V, anterolateral to the nucleus of CN VI, and posterior to the superior olivary nucleus (Figures 11.6 and 14.8). The facial motor nucleus has lateral, medial, and dorsal subnuclei, arranged in columns. The subnuclear innervation pattern is not as well worked out as for the oculomotor nucleus, but the lateral subnucleus is thought to innervate the lower facial muscles and buccinators; the medial subnucleus the posterior auricular, platysma, and occipital muscles, and probably the stapedius; and the dorsal subnucleus the upper facial muscles via the temporal, orbital, and zygomatic branches. Other schemes of organization have been postulated.

Axons of the facial nerve arise from the dorsal surface of the nucleus and travel dorsomedially, moving up and around to encircle the abducens nucleus and forming the internal genu of the facial nerve. The internal loop of CN VII fibers around the CN VI nucleus forms the facial colliculus, a bump in the rhomboid fossa in the floor of the fourth ventricle, a prominent landmark for surgeons working in the area (Figure 11.4). The facial nucleus is in a somewhat aberrant position more anterolaterally than expected, even considering its branchial arch relationships. In embryonic life, the nucleus is more dorsal and medial, near the CN VI nucleus, but with maturation moves to its adult position trailing its axons behind. In their course, the facial nerve axons run in proximity to the nucleus and fibers of CN VI, the pontine paramedian reticular formation,

CN V, and CN VIII as well as the descending and ascending long tracts that course through the pons.

The facial nerve has two components, the motor root, which makes up about 70% of the fibers, and the sensory root, which accounts for 30%. The sensory root forms the nervus intermedius (NI) and contains both sensory and autonomic fibers. The autonomic fibers run near the incoming sensory fibers through the pons. The intrapontine filaments of CN VII thus consist of exiting branchiomotor and parasympathetic fibers, and incoming sensory fibers ([Figure 16.1](#)).

CN VII exits the pons laterally at the pontomedullary junction, just caudal to the roots of CN V between the olive and the inferior cerebellar peduncle ([Figure 11.3](#)). The NI is a small bundle that usually leaves the pons closer to CN VIII than CN VII and runs between the larger trunks across the cerebellopontine angle (CPA). In about 20% of specimens, the NI is not identifiable as a separate structure in the CPA. At the entrance to the IAC, the facial nerve motor root lies in a groove on the anterosuperior surface of the vestibulocochlear nerve, with the NI in between. In this segment, CN VII is a paler white color than CN VIII. The facial nerve at this point lies in close proximity to the anterior inferior cerebellar artery (AICA). In some individuals, the AICA loops down into the IAC. As with the vaginal sheaths of the optic nerve, the subarachnoid space extends along the facial nerve to the geniculate ganglion.

At the bottom or lateral end of the IAC, the nerve pierces the meninges and enters the facial canal, or fallopian aqueduct. The point of entry is the narrowest portion of the canal. The facial nerve and the NI merge as the nerve enters the canal. In traversing the facial canal, the nerve makes two abrupt, tortuous turns, creating two external genus. In its course through the petrous bone, from its entrance into the facial canal until its exit from the stylomastoid foramen, the nerve has three segments: labyrinthine, horizontal or tympanic, and mastoid or vertical. The labyrinthine segment lies laterally between the cochlea and vestibule, toward the medial wall of the tympanic cavity, running perpendicularly to the long axis of the petrous pyramid. The labyrinthine segment ends at the first external genu where the geniculate ganglion lies. At this point, the nerve turns abruptly and runs horizontally for about 1 cm (the horizontal or tympanic segment), then turns backward and arches downward behind the tympanic cavity (mastoid or vertical) segment. The branch to the stapedius muscle arises from the distal tympanic or upper end of the mastoid segment. At the end of the tympanic segment, the nerve encounters the second

external genu as it makes a 90-degree turn to enter the mastoid segment. The mastoid segment then descends toward the stylomastoid foramen, gives off the chorda tympani about 6 mm before its exit, and emerges from the stylomastoid foramen. The tight confines of the bony canal may make the nerve particularly vulnerable to damage from inflammation and edema, a point of possible significance in some CN VII neuropathies (see below). In patients with Bell's palsy, the involved side usually correlates with the side of the narrower facial canal as determined by high-resolution computed tomography (CT). CN VII runs along with the labyrinthine branch of the AICA, but there is evidence to suggest that it is less well vascularized in its intrapetrous segment, particularly in the labyrinthine segment, than elsewhere along its course. This may also have relevance to the pathologic changes in Bell's palsy.

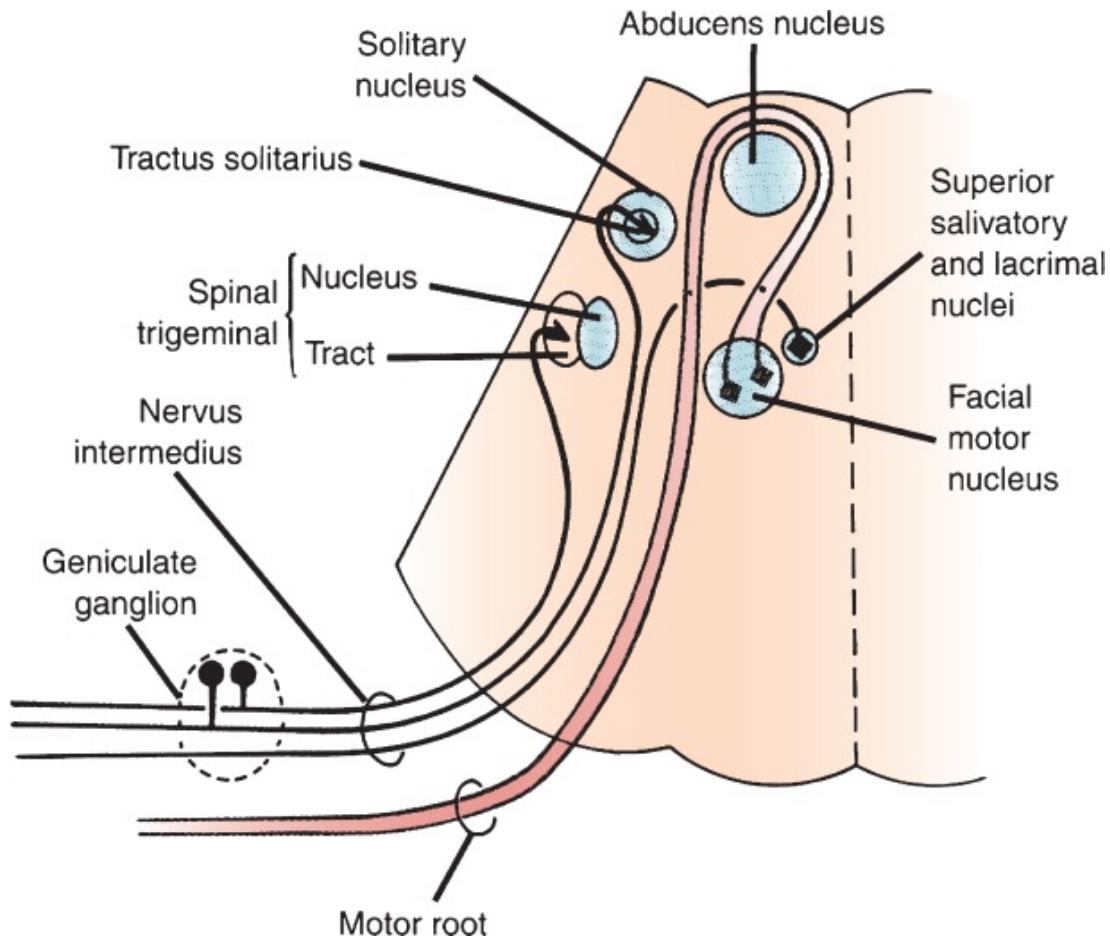


FIGURE 16.1 Components of the facial nerve in the pons. (Modified from Kiernan JA. Barr's *The Human Nervous System: An Anatomical Viewpoint*. 9th ed. Philadelphia: Wolters Kluwer Health/Lippincott, Williams & Wilkins, 2009, with permission.)

There may be anatomical variations in the nerve's course through the petrous bone. It may split into two or three strands at or distal to the geniculate ganglion. The more proximal the division into strands, the more bizarre the subsequent course. Facial motor fibers may run in an enlarged chorda tympani, diminishing the distal facial nerve into a tenuous strand exiting through a narrowed stylomastoid foramen.

Just after exit, the posterior auricular, digastric, and stylohyoid branches arise. The posterior auricular branch supplies the occipitalis, posterior auricular, and transverse and oblique auricular muscles. The digastric and stylohyoid branches supply, respectively, the posterior belly of the digastric and the stylohyoid. The nerve turns forward and passes into the parotid gland. Within the substance of the parotid, it divides into temporofacial and cervicofacial divisions at the pes anserinus (intraparotid plexus) in the cleft between the superficial and deep lobes of the gland ([Figure 16.2](#)). The temporofacial branch crosses the zygoma about 1 cm anterior to the ear, where it is vulnerable to injury.

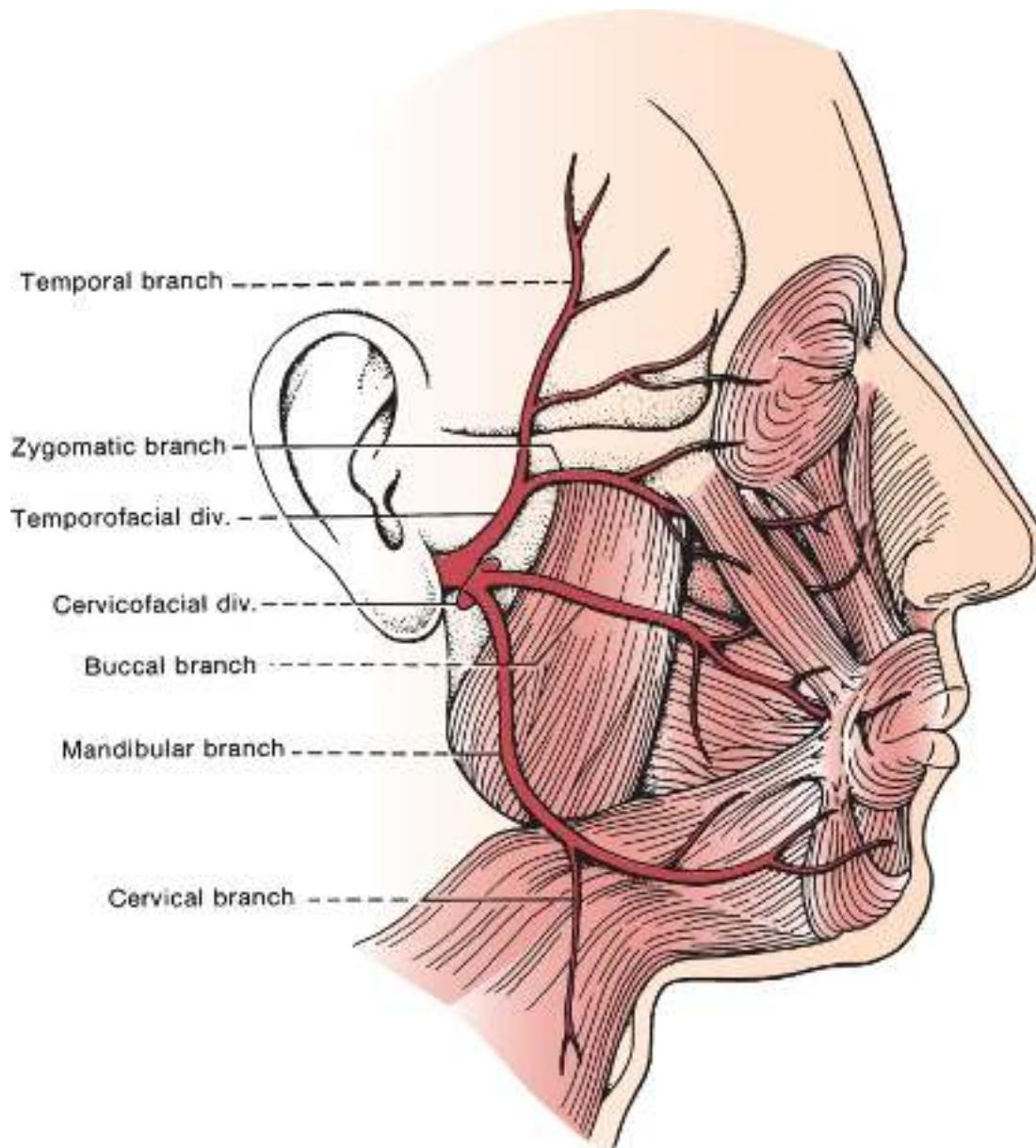


FIGURE 16.2 Branches and distribution of the facial nerve.

The facial nerve supplies all the muscles of facial expression from the scalp and forehead through the platysma, including the extrinsic and intrinsic muscles of the ear. The muscles of facial expression are responsible for all voluntary and involuntary movements of the face except those associated with movement of the jaws and for all play of emotions upon the face. The muscles innervated by the terminal branches are summarized in [Table 16.1](#).

The Nervus Intermedius

The NI is the sensory and autonomic component of the facial nerve. It runs in a position intermediate between CNs VII and VIII across the CPA, moving ever closer to the main facial nerve trunk as it enters the facial canal. At the external first external genu, the NI fuses with the geniculate ganglion. The sensory cells located in the geniculate ganglion are general somatic afferent (GSA) and special visceral afferent (SVA). The GSA fibers carry exteroceptive impulses from the region of the external auditory canal and tympanic membrane. The SVA fibers convey taste from the anterior two-thirds of the tongue. The autonomic component of the NI consists of preganglionic general visceral efferent parasympathetic fibers from the superior salivatory and lacrimal nuclei, which consist of scattered cells in the reticular formation near the caudal end of the motor nucleus. Their axons are bound for the submandibular gland en route to the sublingual and submaxillary glands, the lacrimal glands, and glands in the nasal mucosa.

TABLE 16.1 **Muscles of the Face, Their Actions, and Innervations**

Nerve Branch	Muscle Innervated	Muscle Action
Temporal branch	Frontalis	Raises eyebrows and skin over the root of the nose; draws scalp forward, throwing forehead into transverse wrinkles
	Corrugator (corrugator supercilii)	Draws eyebrow down and medially, produces vertical wrinkles in the forehead (the frowning muscle)
	Upper part of the orbicularis oculi (orbicularis palpebrarum)	Eyelid sphincter; palpebral portion narrows palpebral fissure and gently closes eyelids; orbital portion draws skin of forehead, temple, and cheek toward medial orbit, pulls eyebrow down, draws skin of cheek up; closes eye firmly
	Occipitalis	Draws scalp backward

	Procerus (pyramidalis nasi)	Draws medial eyebrow downward, produces transverse wrinkles over bridge of nose
Zygomatic	Lower and lateral orbicularis oculi	Eyelid sphincter
Buccal	Orbicularis oculi	Eyelid sphincter
	Buccinator	Compresses cheeks, keeps food under pressure of cheeks in chewing
	Zygomaticus	Draws mouth backward and upward
	Nasalis (compressor nares)	Depresses cartilaginous portion of nose, draws the ala toward septum
	Levator anguli oris (caninus)	Raises angle of mouth
	Levator labii superioris (quadratus labii superioris)	Elevates upper lip, dilates nostril
Mandibular	Lower part of the orbicularis oris	Sphincter of the mouth; closes lips; superficial fibers protract lips; deep fibers draw lips in and press them against teeth
	Mentalis	Protrudes lower lip, wrinkles skin of chin
	Risorius	Retracts angle of mouth

	Triangularis (depressor anguli oris)	Depresses angle of mouth
	Depressor labii inferioris (quadratus labii inferioris)	Draws lower lip downward and lateralward
Cervical	Platysma	Pulls lower lip and angle of mouth down; depresses lower jaw; raises and wrinkles skin of neck

Course and Branches of the Facial Nerve

The first branch given off in the facial nerve's course is the greater (superficial) petrosal nerve, which carries preganglionic parasympathetic fibers ([Figure 16.3](#)). These fibers are conveyed by the NI to the geniculate ganglion. They pass through the ganglion without synapsing into the greater petrosal nerve, which goes forward through the hiatus of the facial canal to join the deep petrosal nerve from the carotid sympathetic plexus to form the vidian nerve, or the nerve of the pterygoid canal, which runs to the sphenopalatine ganglion, from where postganglionic fibers proceed to the lacrimal gland.

Distal to the geniculate ganglion, the facial nerve continues to descend. As above, the nerve to the stapedius arises from the distal tympanic or upper mastoid segment and passes forward through a small canal to reach the muscle. Although there is some variability, the chorda tympani usually leaves the main trunk slightly above the stylomastoid foramen; it carries taste and general visceral afferent (GVA) fibers as well as preganglionic parasympathetics. It runs forward and upward in a minute canal in the posterior wall of the tympanic cavity, acquires a mucous membrane investment, and then enters and crosses the middle ear. It is sometimes visible as a small white cord behind the tympanic membrane on otoscopic examination. The chorda tympani runs downward and forward to exit the skull and join the lingual nerve, a branch of the mandibular division of CN V, on its posterior border.

Fibers carrying somatosensory afferents in the chorda tympani have their cell

bodies in the geniculate ganglion. The peripheral processes innervate part of the external auditory canal, the tympanic membrane, lateral surface of the pinna, and a small area behind the ear and over the mastoid process. There is a marked individual variation in this distribution. Their central processes terminate in the spinal tract and nucleus of the trigeminal, and the central connections are identical with those of the trigeminal nerve. CN VII may also subserve deep pain and deep pressure from the face.

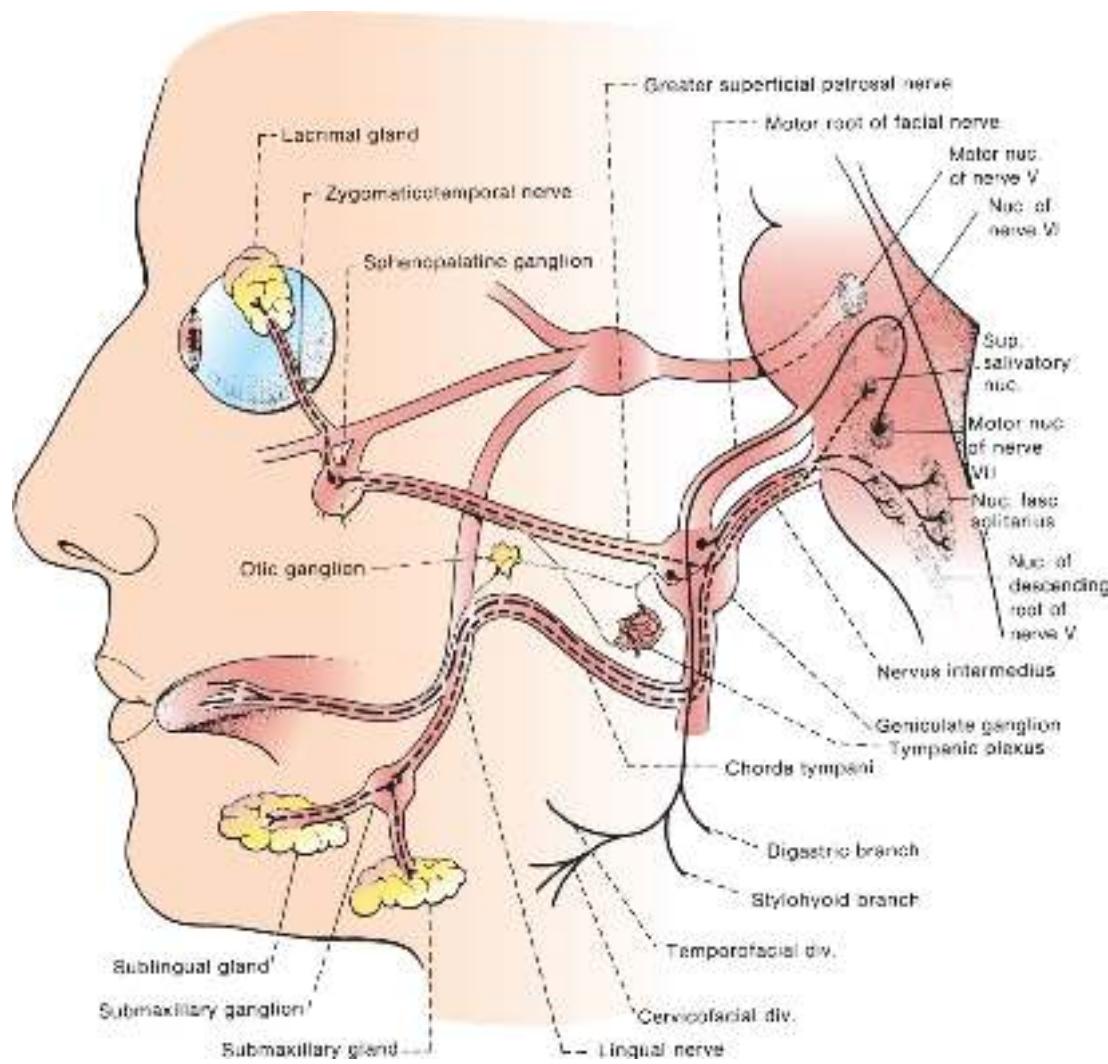


FIGURE 16.3 Course and branches of the facial nerve.

Taste sensation from the anterior two-thirds of the tongue is carried through the lingual nerve to the chorda tympani, then to the geniculate ganglion. CN VII may also carry taste sensation from the mucosa of the soft palate through the sphenopalatine ganglion. Central processes carrying taste and GVA sensation

terminate in the nucleus of the solitary tract. The solitary tract sends communications to the superior and inferior salivatory nuclei, which send parasympathetics to the salivary glands. Other fibers synapse in the reticular formation; next order neurons form a component of the reticulospinal tract bilaterally to synapse with sympathetic neurons in the intermediolateral gray column of the upper thoracic spinal cord. These send sympathetic innervation via the superior cervical ganglion to the salivary glands. Fibers subserving taste sensation ascend with the contralateral medial lemniscus to the thalamus. The primary gustatory cortex, located in the anterior insula and the frontal operculum, mediates the perception of taste. Taste fibers also communicate with the hypothalamus and the olfactory system.

The chorda tympani also carries preganglionic parasympathetic fibers to the submandibular ganglion. Postganglionic fibers convey secretory and vasodilator impulses to the submandibular and sublingual salivary glands and mucous membranes of the mouth and tongue ([Figure 16.3](#)). These glands also receive sympathetic innervation through the superior cervical ganglion and the carotid plexus. The parasympathetic fibers cause vasodilation and a copious, thin, watery secretion high in enzymes; the sympathetic fibers cause vasoconstriction and a scant, thick, mucoid secretion low in enzyme content.

CLINICAL EXAMINATION

Examination of the Motor Functions

Examination of facial nerve motor functions centers on assessment of the actions of the muscles of facial expression. A great deal can be learned from simple inspection. At rest the face is generally symmetric, at least in young individuals. With aging, the development of character lines may cause asymmetry that does not indicate disease. Distinguishing minor, clinically insignificant, facial asymmetry from subtle facial weakness is sometimes challenging. Note the tone of the muscles of facial expression, and look for atrophy and fasciculations. Note the resting position of the face and whether there are any abnormal muscle contractions. Note the pattern of spontaneous blinking for frequency and symmetry. A patient with parkinsonism may have infrequent blinking and an immobile, expressionless, “masked” face. Facial dystonia causes an abnormal fixed contraction of a part of the face, often imparting a curious facial

expression. The procerus sign is seen most characteristically in progressive supranuclear palsy (PSP) and corticobasal degeneration. There is contraction of the forehead muscles, particularly the procerus and corrugator, with knitting of the brows, raised eyebrows, lid retraction, widening of the palpebral fissures, and reduced blinking. The expression is one of surprise, astonishment, perplexity, or consternation ([Figure 16.4](#)). Synkinesis causes abnormal contractions of the face, often subtle, synchronous with blinking or mouth movements. Synkinesis suggests remote facial nerve palsy with aberrant regeneration ([Video 16.1](#)). Spontaneous contraction of the face may be due to hemifacial spasm (HFS) (see below). Other types of abnormal involuntary movements that may affect the facial muscles include tremors, tics, myoclonic jerks, chorea, and athetosis (see below).



Video 16.1 Facial synkinesis following Bell's palsy and after attempted surgical reanimation.



FIGURE 16.4 Procerus sign in a patient with progressive supranuclear palsy.

Observe the nasolabial folds for depth and symmetry and note whether there is any asymmetry in forehead wrinkling or in the width of the palpebral fissures with the face at rest. A flattened nasolabial fold with symmetric forehead wrinkles suggests a central (upper motor neuron) facial palsy; a flattened nasolabial fold with smoothing of the forehead wrinkles on the same side suggests a peripheral (lower motor neuron) facial nerve palsy. Eyelid position and the width of the palpebral fissures often provide subtle but important clinical clues. Eyelid position is discussed further in [Chapter 14](#). A unilaterally widened palpebral fissure suggests a facial nerve lesion causing loss of tone in the

orbicularis oculi muscle, the eye closing sphincter; this is sometimes confused with ptosis of the opposite eye. It is a common misconception that facial nerve palsy causes ptosis.

Some diseases cause a characteristic abnormality of facial expression that can sometimes be recognized at a glance, either because of facial immobility or some peculiar facial expression. Examples of primarily neurologic conditions include parkinsonism and related extrapyramidal disorders (masked facies), PSP (facial dystonia, procerus sign), Möbius' syndrome, myotonic dystrophy (hatchet face, myopathic face, [Figure 16.5](#)), facioscapulohumeral muscular dystrophy (myopathic face, transverse smile), general paresis (facies paralytica), myasthenia gravis (myasthenic snarl, see below), facial nerve palsy (unilateral or bilateral), and Wilson's disease (risus sardonicus, [Chapter 30](#)). There are of course numerous congenital syndromes that cause distinctively dysmorphic facies.

Observe the movements during spontaneous facial expression as the patient talks, smiles, or frowns. Certain upper motor neuron facial palsies are more apparent during spontaneous smiling than when the patient is asked to smile or show the teeth. In infants, facial movements are observed during crying. Have the patient grin, vigorously drawing back the angles of the mouth and baring the teeth. Note the symmetry of the expression, how many teeth are seen on each side and the relative amplitude and velocity of the lower facial contraction. Have the patient close her eyes tightly and note the symmetry of the upper facial contraction. How completely the patient buries the eyelashes on the two sides is a sensitive indicator of orbicularis oculi strength.

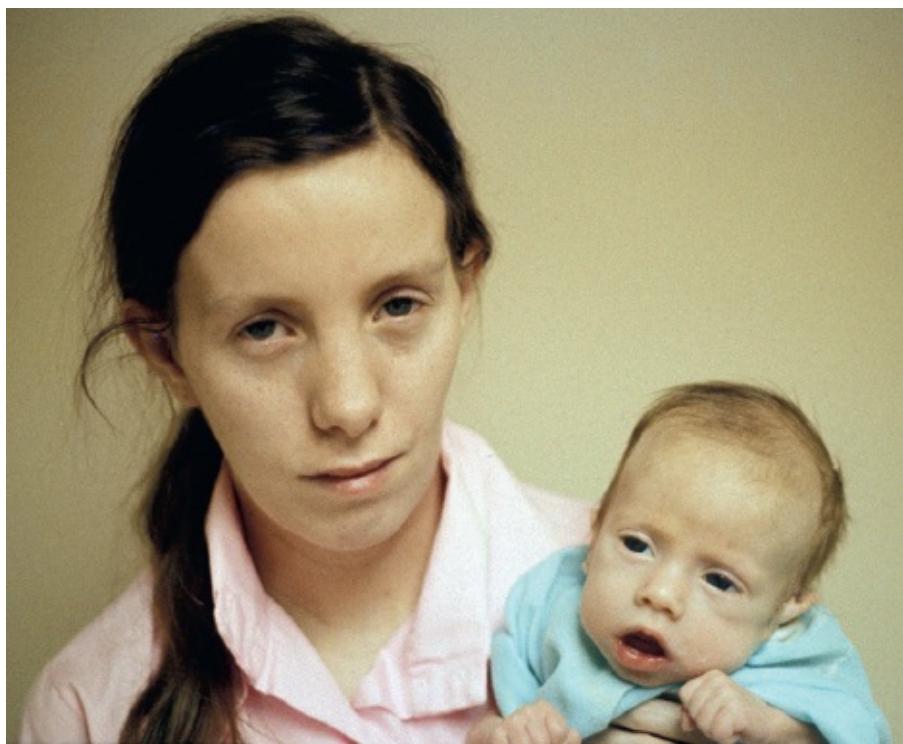


FIGURE 16.5 Myopathic facies in a newly diagnosed young mother with myotonic dystrophy, holding her hypotonic infant, who has the congenital form. The mother has bilateral ptosis, hollowed temporalis, and a slack lower face. The infant has ptosis and the classic “tentèd upper lip.” (Reprinted from Campbell WW. *Clinical Signs in Neurology: A Compendium*. Philadelphia: Wolters Kluwer, 2016, with permission.)

Other useful movements include having the patient raise the eyebrows, singly or in unison, and noting the excursion of the brow and the degree of forehead wrinkling; close each eye in turn; corrugate the brow; puff out the cheeks; frown; pucker; whistle; alternately smile and pucker; contract the chin muscles; and pull the corners of the mouth down in an exaggerated frown to activate the platysma. There is no good command for platysma contraction, and the movement must be demonstrated. The platysma can also be activated by having the patient open the mouth against resistance or clinch the teeth. The patient may smile spontaneously after attempting to whistle, or the examiner may make an amusing comment to assess emotional facial movement. Because of their paucity of facial expression, patients with Parkinson’s disease may fail to smile after being asked to whistle: the whistle-smile (Hanes) sign.

Trying to gently push down the uplifted eyebrow may detect mild weakness. It is difficult to pry open the tightly shut orbicularis oculi in the absence of weakness. Vigorously pulling with the thumbs may sometimes crack open a normal eye. If the examiner can force the eye open with her small fingers, then

the orbicularis oculi is definitely weak. Likewise, it is difficult to force open the tightly pursed lips in a normal individual. When the orbicularis oris sphincter is impaired, the examiner may be able to force air out of the puffed cheek through the weakened lips. Testing ear and scalp movements is seldom useful, although loss of the ability to wiggle the ear in someone previously able to do so has been cited as a sensitive sign of peripheral facial palsy (PFP). The stylohyoid muscle and posterior belly of the digastric cannot be adequately tested. With stapedius weakness, the patient may complain of hyperacusis, especially for low tones. Other tests of motor function and confirmatory signs of facial paresis are discussed in the following sections. It is important in patients with PFP to examine the ear for vesicles or rash, indicative of zoster infection, and to palpate the parotid to exclude a mass lesion.

Examination of the Reflexes

The corneal and other reflexes mediated largely by CN V are discussed in [Chapter 15](#). Frontal release signs such as the snout, suck, and palmomental reflexes are discussed in [Chapter 40](#). Various other reflexes mediated in large part by CN VII can be obtained but are of little practical value. Some merit brief discussion. They are summarized in [Table 16.2](#).

TABLE 16.2	Facial Reflexes
Reflex	Technique
Orbicularis oculi—focal	Best elicited by pulling back, between the thumb and index finger, a fold of skin on the temple lateral to the outer canthus, then briskly tapping the thumb or finger. Sudden stretch of the muscle causes contraction of orbicularis oculi with closing of the eye.
Orbicularis oculi—nonfocal (supraorbital, trigeminofacial, McCarthy's, or	Tapping over outer aspect of supraorbital ridge, over glabella, or around orbital margin; can sometimes be elicited by tapping the forehead as far back as the hairline. Causes bilateral eye blinking. Response can normally

(nasopalpebral reflex, glabellar tap, Myerson's sign—depending on the site of stimulus)	be inhibited; in patients with Parkinson's disease and other conditions, the patient cannot suppress the blinking.
Auditory-palpebral, auro- or acousticopalpebral, cochleopalpebral, or cochleo-orbicularis reflex	Reflex contraction of the orbicularis oculi causing eye closure, usually bilateral but more marked on the ipsilateral side, in response to a sudden loud noise.
Visuopalpebral, visual orbicularis, optocofacial, blink, or menace reflex	Reflex eye closure in response to a strong light or a sudden visual stimulus.
Palpebro-oculogyric reflex (Bell's phenomenon)	Tight eye closure causes eyeballs to turn upward, a normal response but obvious only when eye closure is weak and the rolling of the eyes is seen through the incompletely closed lids. A method for testing reflex upgaze in patients with upgaze deficits.
Chvostek's sign	A spasm or tetanic, cramp-like contraction, of the ipsilateral facial muscles on tapping over the pes anserinus anterior to the ear; various degrees of response may occur. A sign of tetany, but also occurs with hyperreflexia because of upper motor neuron dysfunction. Likely a motor example of Tinel's sign.

Wartenberg wrote at length about the orbicularis oculi reflex, which he considered an important reflex, and the “chaos of nomenclature concerned with this reflex.” A reflex contraction of the orbicularis oculi causing an eye blink—the nonfocal orbicularis oculi reflex—can be elicited in different ways ([Video 38.2](#)). The threshold for reflex contraction is very low, and the reaction is very

quick. Tapping with a finger or percussing with a reflex hammer at many different sites over the forehead and about the eyes may elicit a reflex eye blink. Wartenberg said the muscle “reacts... easily to...a multitude of external stimuli.” Different names were given to methods of eliciting the reflex by stimulating different areas, all essentially the same response. The most frequently used version currently is the glabellar tap. Patients with Parkinson’s disease are unable to inhibit the reflexive eye blinks (Myerson’s sign; not to be confused with Myerson’s reflex). Despite the widespread use of the eponym, it is in fact difficult to find any clear reference linking Myerson to the glabellar tap reflex.

A more specific orbicularis oculi reflex is the focal “deep muscle” response elicited from one side by a percussion that stretches the muscle ([Video 38.2](#)). A fold of the muscle at the temple is held between the thumb and forefinger and then percussed to stretch it back toward the ear. Wartenberg thought this reflex useful because it may be decreased in PFP in proportion to the severity of the palsy, but it is normal or increased with facial weakness of central origin.

Examination of the Sensory Functions

Testing of CN VII sensory functions is limited to taste. Although Hitselberg described hypesthesia of the posterior wall of the external auditory meatus in proximal facial nerve lesions, there is no reliable way to assess the small sensory contribution the nerve makes to the skin of the external ear region. The peripheral receptors are the taste buds embedded in the tongue epithelium and to a lesser extent in the soft palate and epiglottis. Taste buds respond preferentially, but not solely, to one taste quality. Taste is also carried through CN IX and probably CN X.

There are five primary tastes: bitter, sour, sweet, salty, and umami (delicious or savory). Umami has only recently been added to the list. It is a response to compounds of some amino acids, particularly l-glutamate. Umami is a Japanese term that has no English translation. The many flavors encountered in life are a combination of the primary tastes plus olfaction and oral sensory information (“mouth feel”). Sweet and salty substances are most commonly employed for clinical bedside testing because of their ready availability; sour and bitter are more difficult to come by. Chemosensory referral centers typically use four substances for testing: sucrose (sweet), sodium chloride (salty), quinine (bitter), and citric acid (sour). CN VII only subserves taste on the anterior two-thirds of the tongue. When the tongue is retracted into the mouth, there is rapid dispersion

of the test substance outside the area of interest. The tongue must therefore remain protruded throughout testing of an individual substance, and the mouth must be rinsed between tests. If bitter is tested, it should be last because it leaves the most aftertaste.

Some examiners prefer to manually hold the patient's tongue with a piece of gauze to prevent retraction. Because the patient will be unable to speak with the tongue protruded, instructions must be clear in advance. The patient may raise the hand using some signaling system when taste is perceived, point to words written on paper, or make a similar nonverbal response. A damp applicator stick may be dipped into a packet of sugar, artificial sweetener, or salt and coated with the test substance and then placed on one side of the patient's tongue and rubbed around. The patient signals whether she can identify the substance. Most patients will identify the test substance in less than 10 seconds. Taste sensation is less on the tip of the tongue, and the substance is best applied to the dorsal surface at about the junction of the anterior and middle third of the tongue. The sweetness of artificial sweeteners such as saccharine and aspartame is more intense, and they may make better test substances than ordinary sugar. For a demonstration of taste testing technique, see [Video Link 16.1](#). More sophisticated methods are available to test for subtle dysfunction in patients who have primary taste and smell complaints. There are many referral centers that specialize in the management of taste and smell disorders (see [Chapter 12](#)). There are now commercially available filter paper strips impregnated with sweet, sour, salty, and bitter in different concentrations (taste strips). It is seldom necessary or practical to examine taste on the posterior third of the tongue.

The most common situation calling for assessment of taste is the evaluation of facial nerve palsy. If a patient with a peripheral pattern of facial weakness has impaired taste, the lesion is proximal to the junction with the chorda tympani. A lesion at or distal to the stylomastoid foramen (e.g., in the parotid gland) does not affect taste.

Ageusia is the complete inability to taste. With hypogeusia, taste perception is blunted or delayed. Perversions or abnormal perceptions of taste are parageusias. There is marked individual variation in taste. Complete ageusia is rare unless there is also loss of smell. If there is loss of taste, one should first eliminate the possibility of disease of the tongue. Some causes of disturbed taste are listed in [Table 16.3](#). There are many medications that reportedly alter taste; some commonly used in neurologic practice include the following: carbamazepine, phenytoin, tricyclic antidepressants, dexamethasone, hydrocortisone,

penicillamine, lithium, methotrexate, levodopa or levodopa/carbidopa, clozapine, trifluoperazine, baclofen, and dantrolene.

Examination of the Secretory Functions

The secretory functions of CN VII can usually be evaluated by history and observation. Increased tearing is usually apparent; decreased tearing may be determined from the history. Tear production may be quantitated with the Schirmer test. Commercially available filter strips are placed in the inferior conjunctival sac and left in place for 5 minutes. The advancing edge of moisture down the strip is proportional to the moisture in the eye; the results are expressed in millimeters. This test is simple and does not require referral to an ophthalmologist.

TABLE 16.3

Possible Causes of Disturbed Taste

- Oral and perioral infections (e.g., candidiasis, gingivitis, periodontitis)
- Bell's palsy
- Medications
- Dental procedures
- Dentures and other dental devices
- Age
- Nutritional compromise (e.g., vitamin B₁₂ deficiency, zinc deficiency, malnutrition, chronic disease)
- Lesions involving neural taste pathways
- Head trauma
- Toxic chemical exposure
- Radiation treatment of head and neck
- Psychiatric conditions (e.g., depression, anorexia nervosa, bulimia)
- Epilepsy (gustatory aura)
- Migraine headache (gustatory aura)
- Sjögren's syndrome
- Multiple sclerosis
- Endocrine disorders (e.g., diabetes mellitus, hypothyroidism)

Modified from Bromley SM. Smell and taste disorders: a primary care approach. *Am Fam Physician* 2000;61:427–436, 438.

The lacrimal reflex is tearing, usually bilateral, caused by stimulating the cornea. The nasolacrimal reflex is elicited by mechanical stimulation of the nasal mucosa or by chemical stimulation using irritating substances such as ammonia. Abnormalities of salivation are usually suggested by the history. Otolaryngologists and oral surgeons can use special techniques to quantitate salivary flow.

DISORDERS OF FUNCTION

Motor abnormalities, either weakness or abnormal movements, account for the preponderance of clinical abnormalities of facial nerve function. Changes in sensation, primarily taste, and in secretory function, sometimes occur as a sidebar, but are rarely if ever the major manifestation of disease of CN VII. Changes in these functions can help to localize the lesion along the course of the nerve, although this exercise has little practical value. The major branches in sequence are the greater superficial petrosal, nerve to the stapedius, and chorda tympani, after which the nerve continues to the facial muscles. The mnemonic tear-hear-taste-face may help recall the sequence.

Facial Weakness

There are two types of neurogenic facial nerve weakness: peripheral, or lower motor neuron; and central, or upper motor neuron. PFP may result from a lesion anywhere from the CN VII nucleus in the pons to the terminal branches in the face. Central facial palsy (CFP) is due to a lesion involving the supranuclear pathways before they synapse on the facial nucleus. PFP results from an ipsilateral lesion, whereas CFP, with rare exception, results from a contralateral lesion.

Peripheral Facial Palsy

With PFP, there is flaccid weakness of all the muscles of facial expression on the involved side, both upper and lower face, and the paralysis is usually complete (prosopoplegia). The affected side of the face is smooth; there are no wrinkles on

the forehead; the eye is open; the inferior lid sags; the nasolabial fold is flattened; and the angle of the mouth droops ([Figure 16.6](#)). The patient cannot raise the eyebrow, wrinkle the forehead, frown, close the eye, laugh, smile, bare the teeth, blow out the cheeks, whistle, pucker, retract the angle of the mouth, or contract the chin muscles or platysma on the involved side. She talks and smiles with one side of the mouth, and the mouth is drawn to the sound side on attempted movement. The cheek is flaccid and food accumulates between the teeth and the paralyzed cheek; the patient may bite the cheek or lip when chewing. Food, liquids, and saliva may spill from the corner of the mouth. The cheek may puff out on expiration because of buccinator weakness. The facial asymmetry may cause an apparent deviation of the tongue (see [Chapter 20](#) and [Figure 15.7](#)). A patient with an incomplete PFP may be able to close the eye, but not with full power against resistance. Inability to wink with the involved eye is common. The palpebral fissure is open wider than normal, and there may be inability to close the eye (lagophthalmos). During spontaneous blinking, the involved eyelid tends to lag behind, sometimes conspicuously. Very mild PFP may produce only a slower and less complete blink on the involved side. Attempting to close the involved eye causes a reflex upturning of the eyeball (Bell's phenomenon). The iris may completely disappear upwardly. This is a normal response, but only visible in the patient with orbicularis oculi weakness. To elicit the levator sign of Dutemps and Céstan, have the patient look down, then close the eyes slowly; because the function of the levator palpebrae superioris is no longer counteracted by the orbicularis oculi, the upper lid on the paralyzed side moves upward slightly. Akin to Bell's phenomenon is Negro's sign, where the eyeball on the paralyzed side deviates outward and elevates more than the normal one when the patient raises her eyes (not to be confused with the other Negro's sign, cogwheel rigidity).

A sensitive sign of upper facial weakness is loss of the fine vibrations palpable with the thumbs or fingertips resting lightly on the lids as the patient tries to close the eyes as tightly as possible (Bergara-Wartenberg sign). The platysma sign of Babinski is an asymmetric contraction of the platysma, less on the involved side, when the mouth is opened ([Figure 16.7](#)). Labials and vowels are produced by pursing the lips; patients with peripheral facial weakness have a great deal of difficulty in articulating these sounds. Articulation of labial sounds is discussed further in [Chapter 9](#). The House-Brackmann scale, Burres-Fisch index, and facial nerve function index may be useful to try to quantitate the degree of weakness.



FIGURE 16.6 A patient with a peripheral facial nerve palsy on the right. **A.** The patient is attempting to retract both angles of the mouth. **B.** The patient is attempting to elevate both eyebrows.

Because of weakness of the lower lid sphincter, tears may run over and down the cheek (epiphora), especially if there is corneal irritation because of inadequate eye protection. A lack of tearing may signal very proximal involvement, above the origin of the greater superficial petrosal nerve. With severe weakness, the eye never closes, even in sleep. The involvement of the intrinsic and extrinsic ear muscles, stylohyoid and posterior belly of the digastric cannot be demonstrated by clinical examination. Electromyographic needle examination can sample some of these muscles, particularly the posterior auricular and posterior belly of the digastric. Denervation in these muscles indicates a very proximal lesion and may be of help in some cases, particularly in distinguishing Möbius' syndrome from birth-related facial nerve trauma. Weakness of the stapedius may produce hyperacusis, especially for low tones that sound louder and higher.

The facial weakness in PFP is obvious on both voluntary and spontaneous contraction. There is no dissociation. With a severe lesion, the passage of time may lead to atrophy of the involved muscles. With PFP, the motor limb of the direct corneal reflex is impaired, but the consensual is intact; in the opposite eye,

the direct response is intact and the consensual impaired (Table 15.3); in other words, the involved eye does not blink no matter which side is stimulated, and the normal eye does blink no matter which side is stimulated. The various reflexes that involve motor responses of CN VII supplied muscles are impaired. Some patients with PFP complain of numbness of the face. Sometimes, they are describing the wooden feeling that accompanies immobility, but at other times, patients seem to have slight sensory loss that is real and more than logically expected for a lesion of a predominantly motor nerve. The cause of this is unclear.



FIGURE 16.7 On the patient's right side, there is a clear difference between the appearance of the platysma muscle at rest (view at *upper left* in composite photograph) and during voluntary effort to retract both corners of the mouth (view at *lower left*). On the patient's left side, there is only minimal contraction (views at *upper and lower right*). In the frontal view, the fully contracting right platysma (*arrow*) can be directly compared with the paretic muscle on the left (*question mark*). Note also the incomplete retraction of the left corner of the mouth. (Reprinted from Leon-Sarmiento FE, Prada LJ, Torres-Hillera M. The first sign of Babinski. *Neurology* 2002;59[7]:1067, with permission.)

In comatose or otherwise uncooperative patients, facial movements can be elicited by painful pressure over the supraorbital nerves or by other painful stimuli applied to the face to elicit an avoidance response. Pinprick marks on a comatose patient's face are best avoided. The jab of a broken applicator stick is usually sufficient and causes less tissue damage. The groove between the nostrils and the cheek is particularly sensitive for these purposes.

Minimal facial weakness on one side must be differentiated from a facial contracture on the opposite side, which can cause the normal nasolabial fold to appear flattened in comparison. Bona fide facial weakness must also be differentiated from developmental asymmetry, facial hemiatrophy, character lines, and habitual emphasis on the use of one side of the mouth (“Brooklyn facial”). Unequal palpebral fissures from ptosis on one side may be confused with facial weakness on the opposite side causing widening of the fissure; the usual error is the reverse.

Localization of Peripheral Facial Nerve Palsy

PFP can occur from a lesion involving the facial nerve nucleus in the pons or at any point along the infranuclear segment. The weakness of the muscles of facial expression is the same with lesions anywhere along the course of the nerve. Diagnostic localization depends on the associated findings, such as hyperacusis, decreased tearing, impaired taste, and involvement of neural structures beyond CN VII. [Table 16.4](#) summarizes the localization and differential diagnosis of PFP. The most common cause of PFP by far is Bell’s palsy.

Bell’s Palsy

Most cases of idiopathic facial paralysis (Bell’s palsy, for Sir Charles Bell [[Box 16.1](#)]) are likely due to Herpes simplex virus activation, but there is no simple method of confirming this mechanism in clinical practice. Polymerase chain reaction (PCR) testing suggests viral reactivation leading to inflammation and demyelination. Herpes zoster, Ramsay Hunt syndrome (see below), is probably the second most common viral infection associated with PFP. Other viruses implicated include cytomegalovirus, Epstein-Barr virus, human herpes virus 6, and coxsackie. Unfortunately, antiviral treatment has not proved particularly efficacious. An inactivated intranasal influenza vaccine was associated with an increased incidence of Bell’s palsy and subsequently withdrawn from the market. Pathologically, abnormalities are present throughout the bony course of the nerve, but nerve damage is concentrated in the narrow labyrinthine part of the facial canal, probably because of compression related to edema and the tenuous blood supply in that segment. Ischemia has long been thought to play a role in the development of Bell’s palsy. There may be a genetic predisposition in some cases. Bell’s palsy is more prevalent in women who are pregnant or have

recently given birth. The risk is three times greater during pregnancy, especially in the third trimester or in the first postpartum week.

TABLE 16.4 Differential Diagnosis of Lesions of the Facial Nerve

Location of Lesion	Possible Associated Findings	Likely Etiologies	Useful Diagnostic Tests
Nuclear	No localizing associated findings, +/- fasciculations, +/- other evidence of motor neuron disease, dysfunction frequently bilateral	Motor neuron disease, Möbius' syndrome, neoplasm	Needle electromyography
Intrapontine fibers	Normal taste sensation, +/- hyperacusis, +/- decreases lacrimation, facial fasciculations, facial myokymia, ipsilateral CN VI or lateral gaze palsy, ipsilateral weakness of the muscles of mastication, contralateral hemiparesis of arm and leg	Infarction, hemorrhage, neoplasm, syringobulbia, abscess, central pontine myelinolysis, tuberculoma, granuloma, trauma, multiple sclerosis; other demyelinating disorders	MRI, auditory evoked potentials, EMG blink reflex, facial muscle needle electromyography
Cerebellopontine angle or cisternal course, just peripheral to the pons or between the pons and the facial canal	Tinnitus, deafness, and vertigo (CN VIII involvement), facial pain or sensory dysfunction (CN V involvement), loss of taste on the anterior two-thirds of the tongue, decreased salivary and lacrimal secretion (nervus intermedius involvement), hyperacusis (lesion proximal to stapedius branch), ipsilateral ataxia and nystagmus (involvement of the cerebellum or cerebellar connections)	Neoplasm (especially acoustic neuroma), cholesteatoma, head trauma, meningeal inflammation or infiltration	MRI with IAC views, posterior fossa CT myelogram, auditory evoked potentials, EMG blink reflex, facial muscle needle electromyography, CSF examination
Facial canal at the geniculate ganglion	Hyperacusis, loss of taste, decreased tearing, pain in the region of the ear and mastoid, vesicular eruption with Ramsay Hunt syndrome, Battle's sign or raccoon eyes with basilar skull fracture	Bell's palsy, geniculate herpes (Ramsay Hunt syndrome), Guillain-Barré syndrome, petrous bone fracture, neoplasm, diabetes mellitus, sarcoidosis, Lyme disease, HIV infection	MRI (gadolinium may show facial nerve enhancement), EMG blink reflex, needle electromyography, audiogram, acoustic reflex study, CSF examination
Facial canal distal to geniculate ganglion but proximal to origin of nerve to stapedius	Hyperacusis, loss of taste, decreased salivation, normal tearing	Same as previous	Tests same as previous
Facial canal between origin of nerve to stapedius and origin of chorda tympani. Facial canal distal to origin of chorda tympani	No accompanying changes, isolated weakness limited to muscles of facial expression with normal taste, hearing, and tearing.	Same as previous	Same as previous
After emergence from stylo-mastoid foramen	No accompanying findings, involvement may be partial because of selective involvement of a certain division or certain branches of the parotid plexus (pes anserinus) with weakness of some but not all of the muscles of facial expression	Parotid tumor or abscess, trauma	Facial nerve conduction studies, needle electromyography, imaging of parotid

CSF, cerebrospinal fluid; CT, computed tomography; EMG, electromyography; IAC, internal auditory canal; MRI, magnetic resonance imaging.

BOX 16.1

Sir Charles Bell

Bell's palsy is named for Sir Charles Bell, a Scottish surgeon, anatomist, and artist. Early in his career, he published a book on anatomy of facial expression for artists. Among his many contributions (Moritz Romberg proclaimed Bell to be the "Harvey of our century") was a description of the nerve supply to the muscles of the face. He described facial palsy of various etiologies, including one patient who was gored in the face by an ox. He provided the illustrations for his own dissections. It is fitting that the Mona Lisa syndrome refers to the facial synkinesis that sometimes follows Bell's palsy, hypothesized to be the basis for the enigmatic Gioconda half smile in da Vinci's painting.

Certain criteria should be fulfilled to confirm a diagnosis of Bell's palsy. There should be diffuse PFP, onset over a day or 2, paralysis reaching a maximum within 3 weeks, and full or partial recovery within 6 months. A prolonged, progressive course suggests a tumor, as does distal involvement of only some branches or the presence of a parotid mass. Involvement of individual distal branches can also occur from trauma, as by obstetrical forceps.

Symptoms often begin with pain behind the ear, followed within a day or 2 by facial weakness. The pain may rarely precede the paralysis by up to 2 weeks. There is peripheral facial weakness involving both upper and lower face. The paralysis is complete in approximately 70% of patients. Some authorities contend there are often subtle or subclinical abnormalities of other CNs. About 25% of patients report some degree of facial numbness that is often dismissed as an odd sensation related to the immobility. Depending on the relationship of the lesion to the geniculate ganglion, to the takeoff of the chorda tympani, and to the takeoff of the branch to the stapedius, patients may note loss of taste sensation on the ipsilateral anterior two-thirds of the tongue, dryness of the eye, or hyperacusis for low tones. The most common symptoms accompanying Bell's palsy are increased tearing, pain in or around the ear, and taste abnormalities. Trying to localize the lesion by testing taste and lacrimation are not very accurate and of little practical value. In patients studied at surgery, only 6% of lesions were distal to the geniculate ganglion.

Dysgeusia occurs in about 60% of patients, ageusia in about 10%. There may be drooling and difficulty speaking because of the slack facial muscles. Patients

are often unable to close the eye, liquids and saliva may drool from the affected corner of the mouth, and tears may spill down the cheek. The majority of patients with Bell's palsy, Lyme disease, and geniculate herpes will show enhancement of the facial nerve on gadolinium magnetic resonance imaging (MRI). Some enhancement may be seen in normals, but enhancement of the distal intrameatal and labyrinthine segments appears specific for facial nerve palsy.

Age-adjusted incidence rates are higher in the elderly. About 1% of cases are bilateral. About 80% of patients recover fully within 6 months; some have persistent synkinesis because of aberrant regeneration, and the rare patient is left with complete permanent paralysis. The prognosis is age related: best in children, worst in patients over 55. The condition may recur in 6% to 7% of patients. Those without enhancement may have a better prognosis.

Aberrant regeneration is common after Bell's palsy and after traumatic nerve injury. Axons destined for one muscle regrow to innervate another, so that there is abnormal twitching of the face outside the area of intended movement. On blinking or winking, the corner of the mouth may twitch. On smiling, the eye may close ([Video 16.1](#)). These synkinesis can be prominent in some patients; more often, they are subtle, such as a slight twitch of the orbicularis oris synchronous with blinking of the eye. When misdirection is conspicuous, the main effect of smiling on the involved side of the face may be eye closure. The automatic closure of one eye on opening the mouth, the Marin Amat sign, or inverted or reversed Gunn phenomenon (inverse jaw winking), has been explained as a trigeminofacial associated movement. However, it occurs primarily in patients who have had a peripheral facial paralysis and is probably an intrafacial synkinesis.

Aberrant regeneration may also involve autonomic and taste fibers. The syndrome of crocodile tears is a gustatory-lacrimal reflex, characterized by tearing when eating, especially highly flavored foods. It is due to misdirection of salivary axons to the lacrimal gland. Frey auriculotemporal syndrome is similar, but with sweating and flushing over the cheek rather than lacrimation ([Chapter 15](#)). In the chorda tympani syndrome, there is unilateral swelling and flushing of the submental region after eating.

Other Causes of Peripheral Facial Weakness

There are numerous other causes of PFP. Common processes involving the

motor neurons of the CN VII nucleus in the pons include motor neuron disease and Möbius' syndrome. Clinical involvement of facial muscles is more likely in progressive bulbar palsy than in classical sporadic amyotrophic lateral sclerosis (ALS); needle electromyography may show subclinical changes. In spinobulbar muscular atrophy (Kennedy's syndrome), facial fasciculations and facial weakness are often prominent. Facial nerve paralysis, unilateral or bilateral, may be congenital. Möbius' syndrome (congenital oculofacial paralysis) is the association of congenital facial nerve palsy with paralysis of the extraocular muscles, especially the lateral rectus because of hypoplasia or aplasia of the CN nuclei ([Figure 16.8](#)). For a courageous and dramatic video of Möbius' syndrome by an affected patient, see [Video Link 16.2](#). Other CN-innervated muscles may be involved, and there may be other developmental defects. The condition is sporadic. Reportedly, involvement of facial nerve motoneurons can be the only manifestation of an acute attack of paralytic poliomyelitis. PFP has been reported in hereditary neuropathy with liability to pressure palsies.

Lesions involving the facial nerve fibers in the pons may cause PFP. There are usually, but not always, associated findings to indicate the lesion is intramedullary. Fascicular lesions may or may not involve tearing and taste. Many disorders may affect the intrapontine fibers of CN VII ([Table 16.4](#)). Ischemic lesions are common. Millard-Gubler syndrome is ipsilateral PFP and contralateral hemiparesis, which may be due to pontine stroke, hemorrhage, or tumor. A CN VI palsy is often but incorrectly included as part of Millard-Gubler syndrome ([Chapter 21, Box 21.1](#)). Foville syndrome is ipsilateral PFP and horizontal gaze palsy with contralateral hemiparesis ([Chapter 21, Box 21.1](#)). The “eight and a half syndrome” is a one-and-half syndrome ([Chapter 14](#)) in association with a facial palsy due to a pontine lesion. Combined PFP and abducens palsy in isolation, without a hemiparesis, has been reported with an infarction of the caudal pontine tegmentum. A PFP has also been reported in Wallenberg's syndrome because of extension of the infarct into the caudal pons.



FIGURE 16.8 Child with Moebius syndrome with typical masklike facies and downslanted oral commissures. (Reprinted from Thorne C, Chung KC, Gosain A, et al., eds. *Grabb and Smith's Plastic Surgery*. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins, 2014, with permission.)

Other processes that may affect CN VII fibers in the pons include abscess, syringobulbia, demyelinating disease, and trauma. Because of the proximity of the nucleus and fibers of CN VII to the nucleus and fibers of CN VI, pontine lesions frequently cause both an ipsilateral facial paralysis and an ipsilateral lateral rectus paralysis. Pontine lesions are discussed further in the [Chapter 21](#).

Mass lesions in the CPA, such as acoustic neuroma and meningioma, commonly extend to involve CN VII, the NI, CN VIII, CN V, the cerebellar

peduncles, and the cerebellum. Because of the associated hearing loss, there may not be hyperacusis even though the lesion is proximal to the branch to the stapedius. There is usually hearing loss, facial sensory changes, ipsilateral ataxia, and nystagmus. CPA syndromes are discussed further in [Chapter 17](#).

BOX 16.2

Ramsay Hunt Syndromes

Other conditions sometimes referred to as Ramsay Hunt syndrome are deep palmar branch ulnar neuropathy, dyssynergia cerebellaris myoclonica, juvenile Parkinson's disease, and dentatorubropallidoluysian atrophy.

In Ramsay Hunt syndrome (herpes zoster oticus, Hunt syndrome, geniculate herpes), the PFP is due to a reactivation of varicella zoster virus (VZV) involving the geniculate ganglion. Geniculate herpes is one of five conditions eponymically tied to James Ramsay Hunt ([Box 16.2](#)). Because of the very proximal involvement, the facial weakness is accompanied by taste impairment, hyperacusis, and diminution of salivary and lacrimal secretion. Pain in and behind the ear may be prominent. There may be vesicles on the tympanic membrane, in the external auditory canal, on the lateral surface of the pinna, and in the cleft between the ear and mastoid process ([Figure 16.9](#)). Occasionally, the herpetic eruption may also involve the anterior faucial pillar of the palate or the neck. Hunt described two types: an otalgic form with pain in the ear and a prosopalgic form with pain deep in the face, primarily in the posterior orbit, palate, and nose. The latter may result from involvement of sensory fibers in the greater superficial petrosal nerve.



FIGURE 16.9 Vesicles in the external ear canal in a case of geniculate herpes (Ramsay Hunt syndrome).

Some patients develop facial paralysis without ear or mouth rash but associated with serologic or DNA evidence of VZV infection (zoster sine herpete, zoster sine zoster). Preherpetic neuralgia refers to pain and dysesthesias preceding the development of rash. In one study, 14% of patients developed vesicles only after the onset of facial weakness. It is likely that some patients with Bell's palsy have Ramsay Hunt syndrome without a herpetic eruption. It has been estimated that up to one-third of idiopathic PFP cases may be due to zoster sine herpete. Imaging and virologic studies have shown that extensive

viral attack beyond the facial nerve occurs frequently. Tinnitus, hearing loss, nausea, vomiting, vertigo, and nystagmus from involvement of CN VIII are common. Rarely, cochleovestibular symptoms outweigh the PFP, presumably because of VZV reactivation in the ganglia of CN VIII. Other CNs may be affected as well. Compared with Bell's palsy, patients with Ramsay Hunt syndrome often have more severe paralysis at onset and are less likely to recover completely.

Patients with diabetes mellitus have a four- to fivefold increased risk of developing acute PFP, and diabetes is present in about 5% to 10% of patients with PFP. Diabetes is particularly likely in older patients, and those with recurrent or bilateral PFP. Slowly progressive facial weakness can occur with neoplasms involving either the pons or the facial nerve peripherally. Both HIV infection and Lyme disease can occasionally present with facial neuropathy. Lyme disease may cause 10% to 25% of cases of Bell's palsy in hyperendemic areas; there may be no history of tick bite or erythema migrans, and some patients are not seropositive initially. The cerebrospinal fluid (CSF) is often but not invariably normal. PFP because of Lyme disease is particularly prone to be bilateral.

Fractures of the petrous bone because of closed head injury may injure the facial nerve. The fracture may occur longitudinally down the long axis of the petrous pyramid or transversely across it. The facial nerve may be injured in either type. With the more common longitudinal fractures, the facial palsy is usually due to edema, does not occur immediately, and tends to resolve spontaneously. With transverse fractures, the nerve is often lacerated, contused, or severed; the facial palsy comes on immediately and may be permanent. Rupture of the ear drum and bleeding from the ear suggest longitudinal fracture. The tympanic membrane appears bright red, dark red, brown or bluish depending on the color of the fluid in the middle ear ([Figure 16.10](#)). CSF otorrhea is more common with transverse fractures ([Chapter 17](#)).

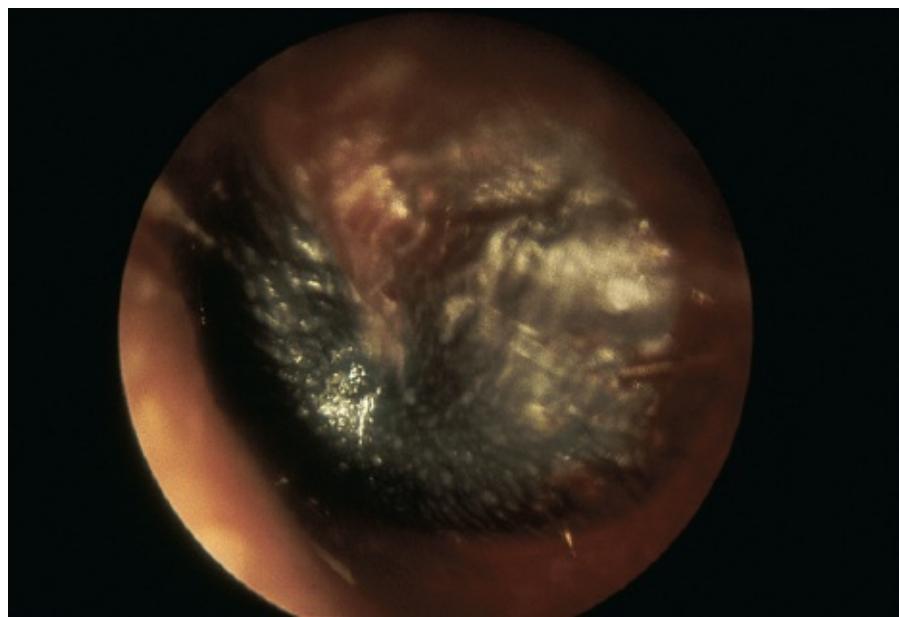


FIGURE 16.10 Hemotympanum due to a left temporal bone fracture. (Reprinted from Chung EK, Atkinson-McEvoy LR, Lai N, et al. *Visual Diagnosis and Treatment in Pediatrics*. 3rd ed. Philadelphia: Wolters Kluwer, 2015, with permission).

Melkersson syndrome (Melkersson-Rosenthal syndrome) is characterized by recurrent attacks of facial palsy, nonpitting facial and lip edema, and a congenitally furrowed and fissured tongue (lingua plicata, scrotal tongue); it is sometimes familial and usually begins in childhood. Its cause is unknown.

Bilateral facial palsy (facial diplegia) refers to bilateral PFP; it is much less common but much more ominous than unilateral PFP. Bilateral facial weakness can also occur because of neuromuscular disorders, including myasthenia gravis, bulbospinal neuronopathy, and muscle disease. Myasthenia gravis may cause marked facial weakness, with difficulty in both closing and opening the eyes. The pattern of perioral muscle involvement is capricious. In some patients, the smile looks like a weak, halfhearted effort, no matter the underlying jocularity, and may be more vertical than horizontal (Figure 16.11). The vertical myasthenic smile may look more like a snarl and is not without social consequences (myasthenic smile, myasthenic snarl). Ectropion, worse in the afternoon and responsive to anticholinesterase agents, is a rare manifestation of myasthenic weakness of the orbicularis oculi (Figure 16.12). Some myopathies are particularly likely to involve the facial muscles. Myopathic facies are particularly typical of facioscapulohumeral muscular dystrophy (Landouzy-Dejerine syndrome). The eyelids droop, but the eyes cannot be tightly closed. The lips cannot be pursed, but protrude and droop tonelessly, leaving an

involuntary protrusion of the upper lip (bouche de tapir). On smiling, the risorius pulls at the angle of the mouth, but the zygomaticus is unable to elevate the lips and the smile is transverse, see [Video Link 16.3](#).



FIGURE 16.11 The vertical myasthenic smile or snarl.

In facial hemiatrophy (progressive facial hemiatrophy, Parry-Romberg syndrome, Wartenberg syndrome), there is either congenital failure of development or a progressive atrophy of the skin, subcutaneous fat, and musculature of one half of the face, sometimes with trophic changes in the connective tissue, cartilage, and bone ([Figure 16.13](#)). Loss of tongue muscle

occurs in some patients. The disorder may be a form of localized scleroderma. Accompanying changes may include trophic changes in the hair, with loss of pigmentation and circumscribed alopecia and vitiligo. The facial atrophy may be accompanied by classic linear scleroderma lesions on the face or elsewhere. Rarely, there is hemihypertrophy instead of hemiatrophy. The disease may be a neural crest migration disorder.



FIGURE 16.12 Myasthenia gravis. **A.** Asymmetric ectropion due to orbicularis oculi weakness. **B.** Improvement after administration of neostigmine. (Reprinted from Solé G, Perez F, Ferrer X. Teaching NeuroImages: reversible ectropion in myasthenia gravis. *Neurology* 2009;73[16]:e83, with permission.)

When bilateral facial weakness is due to disease of CN VII, the differential diagnosis includes bilateral Bell's palsy, sarcoidosis, Lyme disease, diabetes, head trauma, HIV infection, Guillain-Barré syndrome, the Fisher variant of Guillain-Barré syndrome, carcinomatous or lymphomatous meningitis, tuberculous or fungal meningitis, pontine tumor, Melkersson-Rosenthal syndrome, pseudotumor cerebri, Möbius' syndrome, and a long list of other conditions. Leprosy may cause bilateral facial paralysis with greater involvement of the upper face. In Keane's series of inpatients with facial diplegia, the most common causes were Bell's palsy, Guillain-Barré syndrome, meningeal tumor, prepontine tumor, idiopathic cranial polyneuropathy, intrapontine tumor, brainstem encephalitis, and syphilis. Bilateral PFP must be differentiated from other causes of bifacial weakness, such as myopathies and myasthenia gravis.



FIGURE 16.13 Facial hemiatrophy (Parry-Romberg syndrome) with atrophy of the skin, subcutaneous fat, and musculature of one half of the face.

In its course across the middle ear, the chorda tympani may be damaged during middle ear surgery. Interestingly, disturbed taste after middle ear surgery is usually transient, even when the chorda tympani are sectioned bilaterally. However, bilateral chorda tympani lesions may lead to severe and persistent xerostomia because of damage to the autonomic fibers. A syndrome of paroxysmal otalgia because of neurovascular compression of the chorda tympani has been described, with evidence of compression of the nervus intermedius by a branch of the AICA in the IAC demonstrated by magnetic resonance angiography (MRA).

Facial Weakness of Central Origin

In a supranuclear, upper motor neuron or CFP, there is weakness of the lower face, with relative sparing of the upper face. The upper face has both contralateral and ipsilateral supranuclear innervation, and cortical innervation of the facial nucleus may be more extensive for the lower face than the upper. The paresis is rarely complete.

A lesion involving the corticobulbar fibers anywhere prior to their synapse on

the facial nerve nucleus will cause a CFP. Lesions are most often in the cortex or internal capsule. Occasionally, a lesion as far caudal as the medulla can cause a CFP because of involvement of the aberrant pyramidal tract. There is considerable individual variation in facial innervation, and the extent of weakness in a CFP may vary from the lower half to two-thirds of the face. The upper face is not necessarily completely spared, but it is always involved to a lesser degree than the lower face. There may be subtle weakness of the orbicularis oculi, the palpebral fissure may be slightly wider on the involved side, and there may be a decrease in palpable lid vibrations. However, involvement of the corrugator and frontalis is unusual, and the patient should be able to elevate the eyebrow and wrinkle the forehead with no more than minimal asymmetry. Inability to independently wink the involved eye may be the only demonstrable deficit. Occasionally, a patient with incompletely developed Bell's palsy will have relative sparing of the upper face, causing confusion with a CFP.

Even if there is some degree of upper facial involvement in a CFP, the patient is always able to close the eye, Bell's phenomenon is absent, the corneal reflex is present, and the orbicularis oculi reflex may be exaggerated. In CFP, the lower face is weak, the nasolabial fold is shallow, and facial mobility is decreased. However, the lower face weakness is never as severe as with a PFP, which suggests that there may be some direct cortical innervation to the lower face as well as the upper. Separating CFP and PFP is rarely difficult. CFP is typically part of a more extensive paralysis because of a lesion of the upper motor neuron pathways. Rarely, it may occur in isolation without other neurologic abnormalities; this pattern has been reported with a lacunar lesion of the contralateral basis pontis.



FIGURE 16.14 Patient with left thalamic tumor with face at rest (**A**), on voluntarily baring the teeth (**B**), and on reflex smiling (**C**); there is right facial paresis on smiling but not on voluntary contraction, an emotional facial palsy. Patient with a lesion of the corticobulbar fibers in the genu of the left internal capsule with face at rest (**D**), on voluntarily baring the teeth (**E**), and on reflex smiling (**F**); there is right facial paresis on voluntary contraction but not on smiling, a volitional facial palsy. (From Ross RT, Mathiesen R. Images in clinical medicine. Volitional and emotional supranuclear facial weakness. *N Engl J Med* 1998;338[21]:1515. Copyright © 1998 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.)

There are two variations of CFP: (a) volitional, or voluntary; and (b) emotional, or mimetic. In most instances of CFP, the facial asymmetry is present both when the patient is asked to smile or show the teeth, and during spontaneous facial movements such as smiling and laughing. However, spontaneous movements and deliberate, willful movements may show different degrees of weakness (Figure 16.14). When asymmetry is more apparent with one than the other, the facial weakness is said to be dissociated. Facial asymmetry

more apparent with spontaneous expression, as when laughing, is called a mimetic, emotive or emotional facial palsy (EFP) (see [Figure 16.14C](#)); weakness more marked on voluntary contraction, when the patient is asked to smile or bare her teeth, is called a volitional facial palsy (VFP) (see [Figure 16.14E](#)). With VFP, automatic or spontaneous movements may not only be preserved, but at times exaggerated. VFP may result from a lesion involving either the cortical center in the lower third of the precentral gyrus that controls facial movements, or the corticobulbar tract. The lesion thus may be either in the cortex or in the subcortical corticobulbar pathways as they go through the internal capsule, the cerebral peduncle, or the pons above the facial nucleus. The dissociation may be due to bilateral supranuclear innervation for lower facial spontaneous, emotional movements not present for volitional movements. In EFP, the weakness is most marked with spontaneous facial movements, and the patient can contract the lower facial muscles on command without difficulty. The anatomical explanation for EFP is unclear. Facial weakness seen only with emotional movements most commonly results from thalamic or striatocapsular lesions, usually infarction, rarely with brainstem lesions. It has been described in lesions of the frontal lobe anterior to the precentral gyrus involving the supplementary motor area. The fibers that mediate the emotional response travel through pathways other than the corticobulbar tracts. Facial asymmetry has been described in patients with temporal lobe seizure foci; the weaker side is usually contralateral to the lesion.

Abnormal Facial Movements

Some conditions involving the face produce abnormal movements rather than weakness. Common disorders causing abnormal facial movements include aberrant regeneration because of facial nerve palsy, blepharospasm, HFS, and facial myokymia.

Hemifacial Spasm

Facial synkinesis may progress to a stage of HFS. More often, HFS arises de novo, because of intermittent compression by an ectatic arterial loop in the posterior circulation, most often a redundant loop of the AICA. The compression is usually near the anterior aspect of the root exit zone. The pathophysiology is similar to that in some cases of trigeminal neuralgia ([Chapter 15](#)). The arterial pulsations are thought to cause demyelination and focal nerve damage leading to

ephaptic transmission and ectopic excitation. Combined studies using MRI and MRA may demonstrate the neurovascular compression. An MRI study using 3D reconstruction confirmed the AICA as the most common causative vessel, with the posterior inferior cerebellar artery, vertebral artery, internal auditory artery, and veins occasionally causing facial nerve compression at the root entry zone. However, radiographic studies using a 3T MRI has shown that some contact between the facial nerve and nearby vessels, even enough to cause mild nerve deviation, is the rule rather than the exception.

Microvascular decompression is sometimes done and may effectively halt the movements. The lateral spread response is an electrophysiologic phenomenon seen in HFS. Stimulation of the mandibular branch of the facial nerve may cause a compound muscle action potential to appear in the orbicularis oculi. This response does not occur in normals. The lateral spread response is objective evidence of ephaptic transmission from one facial nerve branch to another. During microvascular decompression, the lateral spread response may disappear when the offending vessel is lifted off the nerve, and the status of the response may be used as an indicator of the effectiveness of the decompression. HFS may also occur with other extra-axial or intra-axial lesions, including aneurysm, tumor, multiple sclerosis, or basilar meningitis.

HFS usually develops in older patients, and the condition is twice as common in women than men. Twitching usually begins in the orbicularis oculi, less often in the oris. Initially, the twitching may be subtle and difficult to distinguish from facial synkinesis. HFS may involve the entire facial nerve distribution, or only certain nerve branches; it may propagate from one branch to another. Over months to years, HFS usually spreads to involve all of the facial muscles on one side, but it remains strictly limited to the muscles supplied by the facial nerve. As HFS worsens, it may involve the auricular muscles even when the patient cannot deliberately wiggle the ears; the platysma may also be affected. Fully developed HFS causes repetitive, paroxysmal, involuntary, spasmodic, tonic and clonic contractions of the muscles innervated by the facial nerve on the involved side of the face. The mouth twists to the affected side, the nasolabial fold deepens, the eye closes, and there is contraction of the frontalis muscle ([Video 16.2](#)).



Video 16.2 Hemifacial spasm. (Courtesy Dr. Stephen Reich.)

The spasms may persist in sleep and are often exacerbated by chewing or speaking. Synkinesis following PFP may cause movements resembling HFS. The essential difference is that synkinesis is provoked by a voluntary movement, whereas HFS is a spontaneous, involuntary contraction. HFS is commonly associated with some degree of facial weakness because of underlying nerve damage. Rare patients may have both HFS and trigeminal neuralgia, with lancinating pain accompanying the facial spasms (tic convulsif). Brissaud-Sicard syndrome is HFS with contralateral hemiparesis because of a lesion in the pons.

Babinski's brow lift sign is seen only in HFS and consists of cocontraction of the frontalis and orbicularis oculi muscles causing simultaneous eye closure and paradoxical elevation of the eyebrow during a spasm. This movement is impossible to execute voluntarily and does not occur in blepharospasm, tic or psychogenic movement disorders. The brow lift sign has been referred to as the "other Babinski sign," but at least nine signs bear Babinski's name and this designation has been used for other signs as well, most notably Babinski's platysma sign.

Blepharospasm (nictitating spasm) causes involuntary twitching that primarily involves the orbicularis oculi and frontalis muscles. Blepharospasm is most often idiopathic or "essential" and is a form of focal dystonia ([Chapter 30](#), [Video 30.5](#)). Blepharospasm is always bilateral and fairly symmetric. Meige's syndrome is the association of blepharospasm with oromandibular dystonia. Patients with central nervous system (CNS) Whipple's disease may have an oculofacial, more often an oculomasticatory, myorhythmia (see [Video Link 16.4](#)).

Tic, or habit spasm, can cause a movement resembling HFS or

blepharospasm. Tic often causes retraction of the angle of the mouth, contraction of the orbicularis oculi or platysma, or eye blinking. The movements are somewhat more bizarre and purposeful, and other muscles not innervated by CN VII may be brought into action. Bizarre grimacing movements of the face are usually habit spasms. The movements in HFS and essential blepharospasm are stereotyped. The patient with tic can suppress the movements, at least temporarily, while the movements of HFS and blepharospasm are totally beyond volitional control and cannot be suppressed or imitated.

Spastic Paretic Facial Contracture

Instead of spasm, there may be a facial contracture causing a fixed expression with wrinkling of the forehead, narrowing of the palpebral fissure, drawing up or twisting of the angle of the mouth, and increased depth of the nasolabial fold. A facial contracture may give the faulty impression of weakness on the opposite side. Facial contracture may follow a facial paralysis, or occur de novo. Careful testing may reveal that the affected muscles are still paretic, even though in a state of contracture. This type of spastic paretic facial contracture may occur with a progressive lesion of the pons and is suspicious for neoplasm. When facial myokymia and spastic paretic contracture occur together, the likelihood of pontine neoplasm is very high.

Facial Myokymia

Facial myokymia is a continuous, involuntary muscular quivering that has a rippling, wormlike, appearance ([Chapter 30](#)). It is usually unilateral. Facial myokymia has been reported with numerous conditions, most intrinsic to the brainstem. It is a classic feature of multiple sclerosis but may also occur with pontine tumor, CPA tumors, Guillain-Barré syndrome, facial nerve compression, rattlesnake envenomation, subarachnoid hemorrhage, meningeal neoplasia, basilar invagination and in association with high titers of voltage-gated K⁺ channel antibodies (see [Video Link 16.5](#)). Facial myokymia may occur after cardiac arrest, even in some patients with brain death. With intraparenchymal lesions, the facial nucleus itself is usually intact, but the process disrupts its connections, possibly disinhibiting some neural generator. Mild, usually fleeting, myokymia is common, especially in the orbicularis oculi, and of no clinical significance. These movements often worsen with fatigue and with hyper-

caffeinism. Patients often require reassurance.

Other Abnormal Facial Movements

Focal seizures involving the face may occur with seizure foci in the motor cortex. Facial seizures may be part of a versive seizure or Jacksonian march. Disease of the basal ganglia or extrapyramidal system may involve the facial muscles causing hypokinesia or hyperkinesia ([Chapter 30](#)). Parkinson's disease causes hypokinesia. Forms of facial hyperkinesias include dyskinesias, choreiform, athetoid, dystonic, grimacing, and myoclonic movements and tremors. Oral-facial dyskinesias are common, most often as a tardive manifestation of psychoactive drug use. Facial muscles, especially the platysma, may sometimes be involved in palatal myoclonus, which is a persistent, rhythmic movement in contrast to other forms of myoclonus ([Chapter 30](#)). Facial myoclonus can occur with dolichoectasia of the vertebral artery, with hypocalcemia, serotonin syndrome, and other conditions. Facial fasciculations may occur in any motor neuron disease; perioral and chin fasciculations are frequent in Kennedy's disease.

Sensory Involvement

Except for disturbances of taste, sensory abnormalities are not a common part of facial nerve lesions. Taste may be affected with lesions of the facial nerve proximal to the takeoff of the chorda tympani. Permanent taste disturbances may follow Bell's palsy. Disturbances of taste and smell often occur together. Taste abnormalities are usually due to olfactory dysfunction ([Chapter 12](#)). Dysgeusia may be a direct or indirect effect of malignancy. Hypergeusia and parageusias may occur in psychoses and conversion disorder. Gustatory hallucinations may occur with complex partial seizures and with tumors involving the uncus or parietal operculum. Gustatory and olfactory hallucinations often occur together. Elderly patients sometimes develop dysgeusia of obscure origin that may lead to anorexia and weight loss. Increased taste sensitivity occurs in patients with Addison disease, pituitary deficiency, and cystic fibrosis.

Geniculate neuralgia causes paroxysmal pain deep in the ear, sometimes radiating to the face. "Tic douloureux of the chorda tympani" has also been described. Lesions of the lingual nerve may cause loss of taste together with loss of exteroceptive sensation on the involved side of the tongue; there is also

usually subjective numbness.

Secretory Changes

CN VII is involved in lacrimation and salivation; lesions of the nerve at or proximal to the geniculate ganglion can cause abnormalities of these functions. Absence of salivation occurs only with bilateral lesions. Central lesions, especially those involving the hypothalamus or the autonomic connections, may cause changes in secretory function. Changes in lacrimal and salivary flow are more often the result of systemic processes. Anticholinergic drugs often cause an unpleasantly dry mouth. Keratoconjunctivitis sicca, which occurs in Sjögren's syndrome and other connective tissue disorders, causes deficient secretion of the lacrimal, salivary, and mucosal glands. This in turn causes dryness of the eyes, mouth, and upper respiratory tract. Sialorrhea (ptyalism) is an excess of saliva. It occurs in Parkinson's disease and when patients are unable to swallow, such as in bulbar involvement with motor neuron disease.

An increase or decrease in lacrimal or salivary secretion may occur on a psychogenic basis. Lacrimation, of course, is most frequently the result of an emotional stimulus. Salivation may occur from the smell, taste, sight, or thought of food. Xerostomia is common in depressed and anxious patients.

Video Links

Video Link 16.1. Demonstration of taste testing technique.

[http://www.youtube.com/watch?
v=ldkpd88KSUA&feature=mfu_in_order&list=UL](http://www.youtube.com/watch?v=ldkpd88KSUA&feature=mfu_in_order&list=UL)

Video Link 16.2. Möbius' syndrome. [http://www.youtube.com/watch?
v=3FJPvBcMNAE](http://www.youtube.com/watch?v=3FJPvBcMNAE)

Video Link 16.3. Myopathic facies. http://neurosigns.org/wiki/Myopathic_facies

Video Link 16.4. Oculomasticatory myorhythmia in CNS Whipple's disease.

http://neurosigns.org/wiki/Oculomasticatory_myorhythmia

Video Link 16.5. Facial myokymia after rattlesnake bite.

<https://www.youtube.com/watch?v=KaM3-qy8uqU>

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CHAPTER 17

The Acoustic (Vestibulocochlear) Nerve

The vestibulocochlear, acoustic, or eighth cranial nerve (CN VIII) has two components, the vestibular and the cochlear, blended into a single trunk. The cochlear portion subserves hearing; the vestibular nerve subserves equilibration, coordination, and orientation in space. Both are classified as special sensory afferent nerves. The two components originate in separate peripheral receptors and have distinct central connections. Although they are united along their course through the skull, they differ so greatly both functionally and in their anatomic relationships that they should be considered separately.

THE COCHLEAR NERVE

Anatomy and Physiology

Sound is a form of energy produced by vibrations that create a sinusoidal wave of alternating condensations and rarefactions in a conductive medium such as air. Sound waves converge on the tympanic membrane and are transmitted by the auditory ossicles (malleus, incus, and stapes) to the inner ear, or labyrinth. The labyrinth is a complex of interconnecting cavities, tunnels, ducts, and canals that lies in the petrous portion of the temporal bone ([Figure 17.1](#)). The vestibule, cochlea, and semicircular canals form the bony, or osseous, labyrinth, which is made of compact bone and can be dissected free of the cancellous bone that surrounds it ([Figure 17.2](#)).

The bony labyrinth is filled with perilymph, a thin watery fluid similar to cerebrospinal fluid. The membranous labyrinth is an arrangement of sacs and ducts that lies within the bony labyrinth, generally follows its outline, and is

filled with endolymph (Scarpa's fluid [Antonio Scarpa was an Italian surgeon, anatomist, and artist who first described many structures of the ear]). The membranous labyrinth has two major components: the vestibular apparatus and the cochlear duct ([Figure 17.3](#)). The ossicles span the middle ear cavity and transmit the oscillations of the tympanic membrane to the footplate of the stapes, which sits in the oval window (*fenestra vestibuli*). The ossicles function as an amplifier and help to compensate for the loss of energy as sound waves are transmitted from the air to the perilymph behind the oval window. The tensor tympani muscle, which inserts on the malleus, and the stapedius, which inserts on the stapes, provide reflex protection against sudden, loud noise. The oval window opens into the vestibule of the inner ear, which connects on one side to the cochlea and on the other to the semicircular canals. The cochlea spirals for 2.5 to 2.75 turns to reach its apex. The base of the cochlea faces the internal acoustic meatus and contains myriad fenestrations that admit the filaments of the cochlear nerve. The middle ear cavity acts as an impedance-matching device to transfer sound energy from the low impedance of air to the high impedance of fluid in the cochlea.

The central axis of the cochlea is the modiolus; from it projects a delicate bony shelf, the spiral lamina, which partially divides the cochlear passageway into two parallel channels—the scala tympani and the scala vestibuli. The scala media, or cochlear duct, is part of the membranous labyrinth. It lies in the center of the spirals of the cochlea, completing the partition between the scala tympani and scala vestibuli ([Figure 17.4](#)). At the tip of the modiolus, the cochlear duct ends blindly; a narrow slit at the very apex of the cochlea, the helicotrema (Gr. “hole in a helix”), allows for communication and the flow of perilymph between the scala tympani and vestibuli.

The basilar membrane of the cochlear duct projects from the spiral lamina of the modiolus to the outer wall of the cochlea. The spiral ganglion of the cochlear nerve lies in the spiral canal of the modiolus (Rosenthal's canal). The organ of Corti rests on the basilar membrane and contains inner and outer hair cells. The inner hair cells are the receptors, or end organs, of the cochlear nerve. From the apex of each inner hair cell, a stereocilium extends to just beneath the tectorial membrane ([Figure 17.4](#)). Sound waves induce vibrations in the cochlea, which cause movement of the basilar and tectorial membranes. This movement flexes the stereocilia, which activates the hair cell, causing impulses in the spiral ganglion.

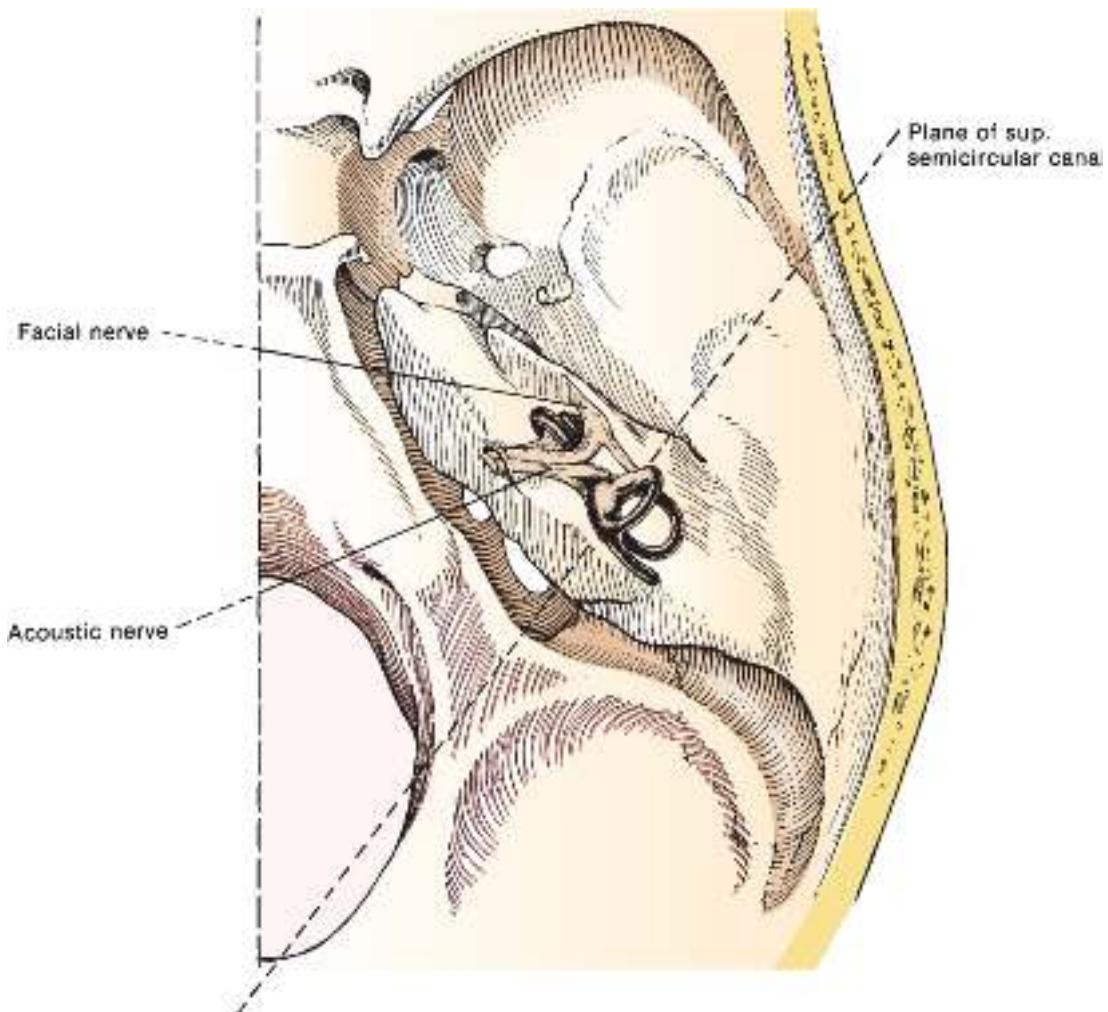


FIGURE 17.1 The right osseous labyrinth in the temporal bone viewed from above.

Because of the varying width of the basilar membrane, sound of a certain frequency induces harmonic oscillations maximal at a certain point along the cochlear duct, which focally activates certain hair cells and encodes the frequency (Box 17.1). The round window (fenestra cochlea) lies below the oval window (Figure 17.2). It is covered by a delicate membrane, the secondary tympanic membrane, which allows for compliance in the perilymph system and permits the waves of vibration initiated at the oval window to dissipate.

The spiral ganglion consists of type I and type II bipolar neurons that lie in the modiolus. Inner hair cells synapse on type I neurons, which make up 95% of the ganglion. Axons of the spiral ganglion cells form the cochlear nerve, which contains some 30,000 fibers (Figure 17.6). Axons from type I cells are myelinated and form the bulk of the nerve. The type II cells connect with the outer hair cells and modulate the activity of the inner hair cells (Box 17.1).

The acoustic nerve traverses the internal auditory canal (IAC), where it lies lateral and inferior to the facial nerve. It crosses the cerebellopontine angle, passes around the inferior cerebellar peduncle, and enters the upper medulla at its junction with the pons near the lateral recess of the fourth ventricle ([Figure 17.7](#)). Each entering fiber bifurcates to synapse in both the dorsal (posterior) and ventral (anterior) cochlear nuclei. The ventral nucleus may be divided into anteroventral and posteroventral portions. This dual termination is the beginning of a great deal of redundancy in the auditory system.

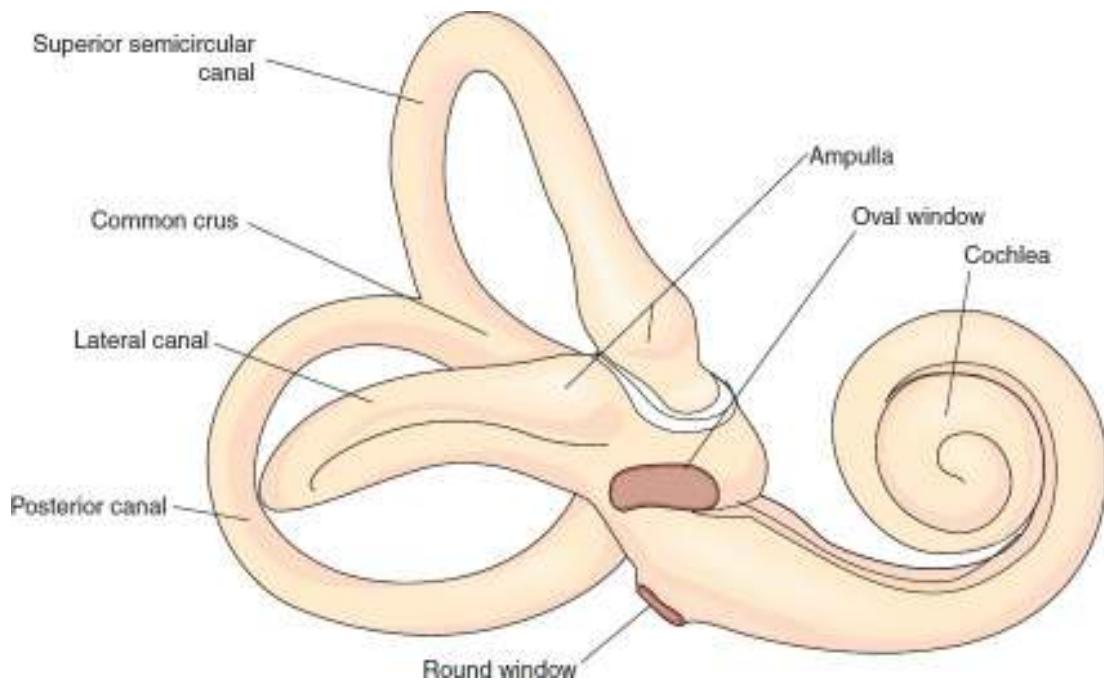


FIGURE 17.2 The right osseous labyrinth, lateral view.

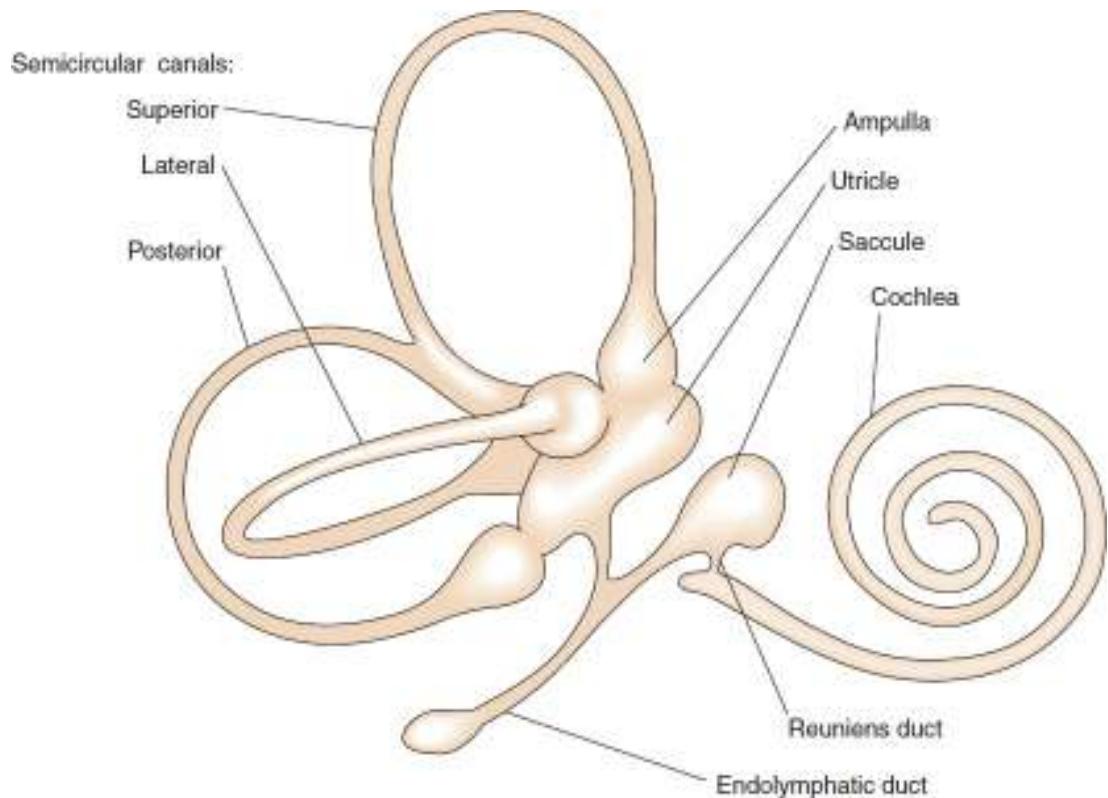


FIGURE 17.3 The membranous labyrinth.

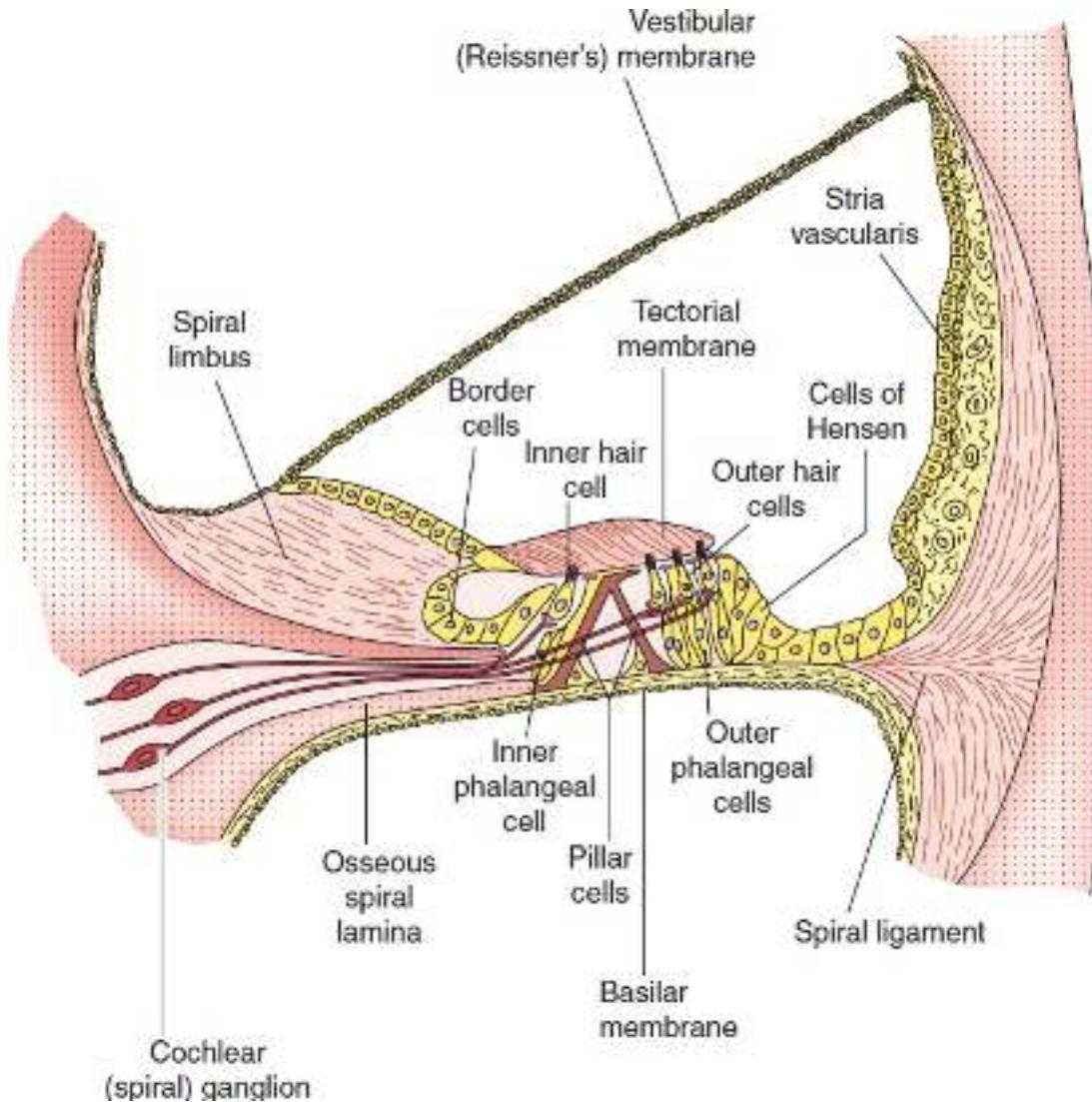


FIGURE 17.4 Structure of the cochlear duct and the spiral organ of Corti. (Modified from Kiernan JA. *Barr's The Human Nervous System: An Anatomical Viewpoint*. 7th ed. Philadelphia: Lippincott-Raven, 1998, with permission.)

BOX 17.1

Tonotopic Organization

The organ of Corti is tonotopically organized. The width of the basilar membrane of the cochlear duct is least at the base of the cochlea, where the spinal lamina of the modiolus extends farthest into the coils of the cochlea. This part of the cochlea is most efficiently activated by high frequencies. Near the apex, the basilar membrane is wider and responds to low-pitched tones. The inner hair cell-spiral ganglion cell complex at a given point along

the organ of Corti is frequency dependent, responding best to a particular pitch and coding for that pitch by its discharges in the cochlear nerve. Tonotopic organization continues to varying degrees throughout the auditory system.

Imagine a spiral staircase in the center of a silo—steps winding around a central core, steps wider at the bottom and progressively narrowing, and from each step a cable of violin string extending to the wall of the silo ([Figure 17.5](#)). The central core represents the modiolus; the steps, the spiral lamina; and the violin strings, the basilar membrane. A low-tone sounding in the silo would set the long strings near the top of the silo in vibration; a high-pitched tone would affect the short strings near the bottom. Coil the silo into a conch to match the turns in the staircase to complete the resemblance to the cochlear duct.

The stereocilia of the outer hair cells are imbedded in the tectorial membrane and have contractile properties. They help adjust and control the oscillations of the membrane and thereby regulate to some degree the activation of the inner hair cells. The outer hair cells receive innervation from the efferent cochlear, or olivocochlear, bundle, which arises from the superior olivary nucleus in the pons. By controlling the outer hair cells, the olivocochlear bundle helps regulate afferent cochlear traffic and may be involved in attentiveness to auditory stimuli.

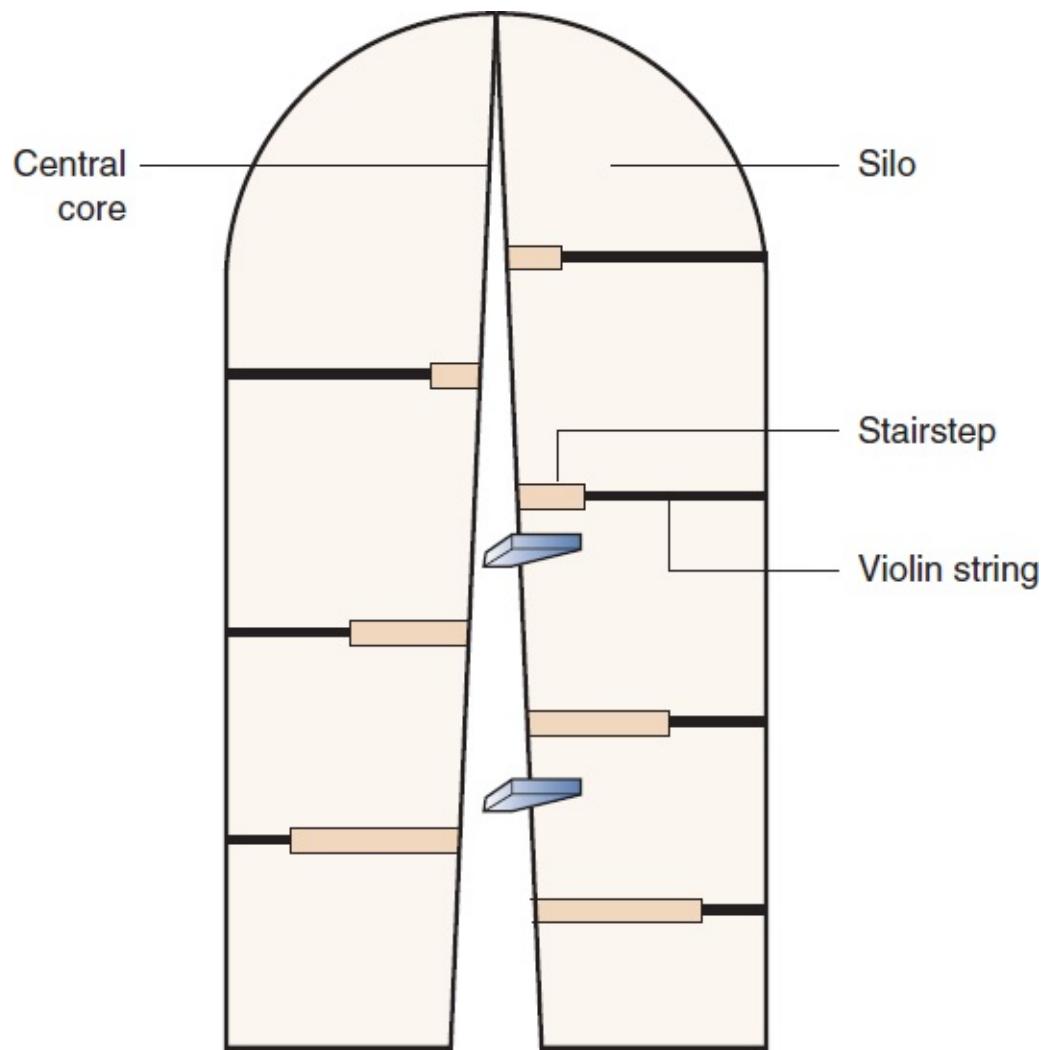


FIGURE 17.5 The cochlear duct and organ of Corti as a spiral staircase in a silo (see Box 17.1).

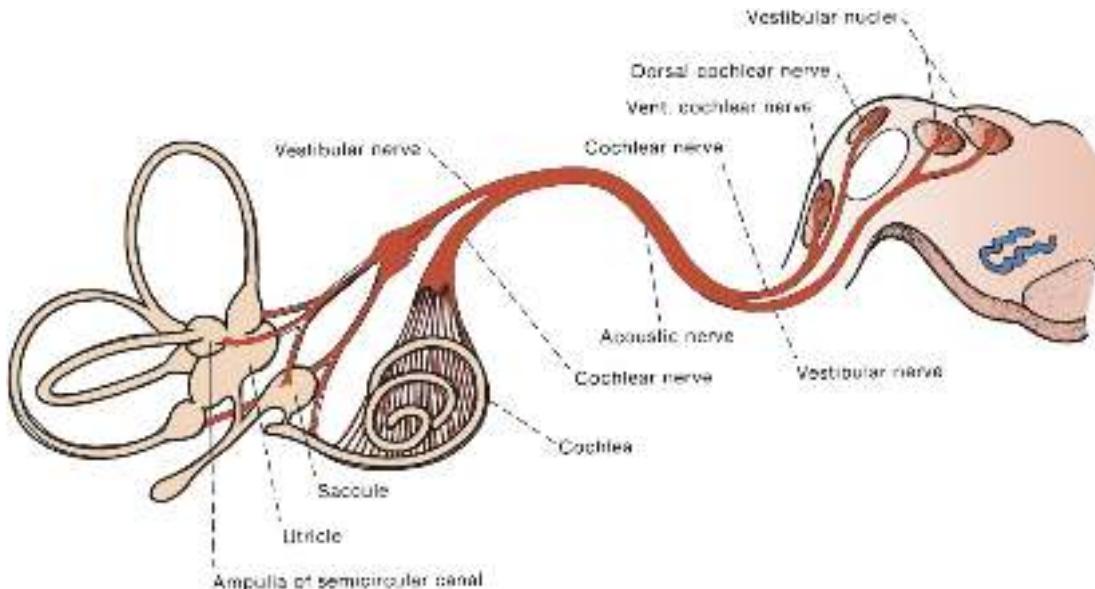


FIGURE 17.6 The acoustic nerve and its connections.

Tonotopic organization is maintained in the auditory nuclei and throughout the higher auditory relay centers; the location of fibers is related to their site of origin in the cochlea, which in turn is a reflection of the activating frequency. In the cochlear nuclei, low-frequency tones are processed ventrally and high frequencies dorsally. Second-order neurons in the cochlear nuclei give rise to the dorsal, ventral, and intermediate acoustic stria. The dorsal acoustic stria consists of fibers from the dorsal cochlear nucleus that pass over the inferior cerebellar peduncle, cross the floor of the fourth ventricle under the striae medullares (fibers of Piccolomini), and then pass ventrally into the pons, near the superior olive nucleus, to join the contralateral lateral lemniscus ([Figure 17.8](#)). The intermediate and ventral acoustic striae arise from the ventral cochlear nuclei. The intermediate stria passes over the inferior peduncle and crosses the tegmentum to join the contralateral lateral lemniscus. Fibers of the ventral stria pass ventral to the peduncle. Some cross the pons as trapezoid fibers to synapse in the contralateral nucleus of the trapezoid body. Others synapse ipsilaterally in the nucleus of the trapezoid body.

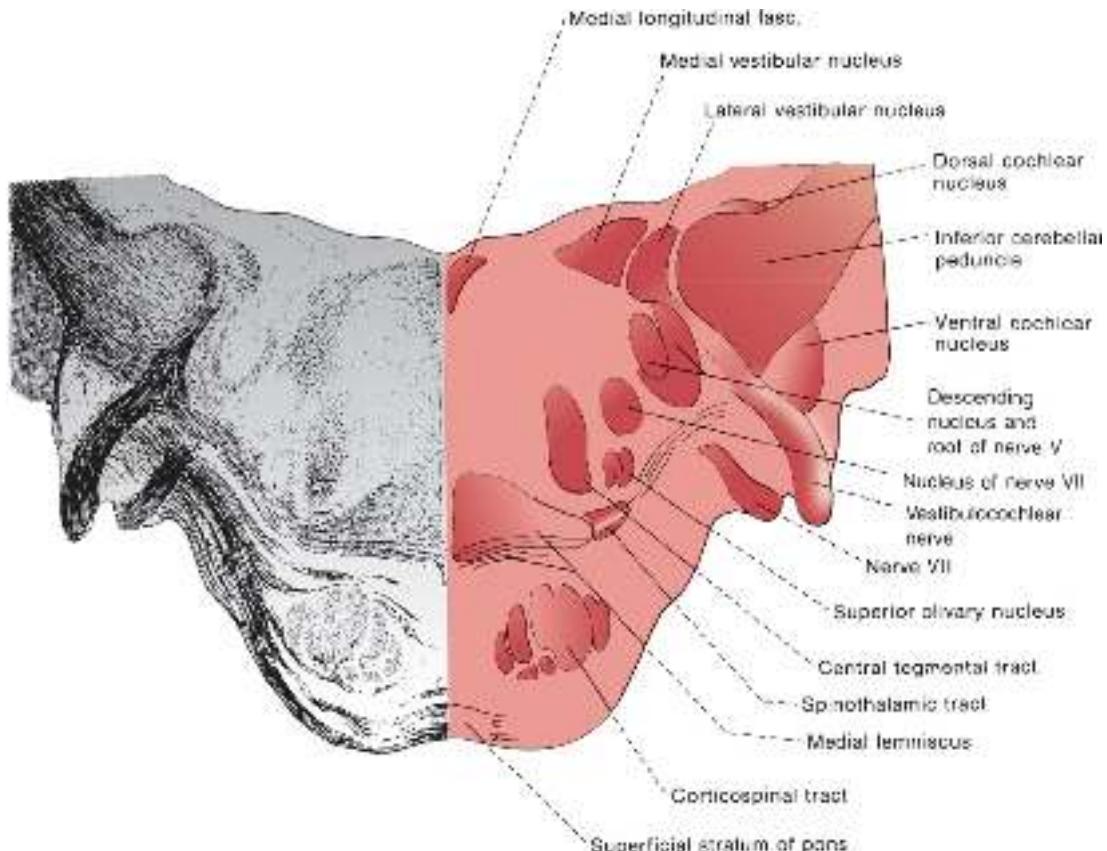


FIGURE 17.7 Section through the junction of the pons and medulla at the level of the cochlear nuclei.

Auditory fibers ascend from the trapezoid body as the lateral lemniscus. Fibers in the dorsal and intermediate acoustic stria run to the contralateral inferior colliculus, most directly, some after a relay in the nucleus of the lateral lemniscus. This crossed, monaural auditory pathway primarily carries information about sound frequency. Fibers of the ventral acoustic stria are both crossed and uncrossed and may synapse in the nuclei of the trapezoid body, superior olive, or lateral lemniscus. The binaural pathway, especially the superior olivary complex component, can determine the time difference between the two ears and aid in the localization of sound. Ascending auditory fibers send collaterals to the brainstem reticular formation and to the nuclei of CNs V and VII; these connections mediate various reflexes related to hearing.

Fibers from the lateral lemnisci ascend to synapse in the central nucleus of the inferior colliculus, an auditory reflex center that is also tonotopically organized. The inferior colliculus is the central relay nucleus of the auditory pathway and receives both ascending and descending input. Axons from the inferior colliculus pass through the brachium of the inferior colliculus to the medial geniculate

body (MGB), a special sensory nucleus of the thalamus that is the final relay station in the auditory pathway. In the MGB, fibers conveying high tones lie medially and low tones laterally. From the MGB, auditory fibers pass through the posterior limb of the internal capsule as the geniculotemporal tract, or auditory radiations, which runs through the sublenticular portion of the internal capsule. The fibers terminate in the cortex of the transverse temporal convolutions (Heschl's gyrus) and the adjacent planum temporale portion of the superior temporal gyrus. The transverse temporal gyri and parts of the planum temporale make up the primary and secondary auditory cortex (Brodmann's areas 41 and 42). The primary auditory cortex is tonotopically organized with high frequencies medial and low frequencies lateral. The auditory association cortex (Wernicke's area in the dominant hemisphere) lies just posterior to the primary auditory cortex.

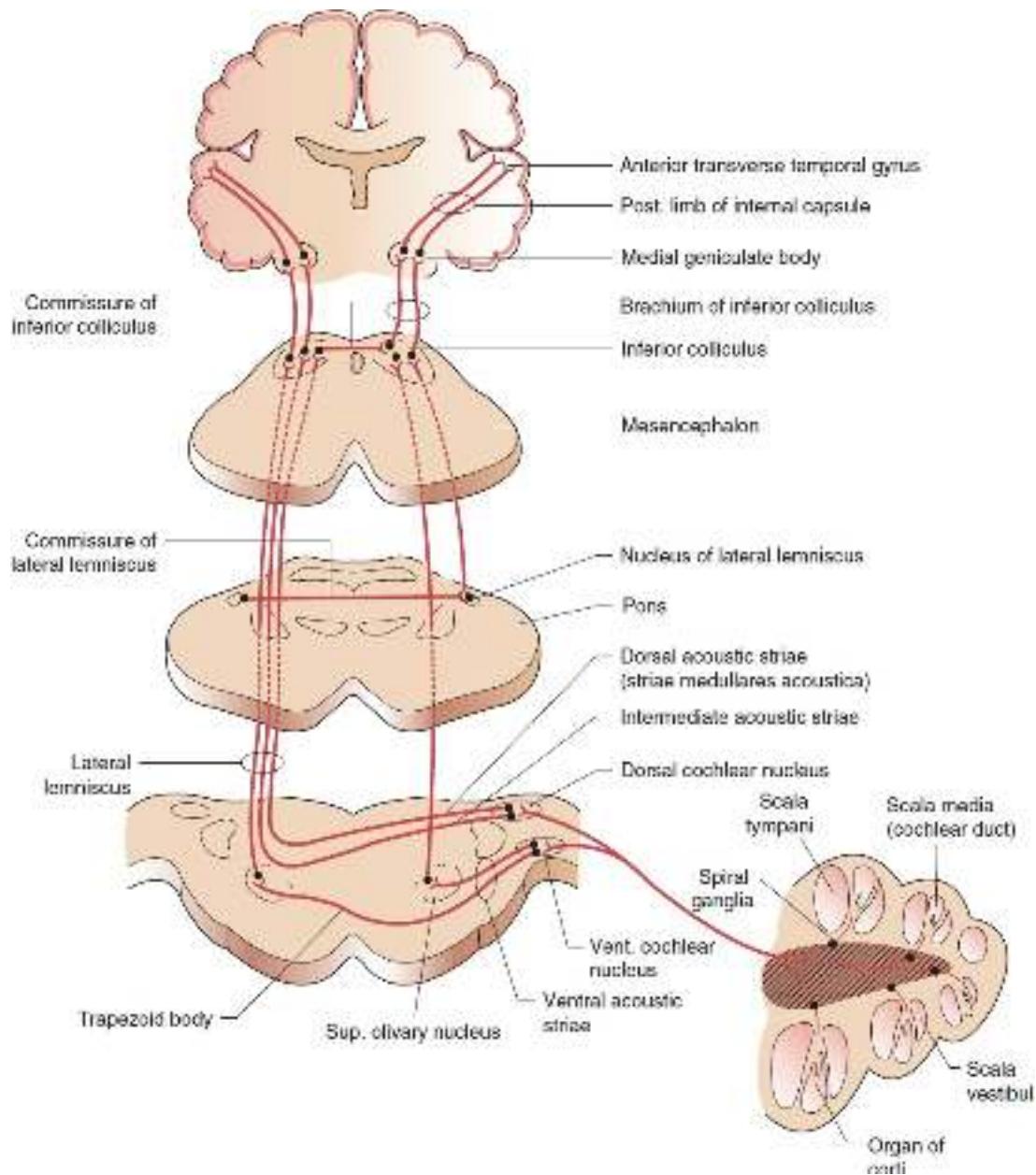


FIGURE 17.8 The cochlear pathway.

There is extensive crossing of the central auditory pathways above the level of the cochlear nuclei. Commissures connect the nuclei of the lateral lemniscus (commissure of Probst) and the inferior colliculi (commissure of the inferior colliculus). There are connections through the brachium of the inferior colliculus between the central nucleus of the inferior colliculus on one side and the contralateral MGB. In addition, there is the direct, tonotopically organized auditory pathway, the core projection, and an additional, less-organized pathway, the belt projection. The core system includes the central nucleus of the inferior

colliculus, portions of the MGB, and the primary auditory cortex. The belt projection includes the pericentral region of the inferior colliculus, the nonlaminated portion of the MGB, and the secondary auditory cortex. The corpus callosum contains fibers that connect the auditory cortices of the two hemispheres.

Descending auditory projections run parallel to the ascending fibers and are concerned with auditory reflexes. Descending pathways include the corticogeniculate, corticocollicular, geniculocollicular, and collicular efferents. The efferent cochlear bundle projects from the superior olive to the cochlea ([Box 17.1](#)).

Clinical Examination

Some information about hearing may be obtained simply by observation and gauging the patient's ability to understand soft and loud tones and low and high pitches; note signs of deafness, such as a tendency to turn the head when listening, lipreading, or speaking with a loud voice. Any history of hearing difficulty, such as trouble using the telephone or hearing conversation in noisy environments, or complaints from family members, should prompt a careful evaluation. Before testing hearing, otoscopic examination should be done to ensure the tympanic membrane is intact and to exclude the presence of wax, pus, blood, foreign bodies, and exudate. The mastoid region should be examined for swelling and tenderness.

Conductive hearing loss (CHL) is that due to impaired conduction of sound to the cochlea and may be due to occlusion of the external auditory canal, middle ear disease (e.g., otitis), or abnormality of the ossicular chain (e.g., otosclerosis). Sensorineural hearing loss (SNHL) is that due to disease of the cochlea (e.g., Ménière's disease) or eighth CN (e.g., acoustic neuroma). As a generality, CHL affects low frequencies and SNHL affects high frequencies. Ménière's disease is a notable exception, causing predominantly low-frequency hearing loss, at least early in the course. Central hearing loss is that due to disease of the central pathways. Central hearing loss is very rare because of the bilaterality and redundancy of the auditory system; unilateral lesions of the central auditory pathways typically do not cause any deficit detectable by routine clinical testing.

There are many ways to assess hearing at the bedside. All are crude compared to the information that can be obtained with a formal audiogram. The subject of audiography is complex. [Box 17.2](#) summarizes some of the basic principles.

Bedside clinical testing of hearing may theoretically use any available instrument that is capable of making a sound. Because the ability to hear and understand speech is the most important functional aspect of audition, whispered voice is useful. Inability to whisper at exactly the same level for testing each ear, and inter- and intraindividual variation in the intensity and pitch of the voice, is a theoretical limitation, but clinically significant hearing loss is usually detectable with this simple technique. Whispered voice has been recommended as an excellent screening test. Inability to perceive a whispered voice has a likelihood ratio (LR) of 6.1 (95% CI, 4.5 to 8.4) for clinically significant hearing loss; normal perception has an LR of 0.03 (95% CI, 0 to 0.24).

Despite its disability for the patient, high-frequency SNHL of the type associated with presbycusis and acoustic trauma is not generally of neurologic significance; the use of high-pitched sounds, such as a ticking watch, seldom provides useful information for neurologic examination purposes. In certain types of deafness, loss of speech discrimination is of clinical significance, even though pure tone and even speech thresholds are normal. Few conditions of neurologic importance cause bilaterally symmetric hearing loss, and an examination designed to detect auditory asymmetry usually suffices. Other useful sounds for bedside testing include finger rub—the noise made by rubbing the thumb and index finger together beside the external auditory meatus—and pure tones created by a tuning fork.

Detailed testing of hearing is done monaurally, ideally while occluding the opposite ear, by pressing the tragus over the canal. For screening purposes in low-yield situations, occlusion of the opposite ear is sometimes omitted, and occasionally, finger rub is done binaurally. In each instance, the patient is asked to compare the sound intensity between the two ears. The examiner may also compare the distance from each ear at which a sound of the same intensity can be heard. An occasionally useful method is to place the earpieces of a stethoscope into the patient's ears. Then, whisper into, scratch softly on, or hold a tuning fork to the chest piece, and ask the patient to compare the sounds heard. One side of the tubing can be occluded to direct the sound into one ear. Ross' method is to stand at a fixed distance (e.g., 6 ft) at a right angle from the patient, have the patient occlude the far ear, and whisper; repeat for the other ear, and compare the auditory acuity on the two sides.

BOX 17.2

Audiometry

Detailed assessment of hearing is done with audiometry, which is usually performed as a battery of tests. The range of human hearing is 20 to 20,000 Hz (about 11 octaves). Speech usually falls in the 300- to 3,000-Hz range. There are many different audiology techniques; those used most commonly for neurologic purposes are pure tone and speech audiometry. An audiogram is a plot of the threshold of audition for short pure tones as a function of frequency on a logarithmic decibel scale. Air conduction (AC), assessed with earphones, tests the entire auditory pathway. Bone conduction (BC) sends a signal directly to the cochlea, bypassing the outer and middle ear structures. The pure tone audiogram displays the severity of any hearing loss in relation to established reference values, and the pattern may suggest the etiology. As with tuning fork testing, a decrease in AC with normal BC, an air-bone gap, indicates conductive hearing loss, and a decrease in both AC and BC indicates sensory or neural loss. The pure tone audiogram is usually normal with lesions involving the central auditory pathways.

Speech audiometry uses spoken words and sentences instead of pure tones. The speech reception threshold is considered the intensity level at which the patient can correctly understand 50% of the material presented. Speech discrimination, or intelligibility, is the proportion of the material the patient can understand when presented at a level that should be easily heard. The loss of discrimination is proportional to the severity of the hearing loss in patients with cochlear lesions. Poor speech discrimination, out of proportion to pure tone hearing loss, is characteristic of a retrocochlear lesion, such as a cerebellopontine angle tumor. In cranial nerve (CN) VIII lesions, discrimination may even paradoxically decline as intensity is raised.

A tympanogram measures the impedance of the tympanic membrane. An abnormal tympanogram is seen in such conditions as otitis media, tympanic membrane perforation, ossicular dislocation, otosclerosis, cerumen impaction, and eustachian tube dysfunction.

The stapedius reflex, or acoustic reflex, measures the change in compliance in response to loud sounds to assess the function of the stapedial muscle. The reflex arc is via CN VIII, brainstem interneurons, and CN VII. In the absence of severe hearing loss, an abnormal stapedius reflex may suggest a lesion of CN VII or VIII or the brainstem.

The AEP, also known as the auditory evoked response, or brainstem

auditory evoked potential/response (BAEP/BAER), is a minuscule potential produced by auditory stimuli and recorded using electroencephalogram (EEG) electrodes. The potential is discernible from the much more prominent background EEG activity because it is time locked to the auditory stimuli. This temporal relationship is only apparent after averaging a large number of responses. The background EEG activity is random and not time locked to the stimuli. It tends to cancel itself out if enough auditory stimuli are given, and the signal (the BAER) gradually emerges from the noise (the background EEG activity). The waves that occur in the first 10 ms after an auditory stimulus are short-latency far-field potentials because of electrical activity at various points along the auditory pathway. These are reproducible and reliable wave forms. BAERs are used primarily for evaluating suspected CN VIII and brainstem lesions. There are five to seven waves in the AEP; the correlation of the waveforms with specific anatomic structures is based primarily on animal studies and remains somewhat uncertain. Wave I is the auditory nerve action potential. Wave II is thought to reflect activity in the cochlear nuclei, although it may be generated by the intracranial segment of the auditory nerve. Wave III is thought to come from the superior olive, and waves IV and V are from the inferior colliculus. The origin of waves VI and VII is unclear, but wave VI may come from the medial geniculate body and wave VII from the auditory radiations.

The relationship of the BAER waveforms to the anatomic pathways allows for lesion localization predicated on changes in interpeak latencies and differences in latencies between the two ears. A delay between waves I and III suggests a lesion between the eighth nerve near the cochlea and the lower pons; an interpeak latency delay between waves III and V suggests a lesion between the lower pons and midbrain. The primary clinical applications of BAERs have been in the evaluation of patients with cerebellopontine angle tumors and demyelinating disease and in coma and brain death. It is also of considerable value in newborn and infant hearing assessment.

When using whispered voice, certain tones are heard better and at a greater distance than others. Sibilants, and the short vowels such as a, e, and i, are heard at a greater distance than broad consonants such as l, m, n, and r, and such vowels as o and u. “Seventy-six” and “sixty-seven” can be heard at a greater

distance than “ninety-nine” and “fifty-three.” One key to the effective use of whisper is unpredictability of the stimulus, for example, the numbers “1, 2, 3” in one ear and “7, 8, 9” in the other. Monosyllables are preferable to common stock questions such as “How are you?” in which hearing a small part may enable the patient to “hear” the rest in context. Alternating words and numbers is a challenging test of hearing.

Tuning forks—typically 128, 256, or 512 Hz—are sometimes used to give more specific information and to assess air conduction (AC) and bone conduction (BC). When testing AC, the tuning fork should be kept in gentle motion to avoid null points. The patient may be asked to compare the loudness of the vibrating fork in the two ears, or the examiner may compare the distance on each side at which the fork begins or ceases to be heard. The gradual dampening of the oscillations makes precision difficult. The examiner with good hearing may compare the patient’s AC and BC with his own (Schwabach test). In evaluating BC, be certain the patient hears rather than feels the tuning fork. How useful tuning fork tests are for general screening has been questioned. But the primary usefulness of both the Weber and Rinne tests (see below) is not as a screening tool but to make an initial differentiation between SNHL and CHL in a patient complaining of unilateral symptoms of hearing loss or tinnitus.

The Rinne test compares the patient’s AC and BC; it can be done in at least two ways. An activated fork may be placed first on the mastoid process and then immediately beside the ear (or vice versa), and the patient is asked which is louder; it should always be louder by the ear. The more time-consuming, traditional method is to place the tuning fork on the mastoid and when no longer heard there move it beside the ear, where it should still be audible. The fork should be heard twice as long by AC as by BC. The Rinne test is normal or positive when AC is better than BC either by subjective assessment of loudness or by the length of time the tuning fork is heard in the two locations. In CHL, BC is better than AC, and the Rinne test is said to be negative. Sound is not conducted normally through the canal or from the tympanic membrane through the ossicular chain to the cochlea, but the sensorineural mechanisms are intact; AC is impaired but BC is preserved. In CHL, BC may even be exaggerated beyond the normal because the middle ear cavity becomes a resonating chamber. In sensorineural deafness, both AC and BC are impaired while retaining their normal relationship of AC better than BC; the Rinne test is positive or normal. With severe sensorineural deafness, BC may be lost whereas slight AC is preserved. Because of inconsistent use of the terms positive and negative, it is

preferable to state that AC is better than BC or that the Rinne test is normal.

In the Weber test, a vibrating tuning fork is placed in the midline on the vertex of the skull. It may be placed anywhere in the midline, over the nasal bridge, the forehead, or the maxilla but works best over the vertex. Normally, the sound is heard equally in both ears or seems to resonate somewhere in the center of the head; it is “not lateralized.” In CHL, the sound is heard better (“lateralized”) to the involved side. A simple way to remember this phenomenon is for the examiner to place a tuning fork over his own vertex and then induce conductive loss by inserting a finger in one ear; the sound will be louder on the side of the occluded canal. In sensorineural deafness, the sound is heard best in the normal ear.

In summary, with unilateral CHL, AC is less than BC (the Rinne test is negative), and the Weber lateralizes to the involved side. In unilateral SNHL, AC is greater than BC (Rinne test positive or normal), and the Weber lateralizes to the normal side ([Table 17.1](#)).

Auditory reflex responses are occasionally useful in evaluating hearing in children, patients with altered mental status, and in hysteria or malingering. The auditory-palpebral reflex is a blink or reflex eye closure in response to a loud, sudden noise. The cochleopupillary reflex is pupillary dilatation, or contraction followed by dilatation, in response to a loud noise. The auditory-oculogyric reflex is eye deviation toward a sound. The general acoustic muscle reflex is a general jerking of the body in response to a loud, sudden noise.

TABLE 17.1

Rinne and Weber Tests

Normally, the auditory acuity is equal in both ears, air conduction is greater than bone conduction (Rinne test normal or positive) bilaterally, and the Weber test is nonlateralizing (midline). The table depicts the pattern on the involved side with *unilateral* conductive or sensorineural hearing loss.

Auditory Acuity	Rinne Test	Weber Test
Conductive hearing loss	Decreased BC > AC (Rinne negative or abnormal)	Lateralizes to the abnormal side

Sensorineural hearing loss	Decreased AC > BC (Rinne positive or normal)	Lateralizes to the normal side
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The laboratory evaluation of hearing is done primarily by electronic audiometry and auditory evoked potentials. These are discussed in [Box 17.2](#).

Disorders of Function

Dysfunction of the cochlear nerve and its connections usually causes either diminution or loss of hearing (hypacusis or anacusis), with or without tinnitus. Hyperacusis occurs most often with paralysis of the stapedius muscle in disorders affecting CN VII, but it may occur as an epileptic aura, in migraine (sonophobia or phonophobia), and in certain psychiatric conditions and drug-related disorders. Dysacusis is impairment of hearing that is not primarily a loss of auditory acuity; rather, it is related to dysfunction of the cochlea or central auditory pathways. Diplacusis is a condition in which there is a difference in the pitch or intensity of the same sound as heard in the two ears or when a single sound is heard as having two components; it is usually due to disease of the cochlea. Paracusis is perversion or distortion of hearing. Paracusis of Willis (paracusis Willisi) is an interesting phenomenon in which the ability to hear improves in the presence of loud noises. Thomas Willis described a patient who heard better when a drum was beating loudly nearby. It is a feature of otosclerosis. Disturbances of hearing because of central nervous system (CNS) lesions are rare.

CHL is due to interference with the transmission of sound to the cochlea. SNHL is due to disease of the cochlea or its central connections. In essence, CHL is due to disease external to the oval window, and SNHL is due to disease central to the oval window. With CHL, there is primarily loss of AC; BC is preserved or even exaggerated ([Table 17.1](#)). The Weber is referred to the involved side. Low tones are lost, as are some of the broad or flat consonants and vowels such as m, n, l, r, o, and u. Impairment of speech discrimination parallels the loss for pure tones. There is no recruitment, and tone decay is normal. Patients with CHL tend to hear speech better in a noisy background than in a quiet setting. Mixed hearing loss, with elements of both CHL and SNHL, is not uncommon. Some causes of hearing loss are listed in [Table 17.2](#).

With unilateral SNHL, AC and BC are both diminished, but AC remains better than BC ([Table 17.1](#)) and the Weber lateralizes to the normal ear. The

hearing loss is worse for higher frequencies (Figure 17.9), and there is greater difficulty with sibilants, sharp consonants, and short vowels (e.g., in the words sister, fish, twenty, water, and date). A clearly enunciated whisper is sometimes more easily understood than a loud, indistinct shout.

TABLE 17.2

Causes of Hearing Loss

Conductive hearing loss

External auditory canal obstruction (e.g., cerumen, foreign bodies, water, blood)

Perforation of the tympanic membrane

Disease of the middle ear

Disease of the nasopharynx with obstruction of the eustachian tube

Sensorineural hearing loss

Disease of the cochlea

Acoustic trauma

Ménière's disease

Infections

Congenital conditions (e.g., congenital rubella)

Presbycusis

Disease of the cochlear nerve or nuclei

Tumors (e.g., acoustic neuroma)

Trauma (e.g., skull fracture)

Infection (meningitis, syphilis)

Toxins or drugs

Presbycusis

Nuclear lesions (e.g., vascular, inflammatory, or neoplastic)

Lesions of the central auditory pathways

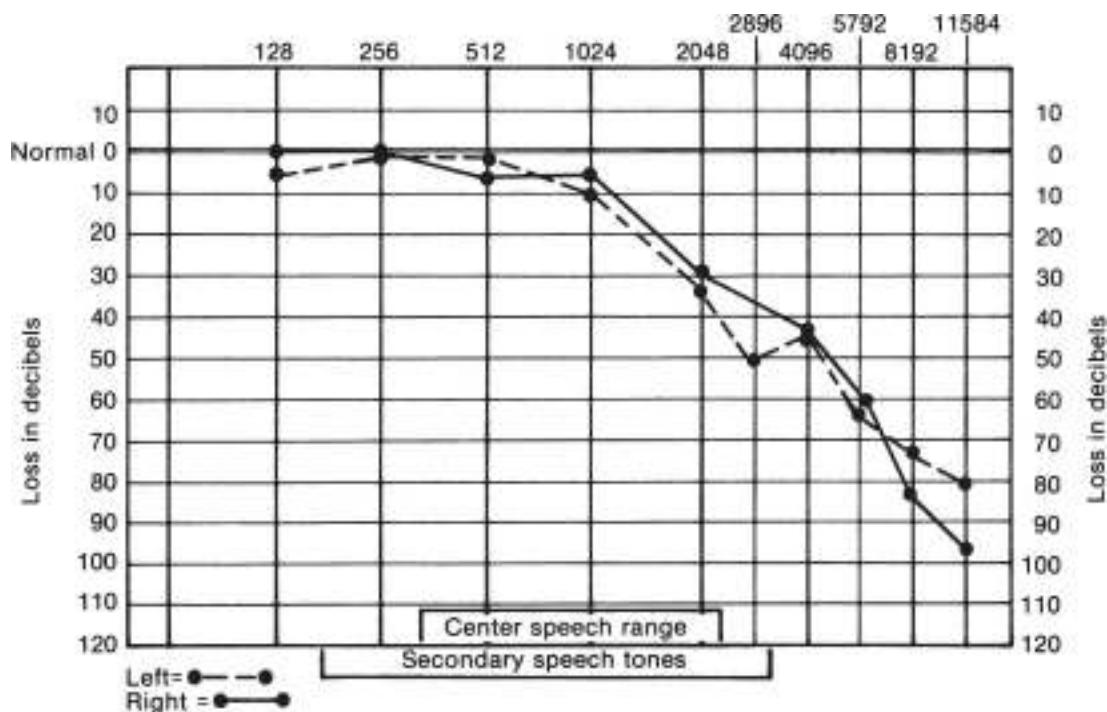


FIGURE 17.9 Audiogram of a patient with sensorineural deafness.

SNHL may be due to disease of the cochlea (end-organ deafness), such as in Ménière's disease, or to disease of CN VIII or more central structures (retrocochlear), as in acoustic neuroma. Typical of cochlear disease is loss of acuity for pure tones with a parallel impairment of speech discrimination, recruitment, and tone decay. Recruitment is an abnormal loudness of sounds because of cochlear dysfunction, which can cause a paradoxical increase in the perception of louder sounds, sometimes accompanied by sound distortion. Recruitment occurs when there is a reduction in the number of hair cells, which causes a loss of the ability to process fine gradations in sound intensity. A small increase in intensity causes an abnormally large recruitment of nerve fibers responding, and the sound is perceived as abnormally loud. Tone decay measures auditory adaption by assessing the ability to maintain the perception of a pure tone continuously. Tone decay does not occur with cochlear lesions. Retrocochlear lesions tend to cause a loss of speech discrimination out of proportion to the loss for pure tones, no recruitment, and abnormal auditory adaptation by tone decay. There is a debate about the existence of a syndrome of purely cochlear Ménière's disease.

SNHL may be bilateral and slowly progressive, as with presbycusis or exposure to ototoxic drugs, for example, aminoglycoside antibiotics or loop diuretics. Gabapentin may cause reversible hearing loss in patients with renal

insufficiency. SNHL may be unilateral and progressive, as in Ménière's disease or acoustic neuroma. It may be unilateral and relatively sudden, over hours to days, in vascular disease (e.g., internal auditory artery [IAA] occlusion), viral infection, or autoimmune hearing loss. The syndrome of sudden, unilateral SNHL is due to dysfunction involving the cochlea or CN VIII with variable, often poor, recovery. The pathogenesis is unknown; autoimmunity, viral infection, and vascular disease are suspected etiologies. The IAA may arise from the anterior inferior cerebellar artery (AICA) or directly from the basilar. Isolated IAA ischemia causes hearing loss often associated with vestibular dysfunction. Ischemia in the AICA distribution produces other CNS manifestations (see [Chapter 21](#)).

The cochlear and vestibular nerves run together in a common sheath from the brainstem to their respective end organs, and disorders of the eighth nerve between the cochlea and brainstem may cause hearing loss. Some disease processes affect both divisions peripherally (e.g., labyrinthitis) or centrally (e.g., brainstem neoplasm). In its course across the CPA, the most important disorder to affect both divisions is a neoplasm. Acoustic neuroma (acoustic neurinoma, acoustic schwannoma) is most common, but neurofibroma, meningioma, facial nerve schwannoma, cholesteatoma, epidermoid cyst, and other tumors may arise here as well. Acoustic neuromas usually present with insidious, progressive hearing loss; rarely, sudden deafness may occur, sometimes as the presenting manifestation, presumably because of intratumoral hemorrhage or IAA ischemia. Vague disequilibrium and imbalance are more common symptoms than true vertigo. Subsequent manifestations depend on the direction of tumor extension. With anterior extension, CNs V and VI are involved. With inferior extension, CNs IX, X, and XI are involved. CN VII is commonly affected in either case, causing all the signs of a far proximal lesion (see [Chapter 16](#)). With medial extension, there is mass effect on the brainstem and cerebellum, often leading to ipsilateral ataxia and evidence of increased intracranial pressure. Other conditions of CN VIII that may cause hearing loss include toxins; superficial siderosis; postinflammatory scarring, as from meningitis; and hereditary conditions. Other conditions that may cause both hearing loss and vertigo include Ménière's disease, labyrinthitis, viral infection (especially herpes), trauma, meningitis, vascular occlusion (internal auditory or anterior inferior cerebellar), Susac's syndrome, Cogan's syndrome, Fabry's disease, perilymphatic fistula, toxins, and drugs.

Lesions of the central auditory pathways (brainstem and central connections)

rarely cause clinical loss of hearing, although detailed audiometric testing and BAERs may show abnormalities. However, midbrain lesions or tumors of the posterior third ventricle—or the aqueduct region with compression of either the medial geniculate bodies or the inferior colliculi—may cause bilateral hearing deficits, presumably because the auditory pathways run close together in this region. Impairment of sound localization contralateral to a temporal lobe lesion has been described. Wernicke's aphasia is characterized by the inability to interpret or comprehend spoken words despite normal hearing; it may occur with dominant temporal lobe lesions. Pure word deafness follows bilateral damage to the posterior-superior temporal lobes bilaterally, causing an inability to comprehend speech with intact hearing and reading. Other cortical syndromes involving hearing include auditory agnosia, amusia, and disturbances in the temporal analysis of sounds.

Pseudohypacusis refers to hearing loss in the absence of any organic disease or hearing loss that is exaggerated. It is more common for real hearing loss to be exaggerated in severity than for it to be feigned with entirely normal hearing. The mainstay of diagnosis is inconsistency in the performance on hearing tests and the absence of verifiable abnormalities on objective tests. A diagnosis of pseudohypacusis is easier to establish in children because they are less able to reproduce factitious abnormalities on repeated testing.

Nonorganic hearing loss may be partial or total and unilateral or bilateral. It is often bilateral and total, and the patient makes no attempt to hear what is said or to read the speaker's lips. In most instances, it is a transient symptom related to acute emotional stress. Psychogenic hearing loss may be associated with other nonorganic symptoms, such as mutism and blindness. When there are also nonorganic motor and sensory disturbances, the hearing loss is usually incomplete and on the same side. In malingering, the deafness is usually unilateral and occurs after trauma in the face of potential secondary gain. Organic posttraumatic hearing loss is typically associated with impairment of vestibular function. Normal labyrinthine responses suggest the claimed hearing loss is either simulated or exaggerated. Inconsistent responses on bedside hearing tests suggest nonorganicity. Discrepancies and inconsistencies on repeated audiometric examinations are typical. The BAER is normal.

Patients simulating bilateral deafness do not behave as a deaf person does. Deaf individuals usually raise their voices during conversation and keep their eyes fixed on the speaker's face and lips, watching for any gesture that may help understanding. A deaf man eager to hear will automatically turn his best ear

toward the speaker. Experienced lip readers have difficulty with sound-alike words; the dissembler may do better than expected because the words are actually heard. Many tests have been devised for detection of nonorganic deafness. The diagnosis is best made audiometrically.

Tinnitus

Tinnitus is spontaneous noise in the ears originating inside the head. There are many types, and the causes are protean. In many cases, no precise etiology can be established. The most common identifiable cause is noise exposure, either acute or chronic. Objective tinnitus refers to noise audible to both the patient and the examiner, as occurs in carotid stenosis. Most tinnitus is subjective tinnitus. It may vary in pitch and intensity and may be continuous or intermittent. It may be described in many ways, such as ringing, buzzing, blowing, whistling, swishing, or roaring. Tinnitus is commonly associated with deafness. It is common in presbycusis and in other types of SNHL and is a fairly constant feature of otosclerosis. It is caused by the abnormal excitation of the auditory apparatus or its afferent pathways, but the exact mechanism is often unclear. Most cases are due to disease of the cochlea or eighth nerve; some are due to CNS disease. Tinnitus is often more noticeable at night when environmental noises are diminished, and it may interfere with sleep. To the patient, tinnitus may be more distressing than the accompanying deafness, and it may cause depression in elderly individuals.

Pulsatile tinnitus is synchronous with the pulse; it is in reality a bruit. Causes include carotid stenosis; arteriovenous malformations, particularly of the dura; glomus tumors; venous hums; and hypertension. Pulsatile tinnitus is fairly common in pseudotumor cerebri, and it occurs occasionally in increased intracranial pressure of other origins. The perilymphatic duct connects the perilymph-filled spaces of the cochlea and an extension of the subarachnoid space in the region of the jugular foramen. Through this channel, pulsations in the subarachnoid space are transmitted to the cochlea. Vascular tinnitus may occasionally be affected by carotid artery compression. Rhythmic tinnitus not synchronous with the pulse may occur with palatal myoclonus (palatal microtremor). Gaze-evoked tinnitus is tinnitus associated with eye movements; it may be due to abnormal communications between the cochlear and vestibular nuclei.

Other causes of tinnitus include cerumen impaction, medications (particularly

ototoxic drugs), Ménière's disease, acoustic neuroma, acute or chronic acoustic trauma, Paget's disease, anemia, labyrinthitis, and Arnold-Chiari malformation. Muscle spasm, contraction of the tensor tympani, nasopharyngeal sounds, and temporomandibular joint clicking may also simulate tinnitus. Tinnitus may be psychogenic. Bizarre types of tinnitus may occur with pontine and cerebral lesions. Auditory hallucinations may occur in lesions of the temporal lobe; these are frequently epileptic auras. More bizarre hallucinations occur in psychotic and drug-induced states. Tinnitus that is unilateral, pulsatile, fluctuating, or associated with vertigo is more likely to indicate a serious underlying condition.

The Vestibular Nerve

The vestibule of the labyrinth connects with five structures that are involved in vestibular function: the utricle, the saccule, and the three semicircular canals. Each of these components lies in the membranous labyrinth, is bathed in endolymph, and contains sensory neuroepithelium. The sensory epithelium consists of cells bearing microvilli, which are referred to as hair cells. The hair cells are the peripheral receptors of the vestibular apparatus. Each hair cell bears a single long kinocilium and an array of shorter stereocilia. The cilia are imbedded in the maculae of the utricle and saccule and in the cupulae of the semicircular canals. Movement of the macula or cupula bends the cilia. Endolymph flows throughout the membranous labyrinth. Changes in endolymph flow in response to external forces or head movement, as well as the effects of gravity and changes in head position, affect neural impulses arising from the areas of sensory epithelium. This is the substrate for vestibular function.

The hair cells function as transducers, converting mechanical deformation of their cilia into receptor potentials. Because of the location of the stereocilia and the kinocilium, each hair cell is structurally polarized. The orientation of each individual hair cell and the arrangement of its microvilli determine its functional response to mechanical stimuli. The cilia contain actin filaments. Bending of the cilia in a specific direction causes the cell to become either depolarized or hyperpolarized. Bending in the opposite direction causes the opposite response. Deformation causes ion fluxes in mechanically sensitive channels in the cilium. Calcium influx because of mechanical deformation depolarizes the cell and causes release of neurotransmitter. A few channels remain open even in the erect cilia, which produces a moderate level of tonic activity in the vestibular system. The receptors send signals by increasing or decreasing this tonic discharge.

The utricle and saccule constitute the otolith organ and are referred to as the static labyrinth. It is designed to detect gravitational effects and linear acceleration and to monitor head position. The utricle is an oblong sac that extends from the posterior-superior portion of the vestibular part of the membranous labyrinth ([Figure 17.3](#)). The saccule is a smaller expansion that lies near the opening of the scala vestibuli of the cochlea. The utriculosaccular duct connects the saccule to the utricle and endolymphatic duct, and the ductus reuniens connects it to the cochlea. The osseous ampulla of a semicircular canal is a bulbous expansion at the point where the canal joins the vestibule, and it is about twice the diameter of the rest of the canal ([Figure 17.2](#)). The semicircular ducts are membranous labyrinth tubules that follow the semicircular canals in the same way the cochlear duct follows the spirals of the cochlea. The ampullae of the ducts open off the utricle.

The utricle and saccule each contain a macule. Covering the maculae is a gelatinous layer, the otolithic or statoconial membrane. Embedded in the otolithic membrane are millions of crystals, the otoliths (statoliths, otoconia, or statoconia). The utricle and saccule respond to linear acceleration and to gravity because of the mass of the otoliths. They monitor the position of the head and movement of the head in relation to gravity. In the ampulla of each semicircular canal is a gelatinous structure called a cupula. The canals do not respond to gravity because there are no otoliths in the semicircular canals and because the cupula has the same specific gravity as the endolymph. Instead, movement of the head causes endolymph to flow, which displaces the cupula and stimulates or inhibits the hair cells.

The macula of the utricle lies horizontally in the floor of the utricle, parallel to the skull base. The macula of the saccule lies vertically in the wall of the saccule. Hair cells are oriented in every conceivable direction. Bending of the cilia either depolarizes or hyperpolarizes the cell, depending on the direction of movement. Because of the multidirectional orientation of the hair cells and the geometry of the maculae, head movement in any direction can be detected. Because of its orientation, the macula of the utricle responds maximally to head movement in the sagittal plane, whereas the macula of the saccule responds maximally to head movement in the coronal plane.

The semicircular canals are the kinetic or dynamic labyrinth and are designed to detect angular acceleration or rotation. The crista ampullaris, or ampillary crest, is a focal thickening in the membrane lining the ampullae of the semicircular canals. The cristae are covered with the sensory neuroepithelium of

the canals. The tips of the cilia of the hair cells are imbedded in the cupula, which forms a dome-shaped cap over the cristae. When rotation of the head occurs, the endolymph lags behind, tilting the cupula and affecting the neural discharges in the hair cells of the cristae.

The semicircular canals are designed to detect rotation. Their orientation in three perpendicular planes and their oval structure guarantee that head movement in any direction will be detected. The three canals are the horizontal (lateral), vertical (anterior or superior), and posterior (inferior). The labyrinth is imbedded deep in the petrous ridge. In turn, the petrous ridge is set at an angle of about 45 degrees from the sagittal plane of the skull. The canals are named because of their anatomical relationships to the labyrinth and to each other, more so than their relationship to the skull. Different names for the same canal compound the difficulty. The following is a useful approximation for the orientation of the canals. The horizontal canal lies horizontally; the anterior and posterior canals stand vertically. The horizontal canal is convex laterally, and it is also called the lateral canal; it actually slants downward from anterior to posterior at an angle of about 30 degrees. The posterior canal arcs posteriorly parallel to the long axis of the petrous bone, toward the base of the petrous pyramid. The anterior canal lies perpendicular to the long axis of the petrous bone, anterior to the other canals, and toward the apex of the petrous bone. In addition, it extends above the other canals and is also known as the superior canal. If the head is placed forward 30 degrees, the lateral canals are horizontal and the vertical canals are vertical.

The canals are maximally stimulated by movement in the plane of their anatomical axis. The horizontal canal best detects rotational head movement in the side-to-side (“no-no”) direction (with the chin tucked to bring the canal fully horizontal). The posterior canal best detects movement in the anteroposterior plane (“yes-yes”), and the anterior canal is oriented to detect lateral tilting movement. The canals on the two sides have been said to form functional pairs. The horizontal canals work together. The anterior canal of one side is approximately parallel to the posterior canal on the opposite side, forming a spatial pair. How closely these angles actually match has been questioned.

The hair cells of both the maculae and the cristae produce a tonic discharge in the vestibular nerve. The discharge rate increases and decreases in response to the bending of the hair cells. Endolymph flow toward the utricle is excitatory. Normally, the two labyrinths are in balance, with symmetric activity in the two vestibular nerves and reciprocal changes induced by head movement. When this

balance is disturbed, the clinical signs and symptoms of vestibulopathy follow.

Afferent impulses from the hair cells travel centrally via the peripheral processes of bipolar neurons in the vestibular (Scarpa's) ganglion in the internal acoustic meatus. Central processes of the vestibular ganglion cells form the vestibular nerve. There are three peripheral divisions of the vestibular nerve, which arise from different portions of the labyrinth. These join to form the vestibular nerve proper ([Figure 17.6](#)). The vestibular component of CN VIII joins the cochlear component in a common sheath; the vestibular component is the larger of the two. The nerve passes through the IAC in company with the facial nerve and the nervus intermedius. It crosses the cerebellopontine angle and enters the brainstem between the inferior cerebellar peduncle and the olive. The cochlear nerve is slightly lateral and caudal to the vestibular component. Within the IAC, CN VIII is lateral and inferior to CN VII. At the pontomedullary junction, CN VIII is slightly lateral and posterior to CN VII.

Entering vestibular fibers pass between the inferior cerebellar peduncle and the spinal tract of CN V. They divide into ascending and descending branches that end primarily in the four vestibular nuclei: lateral, medial, superior, and inferior ([Figure 17.10](#)). The vestibular nuclei lie in the rostral medulla and caudal pons. Some fibers form the vestibulocerebellar tract and pass directly to the cerebellum, without synapsing in the vestibular nuclei, in the juxtarestiform body. The medial (Schwalbe's) vestibular nucleus is the largest subdivision of the vestibular nuclear complex, extending from the medulla into the pons. It lies in the floor of the fourth ventricle, beneath the striae medullares. The inferior (descending, spinal, Roller) nucleus lies lateral to the medial, between the medial nucleus and inferior cerebellar peduncle, and descends further inferiorly to reach lower medullary levels. The lateral (Deiters') and superior (Bechterew's) subnuclei are smaller than the medial and inferior. The lateral nucleus is lateral to the rostral end of the medial nucleus. The superior nucleus extends higher into the pons than other subdivisions, forming a cap on the nuclear complex. Vestibular afferents to the superior and medial subnuclei arise predominantly from the semicircular canals and less so from the otolith organs. Afferents to the lateral and inferior subnuclei arise predominantly from the otolith organs and less so from the semicircular canals. The vestibular nuclei also receive afferent cerebellovestibular fibers through the juxtarestiform body (part of the inferior cerebellar peduncle), primarily from the flocculonodular lobe, as well as afferents from the spinal cord and reticular formation.

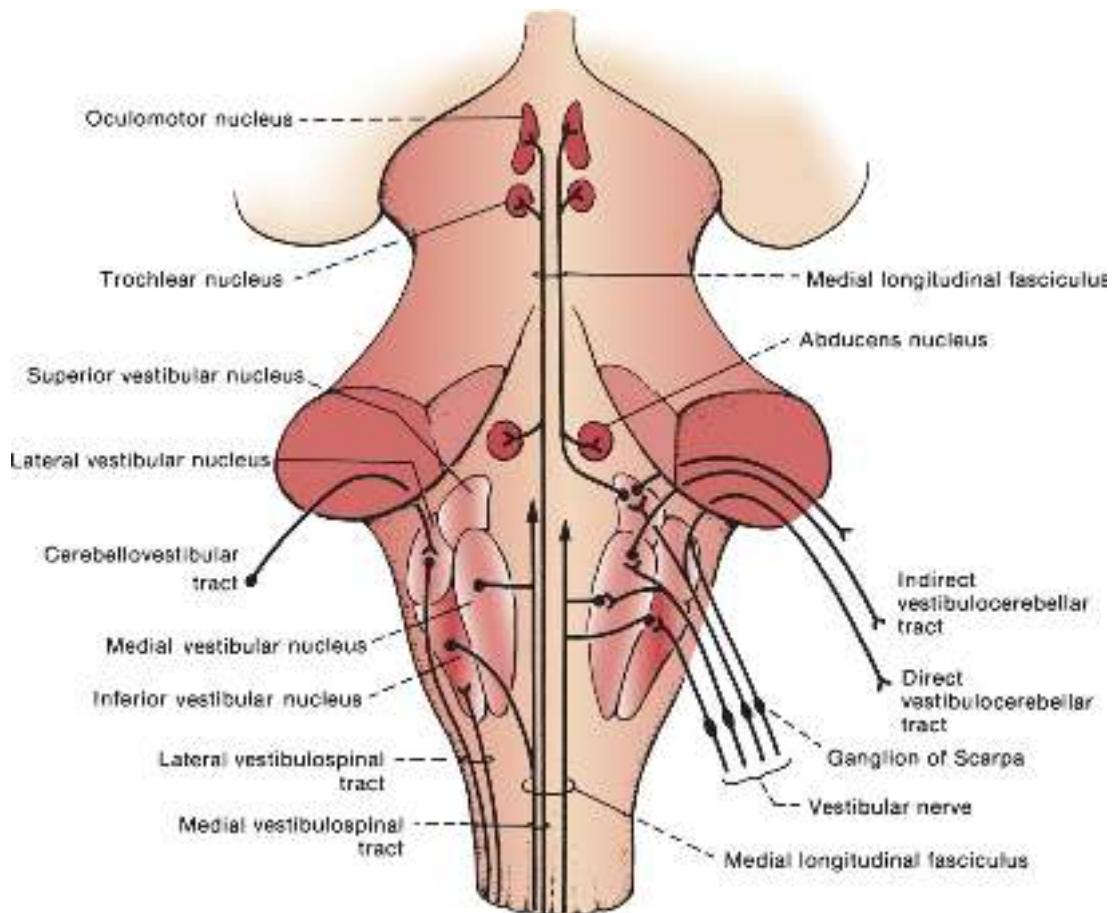


FIGURE 17.10 The vestibular pathway.

The vestibular nuclei make connections with four primary areas: cerebellum, spinal cord, oculomotor system, and cortex. The juxtarestiform body is a collection of fibers medial to the inferior cerebellar peduncle (restiform body). Vestibulocerebellar fibers run through the juxtarestiform body and form part of the mossy fiber input to the cerebellum. The direct (primary) vestibulocerebellar tract bypasses the vestibular nuclei; its fibers terminate primarily in the ipsilateral nodulus, uvula, and fastigial nucleus. The indirect (secondary) vestibulocerebellar fibers arise from the superior, medial, and inferior nuclei and terminate primarily in the flocculus bilaterally and in the same areas that receive the direct vestibulocerebellar input. The vestibular nuclei also receive fibers from the cerebellum. The fastigial nucleus of the cerebellum connects with the vestibular nuclei by the uncinate fasciculus (hook bundle of Russell), which is the major outflow of the fastigial nucleus. The uncinate fasciculus forms a distinctive arc over the superior cerebellar peduncle and then descends in the juxtarestiform body to enter the vestibular nuclei. Multiple areas of the cortex

receive vestibular input, and there is probably no primary vestibular cortex.

All four vestibular subnuclei may send fibers into the medial longitudinal fasciculus (MLF), but the vast majority of the ascending fibers arise from the superior and medial nuclei. This pathway, through connections with the nuclei of CNs III, IV, and VI, and the nuclei of CN XI and upper cervical nerves, is important in regulating movements of the eyes, head, and neck in response to stimulation of the semicircular canals. Fibers from the superior and medial nuclei form the indirect vestibulocerebellar pathway, and the medial nucleus receives cerebellar input through cerebellovestibular fibers.

Fibers from the lateral and inferior vestibular nuclei go down the ipsilateral spinal cord as the lateral vestibulospinal tract, which is important in the regulation of muscle tone and posture by increasing extensor muscle tone, particularly of the trunk. Impulses from the medial vestibular nuclei descend to the cervical and upper thoracic spinal cord through the crossed medial vestibulospinal tract. The inferior nucleus sends bilateral projections into the descending MLF and also provides vestibular input to the cerebellum. The vestibular nuclei also have connections with the reticular formation and through this with the dorsal efferent nucleus of the vagus and with the spinal cord. They also send efferent fibers back to the vestibular ganglion. Ascending vestibular connections extend rostrally to the ventrolateral and ventral posterior thalamic nuclei and from the thalamus to the somatosensory cortex to provide conscious perception of head position and movement. There are also projections to the posterior portion of the superior temporal gyrus that are important in vestibulo-ocular function.

Vestibular Physiology

The utricle and saccule respond to linear acceleration, whereas the semicircular canals respond to angular acceleration. These responses are mediated by hair cells and transmitted to the vestibular ganglion and subsequently to the vestibular nuclei. Under normal circumstances, the neural activity in the labyrinths is equal on both sides. It is convenient to visualize the action of each vestibular system as “pushing” toward the opposite side. When the two labyrinths push equally, the system is in balance and function is normal. When one labyrinth is underactive, the opposite labyrinth pushes the eyes, extremities, and body toward the side of underactivity. The clinical manifestations of vestibular dysfunction include vertigo, oscillopsia, nausea, vomiting, nystagmus,

past pointing, and lateropulsion.

Nystagmus results from a corrective saccade initiated by the frontal eye fields in response to the deviation of gaze toward the side of the less active labyrinth. The fast component of the nystagmus is therefore in the opposite direction from the hypoactive labyrinth. Without visual information to correct for errors (i.e., with eyes closed), patients with an acutely hypoactive labyrinth will have deviation of their extremities toward the underactive side on finger-to-nose testing. When attempting to walk with eyes closed, they will drift toward the side of the hypoactive labyrinth. On the Unterberger-Fukuda stepping test, they will turn toward the hypoactive side.

When both labyrinths are diseased or malfunctioning, as might occur, for example, with ototoxic drug effects, there is no vestibular imbalance and hence no nystagmus, vertigo, past pointing, and the like. Patients with bilateral labyrinthine disease may nonetheless have great difficulty with balance and equilibrium.

TABLE 17.3

Some Causes of “Dizziness”

Symptom Description	Characteristics	Possible Etiologies
Vertigo (spinning, whirling, tilting, falling)	Illusion of motion of self or environment	Dysfunction of the vestibular system, peripheral or central
Disequilibrium (poor balance but not “dizzy”)	Impaired balance, unsteady gait	Bilateral vestibular dysfunction; deafferentation (peripheral neuropathy, posterior column disease); brainstem lesion; cerebellar lesion; extrapyramidal disorder; drug effects
Presyncope (light-headed, drunk, woozy, faint)	Light-headedness; often with systemic symptoms (e.g.,	Global cerebral hypoperfusion (numerous causes)

	diaphoresis, nausea, graying of vision) inciting event	
Multiple sensory deficits	Elderly patient, vague complaints, difficulty walking	Multiple concurrent problems
Ill defined	Histrionic but vague description and nonspecific complaints	Psychogenic

Clinical Examination

Dr. W. B. Matthews said, “There can be few physicians so dedicated...that they do not experience a slight decline in spirits when they learn that their patient’s complaint is giddiness.” The conditions that may present as dizziness range from trivial to life threatening and are often difficult to evaluate and manage. The nebulousness of the patient’s description of dizziness often produces frustration on the part of the clinician, yet in few other conditions are the historical details so pivotal in correct diagnosis. Fortunately, the truly serious conditions that present as dizziness are rare.

Evaluation of the dizzy patient is a very common clinical exercise, and much has been written on the subject. A careful appraisal of the patient’s symptoms is often helpful, but even the skilled clinician is sometimes unsure after hearing the patient’s complaints. The first step in understanding the symptom is to have the patient describe what he means by “dizziness.” Patients use the word dizzy to describe vertigo, as well as a number of other sensations, such as light-headedness or giddiness, sometimes referred to as pseudovertigo. Concomitant dysfunction in several systems may cause dizziness. Conflicting sensory information may certainly cause dizziness; the sensory mismatch from watching a motion picture with dramatic movement in the visual panorama while sitting in a stationary seat illustrates the effect. Simply looking down from a height can cause a sense of dizziness (the subject of the Alfred Hitchcock movie *Vertigo*). It

is important to determine if there are concomitant auditory symptoms; their presence changes the differential diagnosis dramatically.

In a study of 100 dizzy patients in an ambulatory setting, the causes were as follows: vestibulopathy (54), psychiatric disorders (16), multifactorial (13), unknown (8), presyncope (6), disequilibrium (2), and hyperventilation (1). The most common treatable conditions were benign positional, or benign paroxysmal positional vertigo (BPPV), and psychiatric disorders. Other studies have shown a similar distribution. Some of the causes of dizziness are listed in [Table 17.3](#). [Table 17.4](#) lists causes of dizziness because of labyrinthine or vestibular pathway dysfunction. Before discussing vestibular disease, some discussion of nonspecific dizziness is warranted, because patients with such complaints make up a large proportion of the dizzy population.

TABLE 17.4

Some Common Causes of Vertigo

Otologic disorders

Benign paroxysmal positional vertigo

Ménière's disease

Vestibular neuronitis

Neurologic disorders

Migraine-associated vertigo

Vertebrobasilar ischemia

Cerebral hypoperfusion produces a sensation of light-headedness, drunkenness, or impending syncope without spinning, whirling, or any illusion of environmental motion. Such hypoperfusion may occur under a variety of circumstances, all of which may lead the patient to seek medical attention because of "dizziness." In hyperventilation syndrome, hypocapnia-induced cerebral arterial constriction and the resultant hypoperfusion induce light-headedness along with other symptoms, such as chest pain; headache; numbness and tingling of the hands, feet, and circumoral region; and occasionally outright syncope. Frequently, patients are unaware of their overbreathing, but the high minute volume of respiration produces dryness of the mouth, which the patient may describe spontaneously or respond to on specific questioning. Induced hyperventilation may reproduce the symptom complex. Hyperventilation may also induce nystagmus in patients with acoustic neuroma. Orthostatic hypotension because of drugs, prolonged standing, dehydration, increased vagal

tone, or dysautonomia likewise may present as light-headedness or faintness. Accompanying symptoms are few, and only a careful history eliciting the relationship of the dizziness to posture will make the diagnosis. Global cerebral hypoperfusion may also result from decreased cardiac output via any number of mechanisms; arrhythmia is the primary concern.

Elderly patients “deafferented” because of separate disease processes affecting different sensory systems may present with complaints of vague dizziness, unsteadiness, and difficulty with balance, particularly when turning (multiple sensory defect vertigo). Patients can apparently tolerate problems with any one afferent system, but when multiple systems are involved, imbalance and dizziness result. Thus, patients typically will suffer from various combinations of poor vision (e.g., cataracts, macular degeneration), poor hearing (presbycusis), mild peripheral neuropathy, and cervical spondylosis. The term presbylibrium has been applied to poor balance because of aging.

Numerous terms have been employed to describe the clinical phenomenology of vestibular disease; not all are helpful. Vertigo is the sensation of environmental motion (spinning, whirling, lateropulsion, tilt). The term “true vertigo” is sometimes used to describe this symptom. When true vertigo is present, the problem is usually an acute peripheral vestibular disturbance. Objective vertigo creates the sensation that the environment is spinning, whereas subjective vertigo creates the sensation that the patient is spinning. The absence of true vertigo does not exclude peripheral vestibular disease, especially if bilateral pathology exists, such as in ototoxicity because of drugs. Central vertigo is due to CNS disease; peripheral vertigo is due to disease of the peripheral vestibular apparatus or its connections. Patients with CNS lesions may not have true vertigo. Patients with true vertigo, especially when due to a peripheral lesion, often experience vegetative symptoms such as nausea and vomiting, because of projections to the medullary vomiting centers, pallor, and sweating. Acoustic neuroma causes a gradual unilateral loss of vestibular function and is more prone to cause imbalance than true vertigo. Some other serious conditions may present as dizziness without true vertigo, such as cardiac dysrhythmias and dysautonomic orthostasis. Physicians should not make too much of the presence or absence of true vertigo in judging how seriously to take a patient’s complaint of dizziness.

Dizziness may be present constantly or intermittently. If intermittent, as in BPPV, one of the most common causes of dizziness, the episodes may occur so frequently that the initial description may lend the impression the symptoms are

constant. If the episodes are intermittent, the duration of the attacks is important. Attack duration is one of the most important features in distinguishing between central and peripheral vertigo. In vertigo due to BPPV, the attacks last 10 to 30 seconds; in other peripheral vestibulopathies, such as Ménière's disease, the attacks last hours; and in vertebrobasilar insufficiency, the episodes last for minutes. Exploring the precipitating factors is very helpful. Dizziness may be provoked by head or body movement, standing, or lying down or occur spontaneously. The presence of associated symptoms, such as nausea, vomiting, staggering, deviation of the eyes, oscillopsia, disturbances of balance, prostration, tinnitus, hearing loss, autophony (perception of the reverberation of patient's own voice), or loss of consciousness, is important. [Table 3.8](#) reviews some of the pertinent history to explore in a dizzy patient.

Useful bedside testing of vestibular function includes assessment of vestibulospinal reflexes (past pointing, Romberg, Unterberger-Fukuda stepping test), tests of vestibulo-ocular reflexes (VORs) (oculocephalic reflex, head thrust [head impulse] test, dynamic visual acuity, and caloric responses), and searching for nystagmus (spontaneous, positional, or after head shaking). For vestibular tests of ocular function, patients should wear their customary correction. In recalling the expected pattern of responses to some of these, remember that the vestibular system tends to push (eyes, limbs, and body) to the opposite side; when the system is in balance, the eyes are midline and the limbs and body can accurately find a target. When disease is present, the involved labyrinth is usually hypoactive and the uninvolved labyrinth pushes toward the abnormal side. This can be simulated in a normal volunteer with minicalorics, the instillation of 2 to 5 mL of ice water into one ear. Cold irrigation mimics an acute destructive lesion, and for a brief time thereafter, the subject will display the same clinical findings seen in a patient with an acute peripheral vestibulopathy (APV). The caloric demonstration is a useful teaching exercise for a group of trainees. It is also enlightening to do bilateral cold calorics to demonstrate that when both labyrinths are not functioning, normally the affected individual is still quite impaired, despite the lack of labyrinthine imbalance. The bedside tests of vestibular function are listed in [Table 17.5](#).

A systematic examination of the dizzy patient is in use at Washington University that only requires 10 minutes in experienced hands. The components are (a) observation for spontaneous and gaze-evoked nystagmus and fixation suppression; (b) evaluation of extraocular movement; (c) vestibulo-ocular reflex testing; (d) Dix-Hallpike and static positioning (side-lying) tests; (e) limb

coordination, primarily searching for past pointing and ataxia; and (f) gait and Romberg test.

TABLE 17.5 Useful Bedside Tests and Signs to Elicit in the Evaluation of Vestibular Function

Note: Fresnel (or high +) lenses and/or hyperventilation may bring out some of these signs

Observation for spontaneous nystagmus

Evaluation of eye movements

Head thrust test

Dynamic visual acuity

Subjective visual vertical

Vibration-induced nystagmus

Head-shaking nystagmus

Head-tapping test

Past pointing

Dix-Hallpike maneuver

Evaluation of gait, especially tandem

Romberg

Walking straight line, eyes closed

Star walking test

Unterberger-Fukuda stepping test

Calorics

Vestibulospinal Reflexes

Past pointing is a deviation of the extremities caused by either cerebellar or vestibular disease. These two types of past pointing have different patterns ([Video 43.2](#)). Testing is usually done with the upper extremities. A quick and effective technique is simply to have the patient close his eyes while doing traditional cerebellar finger-to-nose testing. If past pointing is present, the limb will deviate to the side of the target because of the absence of visual correction.

This method will usually bring out past pointing if it is present. The traditional method is to have the patient extend the arm and place his extended index finger on the examiner's index finger; then with eyes closed, raise the arm directly overhead; then bring it back down precisely onto the examiner's finger. With acute vestibular imbalance, the normal (more active) labyrinth will push the limb toward the abnormal (less active) side, and the patient will miss the target. The past pointing will always be to the same side of the target and will occur with either limb. With a cerebellar hemispheric lesion, the ipsilateral limbs have ataxia and incoordination; past pointing occurs only with the involved arm and may be to the side of the lesion or erratically to either side of the target. In vestibulopathy, after a period of compensation, the past pointing disappears and may even begin to occur in the opposite direction.

Romberg's test is described in more detail in [Chapter 44](#). In brief, the Romberg compares balance as the patient stands with eyes open and eyes closed. The feet should be brought as close together as will allow the patient to maintain eyes open balance. A normal individual can stand feet together and eyes open without difficulty, but not all patients can. The critical observation is eyes open versus eyes closed. Inability to maintain balance with eyes open and feet together is not a positive Romberg. In unilateral vestibulopathy, if balance is lost with eyes closed, the patient will tend to fall toward the side of the lesion, as the normal vestibular system pushes him over. If the patient has spontaneous nystagmus because of a vestibular lesion, the fall will be in the direction of the slow phase. In peripheral vestibular disease, the direction of the fall can be affected by changing head position; the patient will fall toward the abnormal ear. With a right vestibulopathy and facing straight ahead, eye closure will cause the patient to fall to the right; looking over his right shoulder, he will fall backward; and looking over his left shoulder, he will fall forward. The sharpened Romberg (tandem Romberg) test, which is done by having the patient stand tandem with eyes closed, may be useful in some circumstances.

The patient with an acute vestibulopathy may have difficulty with tandem gait with a tendency to fall to the side of the lesion, but normal straightaway walking may appear unimpaired because visual cues compensate for the vestibular abnormality. But straightaway walking with eyes closed may be informative. A normal individual can walk without visual clues well enough to point his index finger at the palm of the examiner's hand, close his eyes, walk along a path of 20 ft or so, and then touch the finger to the examiner's palm. The patient with acute vestibulopathy may drift toward the side of the lesion and end up well off the

target, the gait equivalent of past pointing.

The Unterberger-Fukuda stepping test is analogous. The patient, eyes closed, marches in place for 1 minute ([Video 43.2](#)). A normal individual will continue to face in the same direction, but a patient with acute vestibulopathy will slowly pivot toward the lesion. In the star walking test, the patient, eyes closed, takes several steps forward then several steps backward, over and over. A normal individual will begin and end oriented approximately along the same line. A patient with acute vestibulopathy will drift toward the involved side walking forward and continue to drift during the backward phase. The resulting path traces out a multipointed star pattern (“star walking”). As with past pointing, the direction of gait drift, pivoting on the stepping test, and similar findings do not reliably indicate the side of the lesion in patients with chronic vestibulopathy after compensation has occurred. These vestibulospinal tests may be abnormal when all other clinical tests of vestibular function are unrevealing.

Vestibulo-Ocular Reflexes

The VOR serves to move the eyes at an equal velocity but in the direction opposite a head movement; this keeps the eyes still in space and maintains visual fixation while the head is in motion (see also [Chapter 14](#)). There are several ways to examine the VOR, including the doll’s eye test, head thrust test, dynamic visual acuity, and calorics.

Oculocephalic Reflex (Doll’s Eye Test)

The oculocephalic response is primarily useful in the evaluation of comatose patients. Turning the head in one direction causes the eyes to turn in the opposite direction. This response indicates that the pathways connecting the vestibular nuclei in the medulla to the extraocular nuclei in the pons and midbrain are functioning and that the brainstem is intact. In an alert patient, visuomotor and ocular fixation mechanisms come into play, limiting the drawing of any conclusions about vestibular function.

Head Thrust Test

The doll’s eye test utilizes slow side-to-side head movements in a comatose patient. The head thrust test is done in an awake patient. Abrupt, rapid

movements are made in each direction while the patient attempts to maintain fixation straight ahead, as on the examiner's nose ([Figure 17.11](#)). The ocular smooth pursuit mechanism cannot compensate for head movements done at such high velocity, but normally, the VOR will maintain fixation and the eyes will hold on target. When the VOR is impaired, the compensatory eye movement velocity is less than the head movement velocity; the eyes lag behind the head movement and a corrective "catch-up" saccade must be made to resume fixation in the eccentric position. For a video of the head thrust test, see [Video Link 17.1](#).

Dynamic Visual Acuity

The ability of the VOR to maintain ocular fixation means that a patient can read even while shaking the head to and fro. The dynamic visual acuity test is performed by obtaining a baseline acuity and then determining the acuity during rapid head shaking. Degradation by more than three lines on the Snellen chart suggests impaired vestibular function. One symptomatic corollary of impaired dynamic acuity is oscillopsia, a visual illusion of environmental motion causing jiggling while walking or in a car, and difficulty reading signs while in motion.

Caloric Tests

Robert Bárány was an otologist who pioneered the understanding of vestibular function and disease. He developed caloric testing for vestibular function in 1906; it is still in use over a century later. He did not in fact describe the maneuver to test for positional vertigo, although his name is linked to it.

Caloric responses are frequently used to check for brainstem integrity in comatose patients. Ice water instilled into one ear canal will abruptly decrease the tonic activity from the labyrinth on the irrigated side. Cold calorics in a comatose patient with an intact brainstem cause tonic deviation of the eyes toward the side of irrigation as the normally active labyrinth pushes the eyes toward the hypoactive, irrigated labyrinth. In an awake patient, cold calorics cause nystagmus with the fast component away from the irrigated side because the cerebral cortex produces a compensatory saccade that jerks in the direction opposite the tonic deviation. The familiar mnemonic "COWS" (cold opposite, warm same) refers to the fast phase of the nystagmus, not to the tonic gaze deviation. Nystagmus is seen only when the cortex is functioning normally.

Warm water irrigation has opposite effects. For a video of the normal caloric response, see [Video Link 17.2](#). Bilateral simultaneous cold calorics induce tonic downgaze and warm calorics upgaze.

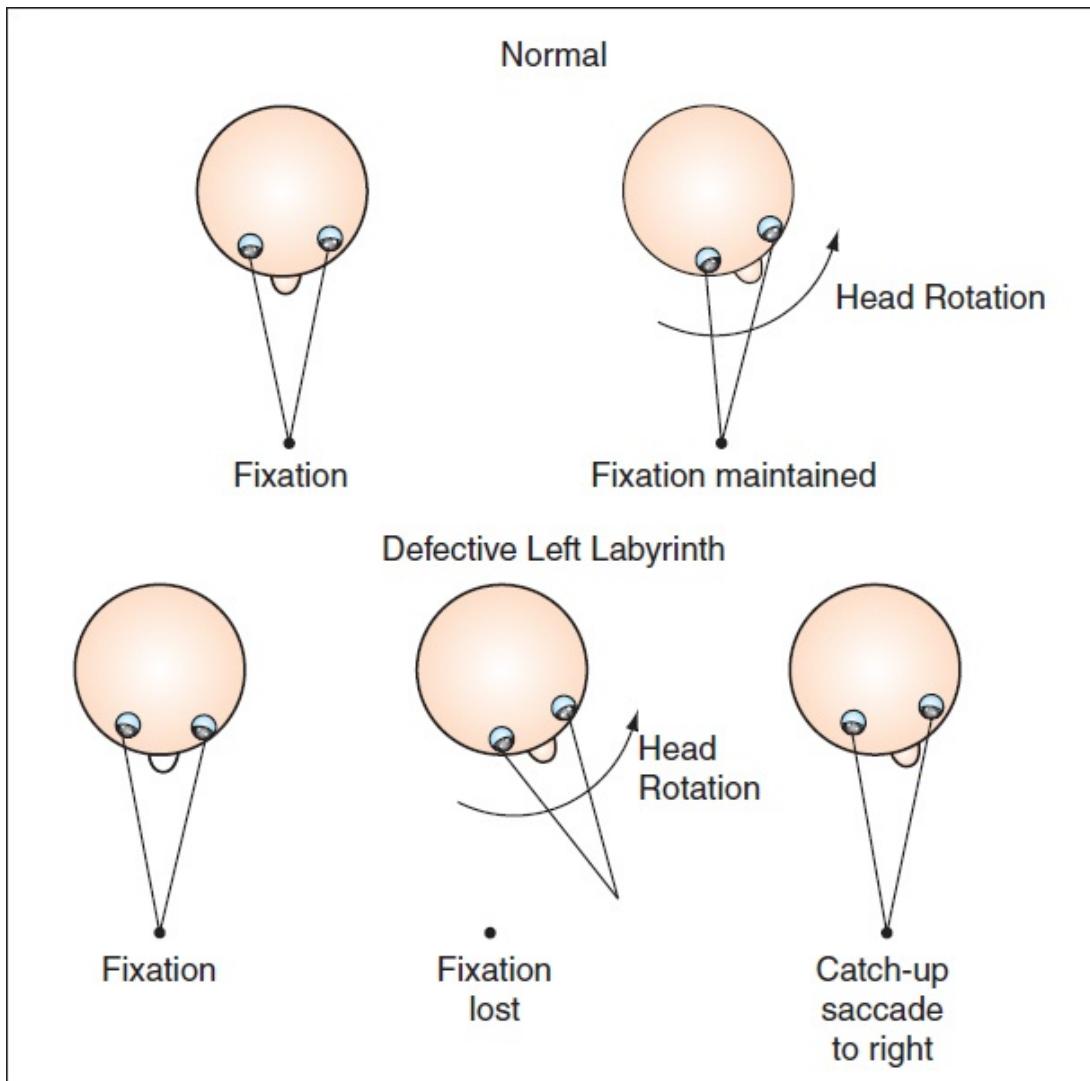


FIGURE 17.11 Head thrust test with a defective left labyrinth. The normal patient maintains fixation throughout. The patient with a defective left labyrinth loses fixation with the rapid head movement and must make a catch-up saccade to the right. (Modified from Barracough K, Bronstein A. Diagnosis in general practice: vertigo. *BMJ* 2009;339:b3493.)

In comatose patients, large volumes of ice water, 30 to 50 mL, are commonly used because it is imperative to elicit the response if it is present. Calorics can also be done to assess vestibular function in dizzy patients, either using much smaller volumes, 2 to 10 mL of an ice and water slush (minicalorics), or larger volumes of water that is less cold. The latency to onset and the duration of the

nystagmus elicited are compared on the two sides. A difference of more than 20% in nystagmus duration suggests a lesion on the side of the decreased response.

Whether in comatose or awake patients, the head is positioned so as to bring the horizontal canal into a position to elicit a maximal response. In comatose patients lying supine, this is done with the head flexed 30 degrees to bring the horizontal canal vertical. For awake patients, the same position may be used, or the head may be extended with the seated patient looking at the ceiling.

Nystagmus

Nystagmus is discussed in greater detail in [Chapter 14](#). The characteristics of vestibular nystagmus will be briefly reviewed. Nystagmus because of vestibular disease may occur spontaneously or be produced by various maneuvers. Careful eye observation may reveal other relevant abnormalities, such as fixation instability, for example, because of macro square jerks, or skew deviation (see [Chapter 14](#)).

Spontaneous Nystagmus

The slow phase of spontaneous vestibular nystagmus is usually in the direction of the lesion, with the fast phase away, because an acute vestibular lesion typically causes hypoactivity of the labyrinth. The findings are similar to those produced by ice water irrigation of the ear and are due to the normal labyrinth pushing the eyes toward the diseased side with the cortex generating a corrective saccade away from the abnormal side. Because of the influence of the three different semicircular canals, vestibular nystagmus may beat in more than one direction, the summation of which creates an admixed rotatory component rarely seen with other conditions. When evaluating nystagmus, the presence of a torsional component suggests a peripheral origin. The amplitude increases with gaze in the direction of the fast phase.

When nystagmus is only present with gaze in the direction of the fast phase (Alexander's law, [Chapter 14](#)), it is termed first degree. Second-degree nystagmus is present in primary gaze. Vestibular nystagmus typically is fine, often present but easily overlooked in primary position. Third-degree nystagmus (fast component opposite to the direction of gaze) rarely occurs with any other nystagmus type. Vertigo, deafness, and tinnitus also help mark nystagmus as

vestibular.

Peripheral vestibular nystagmus (i.e., because of disease of the labyrinth or eighth nerve) is markedly inhibited by visual fixation. Inhibiting fixation with Fresnel (Frenzel is a common misspelling) lenses (strongly convex spectacles that block visual fixation) will often make the nystagmus more obvious by both blocking fixation and magnifying the eyes. When Fresnel lenses are used, torsional nystagmus is often more prominent because vertical and horizontal nystagmus are more easily suppressed by visual fixation. Another technique is to have the patient close the eyelids gently and then partially lift one lid and look for abnormal movements of the scleral vessels. For a video of vestibular nystagmus demonstrating Alexander's law, third-degree nystagmus and fixation suppression, see [Video Link 17.3](#). The fundoscopic examination may bring out subtle vestibular nystagmus. The dim lighting lessens visual fixation, and the disc is magnified. A rhythmic jerking of the disc to the patient's right indicates left beating nystagmus. Formal eye movement studies are done in darkness with recording of the eye movements by electrodes in order to remove the effects of visual fixation. Failure of visual fixation to suppress nystagmus suggests the nystagmus may be of central origin, usually a cerebellar or brainstem lesion. The spontaneous nystagmus because of a central lesion may be purely horizontal or purely vertical.

Nystagmus can sometimes be induced by having the patient rapidly turn the head back and forth with the eyes closed for about 30 seconds and then opening the eyes (head-shaking nystagmus). No nystagmus occurs in normal individuals, but patients with vestibular imbalance may have brief spontaneous nystagmus beating away from the abnormal side. Alternately, the patient may wear Fresnel lenses while shaking the head. For a video of head-shaking nystagmus, see *Head-Shaking Nystagmus* from Dr. Daniel R. Gold, Neuro-Ophthalmology Virtual Education Library [NOVEL], University of Utah, available at [Video Link 17.4](#). Lee et al. recently described a disorder characterized by recurrent spontaneous vertigo and interictal head-shaking nystagmus. Spontaneous nystagmus can occasionally be produced by tapping on the head or by low-frequency vibration applied to the mastoid. Hyperventilation may also help bring out vestibular nystagmus.

Positional Nystagmus

When not present spontaneously, nystagmus can sometimes be elicited by

placing the patient's head into a particular position. To perform the Dix-Hallpike (Hallpike or Nylen-Bárány) maneuver, the patient is moved from a seated position to a supine position with the head extended 45 degrees and turned 45 degrees to one side so that one ear is dependent. The patient is returned to sitting and then the maneuver repeated in the opposite direction. The patient should become symptomatic when the affected ear is dependent. For videos of the Dix-Hallpike test, see Barraclough and Bronstein and *Posterior canal BPPV with fixation and with fixation removed* from Dr. Daniel R. Gold, Neuro-Ophthalmology Virtual Education Library [NOVEL], University of Utah, available at [Video Link 17.5](#).

If vertigo or nystagmus occurs, the patient is held in the provoking position until the symptoms subside, and then, the movement is repeated to assess its recurrence. The side-lying test may be used in patients unable to extend the neck or tolerate the supine position. The head is turned 45 degrees in one direction, then the patient lies down on the opposite shoulder. In BPPV, nystagmus begins after a latency of about 3 to 10 seconds, occasionally as long as 40 seconds; persists for 20 to 30 seconds, rarely as long as a minute; and then gradually abates (fatigues or habituates) after about 30 seconds, even though the head remains in the provoking position. The nystagmus is commonly torsional with the fast component toward the dependent ear (geotropic). For a video of torsional nystagmus in BPPV, see Barraclough and Bronstein. The response is usually much more dramatic in one particular head position. Typically, the patient will experience whirling, occasionally nausea, and rarely vomiting. With BPPV involving canals other than the posterior one, the Dix-Hallpike maneuver may be negative. The roll test, rolling the head of the supine patient to one side, may provoke a response with horizontal canal BPPV.

In canalithiasis, the response is transient, and repeating the maneuver several times consecutively provokes less of a response each time until eventually the nystagmus and vertigo are nil, adaptability. The term habituation is used to refer to either of these phenomena, which are themselves used inconsistently. After a period of 10 to 15 minutes, the response can be elicited again. In cupulolithiasis, latency and fatigability are absent because the adherent otoconia are in constant contact with the cupula.

Positional nystagmus is most often due to peripheral vestibular disease. Although rare, positional vertigo and nystagmus can occur with a central lesion, especially one near the fourth ventricle, but the characteristics of the nystagmus are different. With a central lesion, there may be no latency, and the nystagmus

often begins as soon as the head is placed in the provoking position. Central positional nystagmus is typically vertical (either up- or downbeating), without the rotatory component seen with peripheral lesions. When torsional nystagmus is present, it may be ageotropic, beating away from the ground. In addition, the nystagmus and associated symptoms may persist for a prolonged period, longer than 30 to 40 seconds, sometimes continuing as long as the head position is maintained. With central lesions, there may be a mismatch in the severity of the nystagmus, vertigo, and nausea, in contrast to peripheral lesions where nystagmus, vertigo, and nausea are generally of comparable intensity.

TABLE 17.6 The Characteristics of Central versus Peripheral Positional Nystagmus on Dix-Hallpike Maneuver

Finding	Peripheral	Central
Latency	Yes, typically 3–10 s, rarely as long as 40 s	No
Fatigability* (habituation)	Yes, individual episode typically lasts 10–30 s, rarely as long as 1 min	No
Adaptability* (fatigability)	Yes, maneuver done several times consecutively provokes less of a response each time	No
Nystagmus direction	Direction fixed, typically mixed rotational upbeat with small horizontal component; quick phase of intorsion movement toward the dependent ear, upbeat toward forehead	Direction changing, variable, often purely vertical (either upbeat or downbeat) or purely horizontal
Suppression of nystagmus by visual fixation	Yes	No

Severity	Severe, marked vertigo, intense nystagmus, nausea	Mild vertigo, less obvious nystagmus, inconspicuous nausea
Consistency (reproducibility)	Less consistent	More consistent
Past pointing	In direction of nystagmus slow phase	May be in direction of fast phase

*Adaptability and fatigability are not used consistently in the literature.

Positional nystagmus can be divided into a paroxysmal type that is fleeting, fatigable, often difficult to reproduce, and associated with prominent vertigo and a static type that does not fatigue, persisting as long as the head is maintained in the provoking position, often with little associated vertigo. The static type can occur with either central or peripheral vestibular lesions, but a lack of visual suppression increases the likelihood of a central lesion. Other potentially useful tests in the dizzy patient include Valsalva maneuver (for perilymphatic fistula, see below), tragal compression, hyperventilation, and attempts to provoke Tullio's phenomenon (see below).

The characteristics of peripheral versus central positional nystagmus and related findings are summarized in [Table 17.6](#).

Clinical Investigation

The commonly used quantitative tests for evaluation of vestibular function currently include electronystagmography, rotatory chair testing, and posturography. The tests are summarized in [Box 17.3](#).

Disorders of Function

The primary manifestation of disorders of the vestibular nerve is vertigo and related symptoms such as imbalance. Vertigo will be used in this discussion as a surrogate for all similar symptoms. One of the primary concerns when dealing

with a vertiginous patient is to separate central vertigo, because of CNS disease, from peripheral vertigo, because of peripheral vestibular disease. Disease of the peripheral vestibular apparatus or eighth CN produces peripheral vertigo. Disease of the central vestibular connections produces central vertigo. The vestibular nuclei lie within the CNS in the dorsolateral medulla; disease there may act like either peripheral or central forms. Central vertigo is less common than peripheral. Epidemiologic studies indicate that central causes are responsible for about 25% of the dizziness experienced in patients. Some central causes of dizziness include cerebrovascular disorders, migraine, multiple sclerosis (MS), brainstem lesions, global cerebral hypoperfusion, neurodegenerative disorders, and drug effects.

Certain features are helpful in making the distinction. Central vertigo is typically less severe, and other neurologic signs and symptoms are usually present. Peripheral vestibular disorders cause more nausea, vomiting, and autonomic symptoms than do central disorders. Imbalance tends to be more severe with central lesions, and the patients are often unable to stand or walk. Associated symptoms are helpful if present. Aural symptoms (hearing loss, tinnitus, pain or fullness in the ear) suggest a peripheral cause. Facial weakness or numbness occurs with lesions involving the eighth nerve in the cerebellopontine angle. Processes in the brainstem typically cause prominent neighborhood signs; isolated vertigo is rare. Occasionally, vertigo can be a manifestation of disease of the more rostral vestibular pathways, including the temporal lobe.

BOX 17.3

Electronystagmography and Posturography

Electrooculography (EOG) is a quantitative method of recording the direction, amplitude, and velocity of eye movements by measuring changes in the corneoretinal potential with electrodes. EOG done during stimulation of the labyrinth to cause nystagmus is electronystagmography (ENG). Recordings are done in the dark to minimize visual suppression. The horizontal labyrinth may be stimulated by calorics using air or water or by rotation. It is not possible currently to effectively study the vertical canals or the otolith organ. Rotation can be done actively by the patient turning his head to and fro (active head rotation), by the examiner turning the patient's

head (passive head rotation), or by sitting in a rotation chair. Rotation testing has some advantages over calorics, but a disadvantage is that both sides are tested simultaneously.

Computerized dynamic posturography is a technique that explores the relative importance of the various sensory inputs critical for balance in patients with complaints of dizziness or imbalance. A force platform measures the compensatory movements of the patient's feet while visual, somatosensory, and vestibular perceptions are manipulated. Posturography is not of use in lesion localization and provides no information about etiology.

Distinguishing central from peripheral nystagmus is a common clinical exercise. The most helpful features are of course the presence of aural symptoms and signs in peripheral nystagmus and the presence of CNS symptoms and signs with central nystagmus. Peripheral vestibular nystagmus does not change direction, although it may vary in amplitude depending on the direction of gaze, and is strongly suppressed by visual fixation. Central nystagmus typically changes direction and may not be affected by visual fixation.

Because of the effects of fixation and other compensatory mechanisms, peripheral nystagmus is seldom prominent after the first 12 to 24 hours, but central nystagmus may persist for weeks or months. The vestibular apparatus pushes not only the eyes but also the limbs and the body to the opposite side. With APV, the patient will past point, fall on Romberg, turn on the stepping test, and drift while walking eyes closed in the direction of the nystagmus slow phase. Failure to follow these rules (e.g., past pointing in the direction of the fast phase) suggests a central lesion but can occur with a compensated peripheral lesion. Peripheral nystagmus is often positional, and the vertigo and vegetative symptoms are in proportion to the nystagmus. With positional nystagmus, latency to onset, fatigability, and adaptability all support a peripheral process. Minimal vertigo with prominent nystagmus, or lack of latency, fatigability, and adaptability, suggests a central process. Peripheral nystagmus often has a rotary component, and the horizontal nystagmus beats in the same direction in all fields of gaze (may even be third degree). Central nystagmus tends to change directions. Visual fixation inhibits peripheral nystagmus but has no effect on central nystagmus.

Involvement of the vestibular nuclei may cause vertigo that has central features. Common processes that involve the brainstem and that are likely to

cause vertigo include ischemia, demyelinating disease, and neoplasms. Less common brainstem lesions causing central vestibular dysfunction include arteriovenous malformation, syringobulbia, hematoma, and spinocerebellar degeneration. Lesions in the cerebellopontine angle affect both the auditory and vestibular portions of CN VIII.

Vertebrobasilar transient ischemic attacks, or “vertebrobasilar insufficiency,” commonly cause vertigo, most often along with other signs and symptoms. Rarely, patients may have transient vertigo without accompanying symptoms. A three-step bedside examination is touted as a reliable way to distinguish brainstem stroke from APV: the HINTS—head impulse, nystagmus, test of skew. A syndrome of acute vertigo mimicking labyrinthitis may occur with acute cerebellar infarction or hemorrhage. In acute cerebellar lesions, the patient will tend to fall toward the side of the lesion on Romberg testing; the nystagmus may also be maximal with gaze toward the lesion. As a result, the patient may fall in the direction of the fast phase, opposite the pattern seen in APV.

Dizziness, vertigo, and disequilibrium occur commonly in patients with MS. In one instance, an MS lesion in the medulla caused clinical symptoms mimicking vestibular neuronitis. However, MS patients are not immune from developing the common syndrome of BPPV, and peripheral vestibulopathy may be a more common cause of vertigo in such patients than MS exacerbation.

There is a relationship between migraine and episodic vertigo. Motion sensitivity is common in migraineurs, and episodic vertigo occurs in as many as 25%. Isolated attacks of vertigo have been labeled as a migraine equivalent. Migraine-associated vertigo may be a symptom of migraine or a related disorder (vestibular migraine, migrainous vertigo, or migraine-related vestibulopathy). Epidemiologically, there is a strong link between vertigo and migraine, but whether migraine-associated vertigo exists as a migraine equivalent is unsettled. Migraine-associated vertigo is a separate entity from basilar artery migraine.

Occasionally, migraine patients may also develop cochlear symptoms, perhaps because of spasm of the labyrinthine microvasculature. Migraine can mimic Ménière’s disease. In some patients, there may be a channelopathy involved. There is a malignant form of migraine-associated vertigo that can be very disabling.

Disorders of the peripheral vestibular apparatus are the most common causes of vertigo and related symptoms. [Table 17.4](#) lists some of the causes of peripheral vertigo. In BPPV, the most common peripheral vestibulopathy, vertigo is induced by assumption of a particular head position or by rapid head

movement. Classically, such patients experience vertigo when first lying down or when rolling over in bed at night, bending over, or looking up. Between paroxysms of vertigo, patients may complain of poor balance or light-headedness. BPPV attacks are brief, generally 10 to 30 seconds, and frequent. BPPV probably results from otoliths that have become detached from the macula of the utricle and formed free-floating debris that settles into one of the semicircular canals (canalithiasis) or becomes adherent to the matrix gel of the cupula (cupulolithiasis). Movement of the debris causes the attacks of vertigo. Otolith movement causes endolymph movement and stimulation of the hair cells of the cupula. The result is vertigo until the otoconia settle to the bottom, hence the brief duration of the attacks. The Dix-Hallpike maneuver causes the debris to move and reproduces the symptoms. The disorder predominantly affects the posterior semicircular canal, the most dependent portion of the vestibular labyrinth, and a movement of the head backward causes vertigo. Between 10% and 30% of cases involve the horizontal canal and about 1% the anterior canal. In a series of 240 patients, the most common identifiable etiologies were head trauma (17%) and viral neurolabyrinthitis (15%). Rarely, patients with posterior fossa tumors have a clinical picture nearly identical to BPPV. In horizontal canal BPPV, there is horizontal nystagmus beating toward the down ear on rapid turning of the head to either side in the supine position. Most cases of horizontal canal BPPV are due to cupulolithiasis rather than canalithiasis.

In vestibular neuronitis (neuritis, neurolabyrinthitis), APV, or labyrinthitis, more severe attacks prostrate the patient for several days. Although often used interchangeably, technically, labyrinthitis is accompanied by cochlear dysfunction with hearing impairment, whereas vestibular neuronitis is purely vestibular. An attack typically causes constant vertigo lasting for days and is accompanied by nausea, vomiting, and sweating. The patient looks and feels extremely ill. The patient will have horizontal-torsional nystagmus in primary gaze and other evidence of vestibular imbalance. During the acute phase, the involved labyrinth may be hyperactive, and after resolution, the involved labyrinth is hypoactive.

The acute phase slowly remits over weeks. Improvement is due to recovery of nerve function and CNS compensation. Mild, brief attacks of vertigo similar to BPPV may plague the patient for months to years after seeming recovery. APV is often a viral or postviral inflammation of the vestibular portion of CN VIII. It may be simulated by hemorrhagic or ischemic disease of the brainstem or cerebellum, MS, or the effects of a drug or toxin. Some instances of apparent

labyrinthitis are likely due to IAA ischemia. Ramsay Hunt syndrome (see Chapter 16) may also involve CN VIII and other CNs as well.

In Ménière's disease, the attacks of vertigo typically last minutes to several hours, much longer than the typical symptoms of BPPV but much shorter than with APV. Patients describe other symptoms, either along with the vertigo or independently, including hearing loss (classically fluctuating), tinnitus, and a sensation of vague pain or fullness in the ear. The association of hearing loss and vertigo is classic. Many famous people have been affected, most notably Jonathan Swift (Box 17.4). Some patients have purely vestibular Ménière's; whether there is a purely cochlear form is controversial. Inner ear disease can occasionally cause drop attacks. The distinction between Ménière's disease and Ménière's syndrome is no longer stressed. One of Ménière's original patients suffered a hemorrhage into the labyrinth. It was Hallpike who found endolymphatic hydrops in a patient with Ménière's syndrome, establishing Ménière's disease as an entity. Modern MRI has confirmed the presence of endolymphatic hydrops in patients with Ménière's disease. The cause of the hydrops remains obscure.

Other conditions that may cause vertigo and be confused with CN VIII disease include perilymphatic fistula and superior semicircular canal dehiscence. In perilymphatic fistula, there is an abnormal communication between the inner and middle ear. Patients develop episodic vertigo with or without hearing loss, often provoked by Valsalva or straining. Vertigo and nystagmus may be induced by loud sounds (Tullio's phenomenon) because of physical activation of the vestibular system by sound vibrations. Superior semicircular canal dehiscence is due to a defect of the temporal bone overlying the superior canal, allowing pressure induced by sound to be transmitted to the inner ear. Vertigo and nystagmus may be induced by Valsalva or sound. An otolithic crisis of Tumarkin is a sudden drop to the ground followed by immediate recovery that may occur in Ménière's disease.

BOX 17.4

Ménière's Disease

Well-known affected individuals include Emily Dickinson, Peggy Lee, Alan Shepard, and Vincent Van Gogh. Swift wrote extensively about his “giddiness” and his deafness, which plagued him from an early age. Swift

wrote something to the effect that “my friend the giddiness would come to visit, then my friend the hearing loss, and eventually they became such good friends they came to visit together.”

Other rare causes of vertigo include seizure disorder, especially partial complex seizures of temporal lobe origin (tornado epilepsy), episodic ataxia, benign paroxysmal vertigo of childhood, hypothyroidism, mal de debarquement (mal de mer), and phobic postural vertigo.

Video Links

Video Link 17.1. Head thrust test. http://neurosigns.org/wiki/Head_impulse_test

Video Link 17.2. Normal caloric responses. <http://www.youtube.com/watch?v=H4iQkFUgG6k>

Video Link 17.3. Vestibular nystagmus. <http://www.youtube.com/watch?v=mghGeKkNBzQ>

Video Link 17.4. Head-shaking nystagmus.
https://collections.lib.utah.edu/details?id=187675&q=sort_type_t%3A%2AMovingImage%2A+AND+head+shaking+nystagmus

Video Link 17.5. The Dix-Hallpike test. https://collections.lib.utah.edu/details?id=187762&q=sort_type_t%3A%2AMovingImage%2A+AND+head+shaking+nystagmus

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CHAPTER 18

The Glossopharyngeal and Vagus Nerves

The glossopharyngeal (CN IX) and vagus (CN X) nerves are intimately related and similar in function. Both have motor and autonomic branches with nuclei of origin in the medulla. Both conduct general somatic afferent (GSA) as well as general visceral afferent (GVA) fibers to related or identical fiber tracts and nuclei in the brainstem, and both have a parasympathetic, or general visceral efferent, and a branchiomotor, or special visceral efferent (SVE), component. The two nerves leave the skull together, remain close in their course through the neck, and supply some of the same structures. They are often involved in the same disease processes, and involvement of one may be difficult to differentiate from involvement of the other. For these reasons, the two nerves are discussed together.

THE GLOSSOPHARYNGEAL NERVE

Anatomy and Physiology

The glossopharyngeal, as its name implies, is distributed principally to the tongue and pharynx. It conveys general sensory as well as special sensory (taste) fibers from the posterior third of the tongue. It also provides general sensory innervation to the pharynx, the area of the tonsil, the internal surface of the tympanic membrane, and the skin of the external ear. It conveys GVA_s from the carotid body and the carotid sinus. Its skeletomotor neurons innervate the stylopharyngeus muscle, and its parasympathetic component innervates the parotid gland.

Upper motor neuron influences on CN IX arise from the primary motor

cortex and descend in the corticobulbar tracts to synapse in the rostral portion of the nucleus ambiguus in the dorsolateral medulla ([Figure 18.1](#)). The cortical innervation is bilateral. The cells in the nucleus ambiguus are branchiomotor and innervate muscles derived from the third, fourth, and fifth branchial arches. In keeping with the tendency of SVE axons to create internal loops, the fibers of CN IX first head posteromedially toward the floor of the fourth ventricle and then turn and sweep laterally and forward. The nerve emerges from the medulla as three to six rootlets in the groove between the inferior olive and the inferior cerebellar peduncle, between and in line with the emerging fibers of CN VII above and CN X below ([Figure 11.3](#)). These rootlets unite to form a single nerve, which leaves the skull through the jugular foramen.

CN IX exits the skull through the jugular foramen, lateral and anterior to CNs X and XI within a separate dural sheath. After leaving the skull, CN IX enters the carotid sheath, descends between the internal jugular vein and internal carotid artery, dips beneath the styloid process, and then passes between the internal and external carotid arteries. It curves forward, forming an arch on the side of the neck to reach the lateral pharyngeal wall, and then disappears under the hyoglossus muscle to divide into its terminal branches. Two ganglia lie on the nerve just caudal to the jugular foramen: the superior (jugular) and inferior (petrosal) glossopharyngeal ganglia ([Figure 18.2](#)). The superior glossopharyngeal ganglion is small, is inconstant, has no branches, and is often fused with the inferior ganglion. CN IX has six terminal branches: (a) the tympanic nerve (Jacobson's nerve), (b) carotid, (c) pharyngeal, (d) muscular, (e) tonsillar, and (f) lingual branches. CN IX has important connections with CNs V, VII, and X and the cervical sympathetics.

The branchiomotor fibers of CN IX go to the pharynx. The muscular branch follows along the posterior border of the stylopharyngeus muscle and then terminates in the belly of the muscle. Most of the pharyngeal muscles are supplied by both CNs IX and X. If CN IX supplies any muscle alone, it is the stylopharyngeus. The actions of the stylopharyngeus are described in [Table 18.1](#).

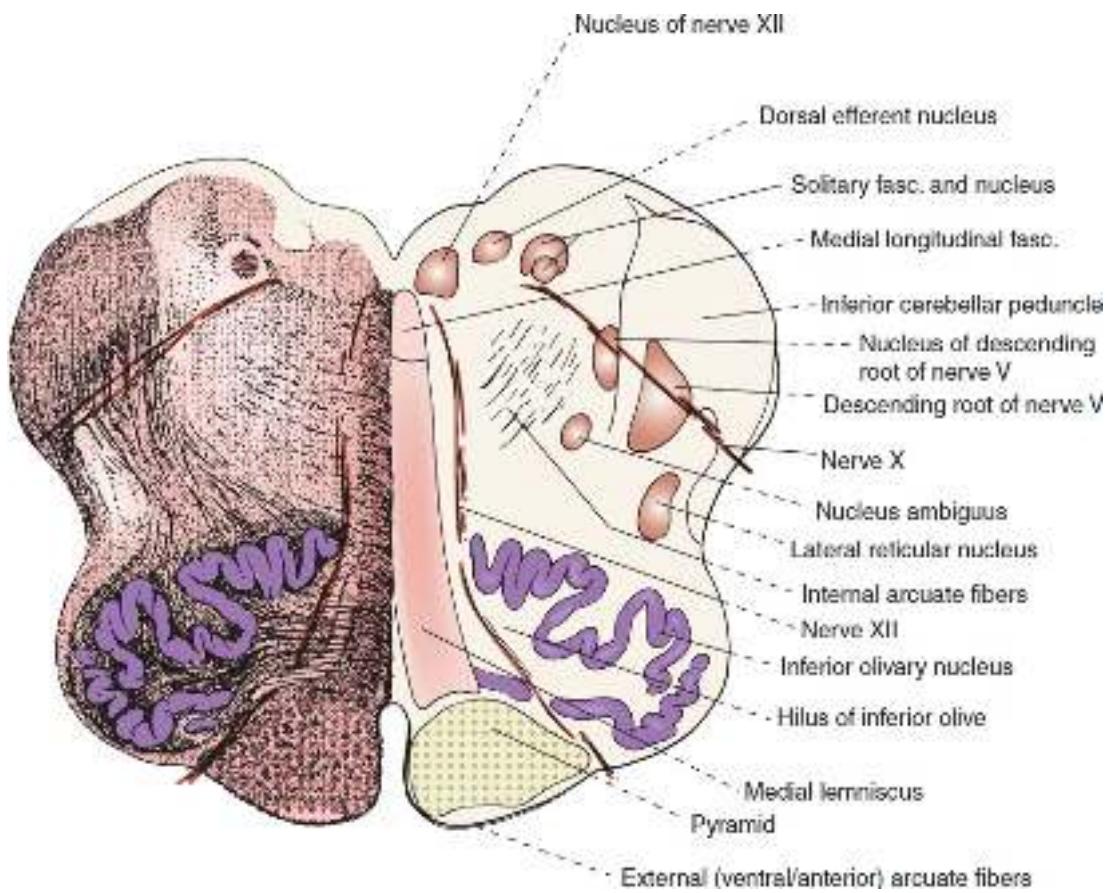


FIGURE 18.1 Section through the medulla at the level of the inferior olfactory nucleus.

CN IX supplies parasympathetic innervation to the parotid gland and to the mucous membranes of the posterior-inferior mouth and pharynx (Figure 18.2). The parasympathetic nuclei in the lower brainstem are the superior and inferior salivatory and the dorsal motor nucleus of CN X (DMNX), also known as the dorsal motor or dorsal efferent nucleus of the vagus. The autonomic fibers of CN IX arise primarily from the inferior salivatory nucleus, with some from the DMNX. The parasympathetics pass through the superior and inferior glossopharyngeal ganglia without synapsing. Just below the inferior ganglion, they exit to form the tympanic nerve, which ascends to the tympanic cavity through a small canal on the undersurface of the temporal bone between the carotid canal and the jugular fossa (tympanic canaliculus). The tympanic nerve ramifies in the tympanic cavity to form part of the tympanic plexus. The lesser petrosal nerve is a continuation of the tympanic nerve that leaves the tympanic plexus, enters the middle cranial fossa briefly, and then exits through the foramen ovale to synapse in the otic ganglion. Postganglionic fibers join the auriculotemporal branch of the mandibular division of CN V for distribution to

the parotid gland; this is the nerve involved in gustatory sweating ([Chapter 15](#)).

Sensory neurons of CN IX are located in the superior and inferior glossopharyngeal ganglia. There are GSA fibers that convey ordinary exteroceptive sensation; GVA fibers that convey information from the carotid body and carotid sinus, as well as visceral sensation from the pharynx; and special visceral afferents that convey taste sensation. The GSA fibers convey exteroceptive sensation from the mucous membranes of the tympanic cavity, mastoid air cells, and auditory canal via the tympanic plexus and tympanic branch. Sensation from the pharynx, tonsil, and posterior third of the tongue travels via the pharyngeal, tonsillar, and lingual branches. Central processes of these cells terminate in the trigeminal nuclei, and their central connections are the same as for other GSA fibers. One of the most important functions of CN IX is to carry visceral afferent fibers from the carotid body and sinus involved in the reflex control of heart rate, blood pressure, and respiration. The carotid branch of CN IX (carotid sinus nerve) arises just below the jugular foramen and descends on the internal carotid artery to the carotid sinus and carotid body. It conveys impulses from carotid body chemoreceptors and carotid sinus baroreceptors and terminates centrally on cells in the middle third of the nucleus of the solitary tract. Other fibers carrying visceral afferent fibers from the mucous membranes of the pharynx, soft palate, and posterior third of the tongue pass through the petrous ganglion to terminate in the solitary tract and nucleus. The lingual branches of CN IX carry taste fibers (primarily sour and bitter) from the circumvallate papillae, mucous membranes of the base and taste buds on the posterior third of the tongue, glossoepiglottic and pharyngoepiglottic folds, and lingual surface of the epiglottis. These fibers terminate in the rostral part of the nucleus of the solitary tract (gustatory nucleus). Their central connections are the same as for the taste fibers of CN VII.

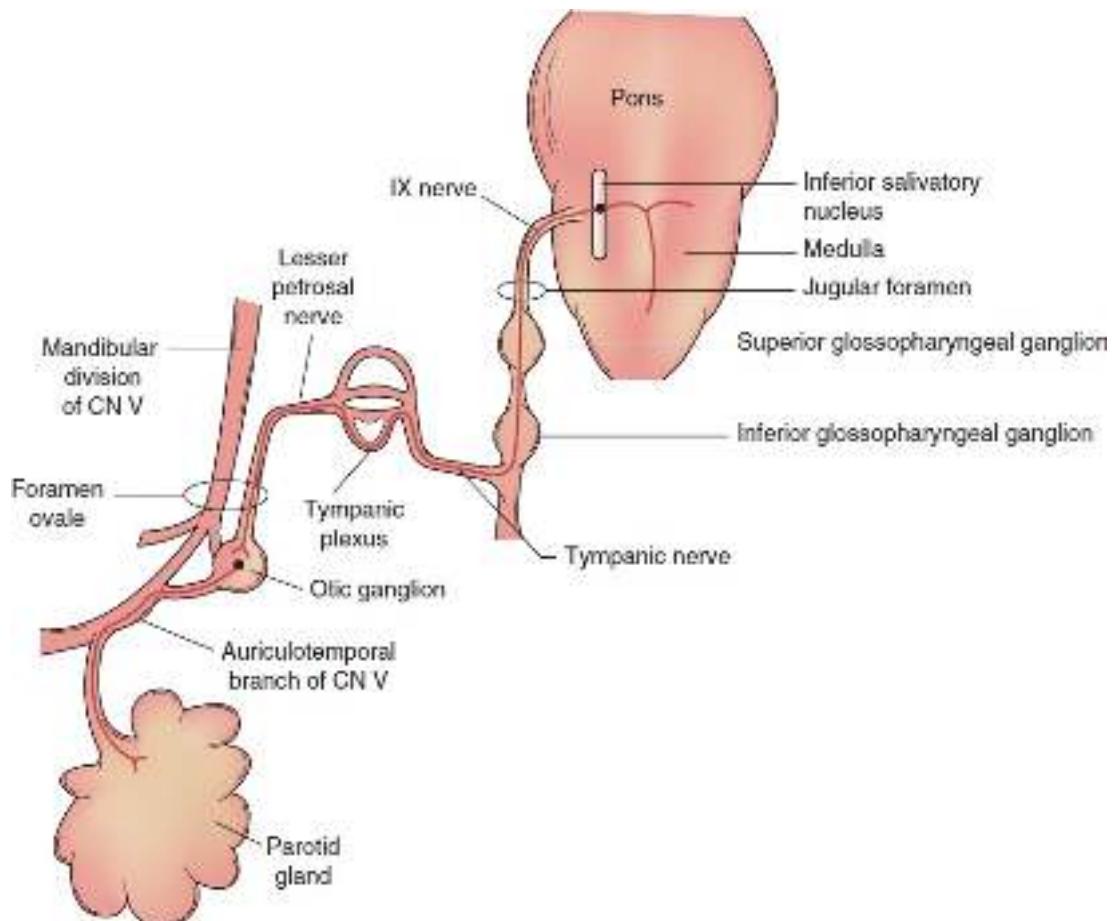


FIGURE 18.2 Peripheral distribution of the parasympathetic branches of the glossopharyngeal nerve.

Clinical Examination

CN IX is difficult to examine because most or all of its functions are shared by other nerves and because many of the structures it supplies are inaccessible. It is possible to examine pain and touch sensation of the pharynx, tonsillar region and soft palate, and the gag reflex. Bedside testing of taste on the posterior third of the tongue is difficult and seldom attempted. It is not possible to isolate the motor functions from those of the vagus. The small area of cutaneous exteroceptive sensory supply is shared by other nerves. Patients with CN IX lesions might theoretically have detectable sensory loss, but it is not possible to find in patients who have undergone ninth nerve section for glossopharyngeal neuralgia.

The only muscle to receive its motor innervation purely from CN IX is the stylopharyngeus. The only deficit that might be detectable is a slight lowering of

the palatal arch at rest on the involved side. Other palatal motor functions are subserved by either CN X or the two nerves working together. The salivary reflex is flow of saliva from the parotid duct after gustatory stimuli. The afferent limb is through taste fibers and the efferent through the parasympathetic outflow of the superior and inferior salivatory nuclei.

TABLE 18.1 Branches of the Glossopharyngeal and Vagus Nerves, the Muscles Innervated, and Their Actions

Nerve Branch	Muscle Innervated	Muscle Action
CN IX		
Muscular branch	Stylopharyngeus	Raises and dilates the pharynx
CN X		
Pharyngeal branch	Musculus uvulae	Shortens and bends the uvula backward; helps to block off the nasal passages in swallowing
	Levator veli palatini	Raises the soft palate and pulls it backward; blocks off the nasal passages in swallowing
	Palatopharyngeus	Pulls the pharynx and the thyroid cartilage upward and depresses the soft palate; draws the pharyngopalatine arches together and closes faucial orifice
	Salpingopharyngeus	Blends with palatopharyngeus, raises upper and lateral portion of the pharynx
	Palatoglossus	Elevates posterior part of the

		tongue and narrows the fauces; depresses the soft palate
	Superior, middle, and inferior constrictors of the pharynx	Flattens and contracts the pharynx in swallowing; forces food into the esophagus in the final act of deglutition; affects speech by changing the shape of the pharyngeal resonator
Superior laryngeal nerve	Cricothyroid	Chief tensors of the vocal cords; elongate the cords by increasing the distance between the vocal processes and the angle of the thyroid
Recurrent laryngeal nerve	Posterior cricoarytenoids	Chief abductors; separate vocal cords and open the glottis by rotating the arytenoids cartilages outward
	Lateral cricoarytenoids	Chief adductors; close the glottis by rotating the arytenoids cartilages inward
	Thyroarytenoids (vocalis)	Pull arytenoids forward to shorten and relax the vocal cords
	Arytenoid	Unpaired; slides arytenoids together and closes the glottic rim

The gag reflex is elicited by touching the pharynx or palate. Some sources make a distinction between the pharyngeal reflex and the palatal reflex, referring only to the former as the gag reflex. In common clinical usage, no distinction is made between these two and either is referred to as the gag reflex. The reflex is elicited by touching the lateral oropharynx in the region of the anterior faucial pillar with a tongue blade, applicator stick, or similar object (pharyngeal reflex),

or by touching one side of the soft palate or uvula (palatal reflex). The pharyngeal reflex is the more active of the two. The reflex also occurs with touching the base of the tongue or posterior pharyngeal wall. The afferent limb of the reflex is mediated by CN IX and the efferent limb through CNs IX and X. The reflex center is in the medulla. The motor response is constriction and elevation of the oropharynx. This causes the midline raphe of the palate and the uvula to elevate and the pharyngeal constrictors to contract. The activity on the two sides is compared. The gag reflex is protective; it is designed to prevent noxious substances or foreign objects from going beyond the oral cavity. There are three motor components: elevation of the soft palate to seal off the nasopharynx, closure of the glottis to protect the airway, and constriction of the pharynx to prevent entry of the substance.

When unilateral pharyngeal weakness is present, the raphe will deviate away from the weak side and toward the normal side. This movement is usually dramatic (see [Video Link 18.1](#)). Minor movements of the uvula and trivial deviations of the midline raphe are not of clinical significance. In normal adults, both palatal and pharyngeal reflexes are usually present, but there may be inter- and intraindividual variation in the intensity of the stimulus required. The gag reflex may be bilaterally absent in some normal individuals. Unilateral absence signifies a lower motor neuron lesion. Like most bulbar muscles, the pharynx receives bilateral supranuclear innervation, and a unilateral cerebral lesion does not cause detectable weakness.

The gag reflex is often used to predict whether or not a patient will be able to swallow. A poor gag reflex in an awake patient with an acute deficit may be a predictor of swallowing difficulties. In fact, the gag reflex has little to do with normal swallowing. Normal deglutition is a smooth coordinated sequence of muscle contractions that propel a bolus of food from the mouth into the esophagus. A normal swallow bears little resemblance to the chaos of a gag reflex. Higher cortical centers have to inhibit the gag response during normal swallowing. The gag reflex is useful but limited in assessing airway protection. A decreased gag reflex in a patient with depressed consciousness may portend inadequate guarding of the airway and increased aspiration risk, but the status of the gag reflex is not a completely reliable indicator. Patients with an apparently intact gag reflex may still aspirate, and a patient with a depressed gag reflex may not.

Davies et al. found that the gag reflex is absent in 37% of normals, which may explain its low predictive value in the assessment of aspiration risk. Leder

and Espinosa concluded that the clinical examination, a major component of which is the status of the gag reflex, underestimated the probability of aspiration in patients who were at risk and overestimated it in patients who were not. The trigeminal nerve contributes to palatal sensation and may allow for paradoxical preservation of the gag reflex in the face of a CN IX lesion. The gag reflex may be hyperactive in some normal individuals, even to the point of causing retching and vomiting. A hyperactive gag reflex may occur with bilateral cerebral lesions, as in pseudobulbar palsy and amyotrophic lateral sclerosis (ALS).

Disorders of Function

Unilateral supranuclear lesions cause no deficit because of the bilateral corticobulbar innervation. Bilateral supranuclear lesions may cause pseudobulbar palsy ([Chapter 21](#)).

Isolated lesions of CN IX are extremely rare if they ever occur. In all instances, the nerve is involved along with other CNs, especially CN X. Nuclear and infranuclear processes that may affect CN IX include intramedullary and extramedullary neoplasms and other mass lesions (e.g., glomus jugulare tumor), trauma (e.g., basilar skull fracture or surgical dissection), motor neuron disease, syringobulbia, retropharyngeal abscess, demyelinating disease, birth injury, and brainstem ischemia. Surgical section or other trauma to the carotid branch may cause transient or sustained hypertension. Involvement of CN IX may be related to the cardiovascular dysautonomia that sometimes accompanies Guillain-Barré syndrome. CN IX may be involved along with other CNs in lesions of the skull base, for example, the jugular foramen syndrome ([Chapter 21](#)).

Perhaps, the most important lesion of the ninth nerve is glossopharyngeal (or vagoglossopharyngeal) neuralgia or “tic douloureux of the ninth nerve.” In this condition, the patient experiences attacks of severe lancinating pain originating in one side of the throat or tonsillar region and radiating along the course of the eustachian tube to the tympanic membrane, external auditory canal, behind the angle of the jaw, and adjacent portion of the ear. As in trigeminal neuralgia, there may be trigger zones; they are usually in the pharyngeal wall, fauces, tonsillar regions, or base of the tongue. The pain may be brought on by talking, eating, swallowing, or coughing. It can lead to syncope, convulsions, and rarely cardiac arrest because of stimulation of the carotid sinus reflex. Glossopharyngeal neuralgia must be differentiated from other craniofacial neuralgias and from pain because of a structural lesion of the nerve. Some authorities differentiate

between glossopharyngeal neuralgia, in which the pain radiates from the throat to the ear, and Jacobson's neuralgia, in which the pain is limited to the ear and eustachian tube. Glossopharyngeal neuralgia is most often idiopathic but has been reported with lesions involving the peripheral distribution of the nerves. Multiple sclerosis only rarely causes glossopharyngeal neuralgia, although it is commonly associated with trigeminal neuralgia.

Carotid sinus hypersensitivity is due to inadvertent activation of the baroreceptors in the carotid sinus causing bradycardia and hypotension. Identifiable etiologies may include constriction around the neck (e.g., tight collar) or a mass in the neck impinging on the sinus, but many cases are idiopathic.

THE VAGUS NERVE

Anatomy and Physiology

The vagus (L. “wandering,” because of its wide distribution) is the longest and most widely distributed CN ([Figure 18.3](#)). Some of the nuclei of origin are the same as for CN IX, and it shares many functions with CN IX. It connects with four brainstem nuclei: the nucleus ambiguus, the DMNX, the nucleus of the spinal tract of CN V, and the nucleus of the solitary tract. It conveys exteroceptive GSA sensation from the pharynx, larynx, ear, and meninges and GVA fibers from the larynx, viscera of the thorax and abdomen, and receptors in the aorta. CN X carries skeletomotor axons from the nucleus ambiguus to the pharynx and larynx and parasympathetic axons from the DMNX to the smooth muscles and glands of the pharynx and larynx and to the thoracic and abdominal viscera. Its terminal ramifications reach the splenic flexure of the colon.

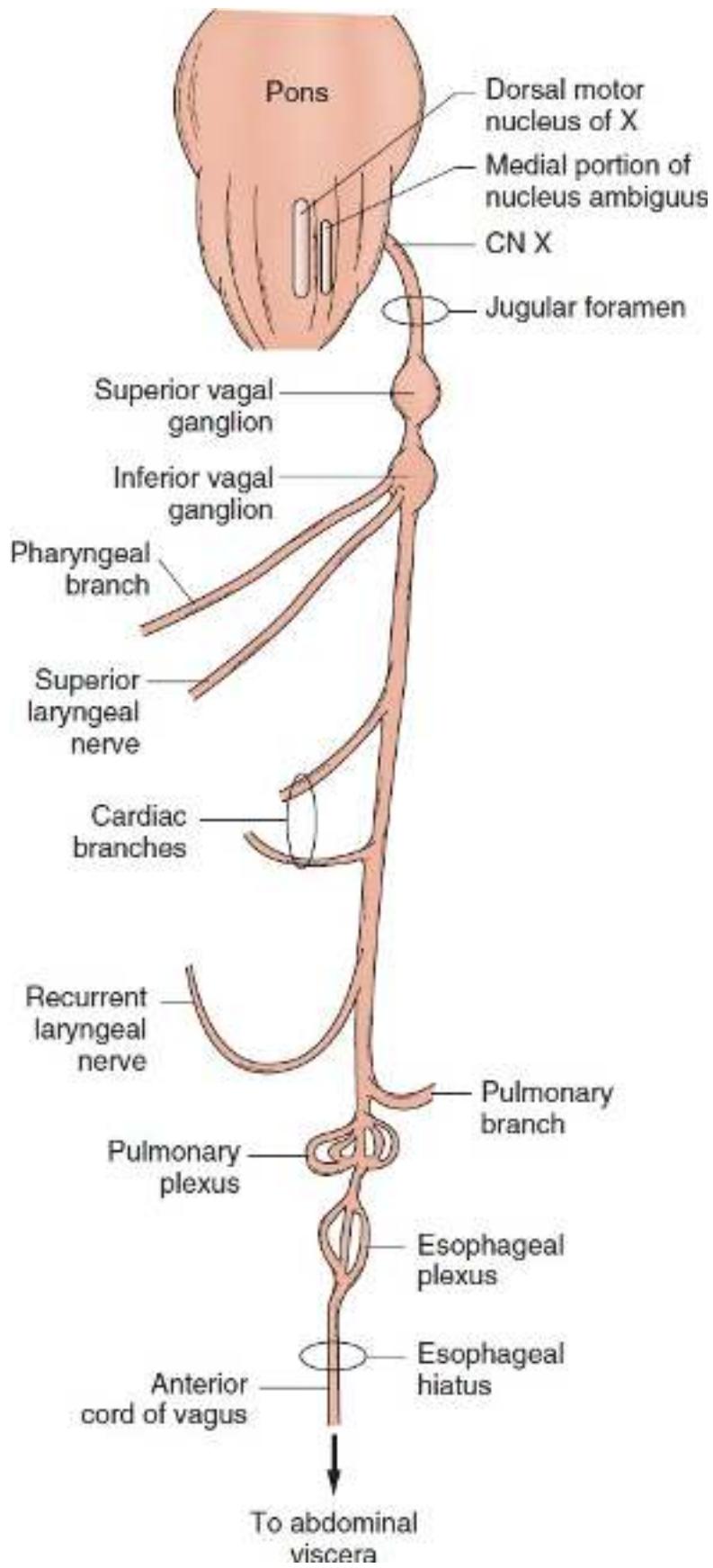


FIGURE 18.3 Peripheral distribution of the branches of the vagus nerve.

The vagus emerges from the medulla as a series of rootlets just below those of the glossopharyngeal. CN X leaves the skull through the jugular foramen in the same neural sheath as the cranial root of CN XI and behind CN IX. In the jugular foramen, the nerve lies close to the jugular bulb, a dilatation of the internal jugular vein that houses the glomus jugulare (tympanic body). The glomus jugulare has functions similar to the carotid body. CN X descends the neck in the carotid sheath, lying between the carotid artery and internal jugular vein to the upper border of the thyroid cartilage and then between the vein and common carotid to the base of the neck. Branches leave in the jugular foramen to supply the meninges and ear; other branches leave distal to the foramen to supply the pharynx and larynx. The major portion of the nerve enters the thorax. The vagus has two sensory ganglia. The superior (jugular) vagal ganglion is located in the jugular fossa of the temporal bone; the inferior (nodose) ganglion is located just distal to the jugular foramen. There are 10 major terminal branches that arise at different levels: (a) meningeal, (b) auricular, (c) pharyngeal, (d) carotid, (e) superior laryngeal, (f) recurrent laryngeal, (g) cardiac, (h) esophageal, (i) pulmonary, and (j) gastrointestinal. The terminal branches are summarized in [Table 18.2](#).

The Motor Portion

The cortical center regulating vagus function lies in the lower portion of the precentral gyrus; the supranuclear innervation is bilateral but primarily crossed. Fibers descend in the corticobulbar tracts to synapse in the nucleus ambiguus. The vagal branchiomotor fibers follow the same looping intramedullary course as the fibers of CN IX. There are three major branchiomotor branches: pharyngeal, superior laryngeal, and recurrent laryngeal. The actions of the muscles innervated by the vagus are summarized in [Table 18.1](#).

The pharyngeal branch runs between the internal and external carotid arteries and enters the pharynx, where it ramifies to form the pharyngeal plexus. The plexus also receives fibers from the external laryngeal branch, CN IX, and the sympathetic trunk. The vagus, with a contribution from the bulbar portion of CN XI, supplies all the striated muscles of the soft palate, pharynx, and larynx except for the stylopharyngeus (CN IX) and tensor veli palatini (CN V).

TABLE 18.2**The Terminal Branches of the Vagus Nerve**

Nerve	Anatomy
Meningeal branch	Arises from jugular ganglion; recurrent course upward through the jugular foramen; supplies dura of the posterior fossa
Auricular branch	Arises from superior vagal ganglion; receives filament from the inferior ganglion of CN IX; supplies GSA fibers to posterior part of the tympanic membrane, external acoustic meatus, and the skin of the posterior pinna; communicates with posterior auricular branch of CN VII
Pharyngeal branch	Arises from the inferior vagal ganglion; passes across internal carotid artery to the upper border of the middle pharyngeal constrictor; divides into numerous filaments that join branches of CN IX, superior laryngeal nerves and sympathetic nerves to form pharyngeal plexus. Motor innervation to all muscles of the soft palate and pharynx except for stylopharyngeus and tensor veli palatini; sensory innervation to mucous membrane of the pharynx
Carotid body branches	Arise from the inferior vagal ganglion, carry impulses from baro- and chemoreceptors to middle third of the nucleus of the solitary tract; form plexus with branches of CN IX
Superior laryngeal branch	Arises from the inferior vagal ganglion; divides into external and internal branches. Smaller external branch innervates cricothyroid muscle and sends branches to pharyngeal plexus. Internal branch provides sensory innervation to internal surfaces of the larynx as far down as the vocal folds
Recurrent laryngeal	Arise in the thorax and ascend back to the larynx; on the right, winds backward around subclavian

nerves	artery; on the left, loops around aortic arch; both ascend between the esophagus and trachea, behind common carotid artery and thyroid gland to the larynx; distributed to all muscles of the larynx except the cricothyroid; supply sensation to the mucous membrane of the larynx below the vocal folds
Cardiac branches	Superior and inferior branches; superior arises from the vagus; inferior arises from the trunk of the vagus and recurrent laryngeal on the right, on the left from the recurrent laryngeal only; communicates with cardiac branches of the sympathetic nervous system to form the cardiac plexus
Pulmonary branches	Arise in the thorax; communicate with filaments from the sympathetic division to form the pulmonary plexuses
Esophageal branches	Arise in the thorax; join filaments from the splanchnic nerves and thoracic sympathetics to form esophageal plexus
Gastrointestinal branches	Arise in the abdomen; form gastric, celiac, and hepatic plexuses

The superior laryngeal nerve arises distal to the pharyngeal branch and divides into an internal and external branch. The internal branch is primarily sensory. The external branch supplies the cricothyroid. All of the other intrinsic laryngeal muscles are supplied by the recurrent nerves, except for the arytenoid, which may receive some fibers from the internal branch of the superior laryngeal. The recurrent laryngeal nerves both descend deep into the thorax and then loop back to the larynx. On the right, the recurrent laryngeal arches around the subclavian artery and on the left around the aortic arch. Each nerve gives off cardiac, tracheal, and esophageal branches, ending on each side as the inferior laryngeal nerve to supply the intrinsic muscles of the larynx.

The Parasympathetic Portion

The parasympathetic component of CN X arises from the DMNX, a long cell column just dorsolateral to the hypoglossal nucleus extending from the upper pole of the inferior olive to the lower portion of the medulla. Some parasympathetic neurons lie immediately adjacent in the medial part of the nucleus ambiguus. The neurons in the nucleus ambiguus innervate the heart, and those in DMNX supply the other vagally innervated viscera. The fibers stream ventromedially and merge with the branchiomotor fibers coming from the nucleus ambiguus. The autonomic fibers leave the medulla as preganglionic fibers of the craniosacral division of the autonomic nervous system. They terminate in ganglia close to the viscera they supply and send short postganglionic fibers directly to the muscular and glandular structures they innervate. The vagus is the longest parasympathetic nerve in the body and mediates many important functions, which are discussed in [Chapter 45](#). In brief, a vagal discharge causes bradycardia, hypotension, bronchoconstriction, bronchorrhea, increased peristalsis, increased gastric secretion, and inhibition of adrenal function. The vagal centers in the medulla that control these functions are themselves under the control of higher centers in the cortex and hypothalamus. Inhibition of vagal function produces the opposite effects.

In its course through the thorax, the right vagus nerve gives off pulmonary and esophageal branches, passes through the esophageal opening in the diaphragm posterior to the esophagus, and then divides into gastric and celiac branches. The left vagus also gives off pulmonary and esophageal branches and then enters the abdomen anterior to the esophagus and divides into several gastric branches.

The Sensory Portion

The superior vagal ganglion is located in the upper part of the jugular foramen. It communicates through several delicate branches with the cranial portion of CN XI and with the petrous ganglion of CN IX, with CN VII, and with the superior cervical ganglion. The inferior vagal ganglion lies just beneath the jugular foramen. The cranial root of the CN XI passes through it to join CN X. The inferior ganglion also communicates with CN XII, the superior cervical ganglion, and the loop between C1 and C2. Both vagal ganglia are sensory, containing unipolar neurons that mediate general somatic, special visceral, and

general visceral afferents. The branchiomotor and parasympathetic axons pass through the ganglia without synapsing. The superior ganglion primarily conveys somatic sensation, and most of its communication is with the auricular nerve. The inferior ganglion relays general visceral sensation and taste.

The somatic sensory portion of the vagus conveys pain, temperature, and touch sensation from the pharynx, larynx, ear canal, external surface of the tympanic membrane, and meninges of the posterior fossa. In the larynx, GSA fibers from above the vocal folds travel in the internal laryngeal branch of the superior laryngeal nerve; fibers from below the vocal folds travel with the recurrent laryngeal nerve. Visceral afferents follow the same pathways. General sensory fibers from the region of the ear, ear canal, and tympanic membrane travel in the auricular branch (nerve of Arnold). Stimulation of the auricular branch, as by tickling the ear canal, can produce reflex activation of DMNX with coughing, vomiting, and even syncope (*mitempfindung*; see [Chapter 31](#)). The GSA fibers in CN X synapse in the nucleus of the spinal tract of CN V and are relayed to the thalamus and to the sensory cortex.

Fibers carrying GVAs from the pharynx, larynx, vagally innervated viscera, and baroreceptors and chemoreceptors in the aorta travel over the peripheral processes of neurons in the inferior vagal ganglion. The central processes terminate in the caudal portion of the solitary tract. Collaterals to the reticular formation, DMNX, and other CN nuclei mediate important visceral reflexes and are involved in the regulation of cardiovascular, respiratory, and gastrointestinal function. There are some taste fibers from the region of the epiglottis and arytenoids, which travel with the taste fibers of CN IX to terminate in the rostral solitary tract.

Normal Functions

Normal functions mediated by CNs IX and X include swallowing, phonation, and airway protection and modulation. The complex process of swallowing is divided into two stages, controlled primarily by CNs IX, X, and XII. In the first stage, the food bolus is driven back into the fauces by tongue action. During the second stage, the epiglottis closes over the entrance to the larynx, and the bolus glides along its posterior surface. The muscles of the soft palate and nasopharynx close above the bolus to prevent passage into the nasopharynx. The bolus is directed downward and backward into the pharynx, and then the constrictors contract to propel it downward into the esophagus.

The larynx is composed of several cartilages. The thyroid and cricoid cartilages form part of the outer casing. The arytenoids are paired cartilages lying in the interior; they have a muscular process and a vocal process. The true vocal cords are mucous membranes that cover the vocal ligaments, which extend from the vocal processes of the arytenoids to the thyroid cartilage. The larynx is controlled by myriad small muscles. The arytenoids may either slide or pivot; either action changes the configuration of the vocal cords. The glottic rim is the passageway between the vocal cords. Contraction and relaxation of the intrinsic laryngeal muscles change the tension or shape of the vocal cords and alter the aperture of the glottic rim. The muscles of the larynx perform three basic functions: They abduct and open the glottic rim to allow air entry and exit, they adduct and close the glottic rim to protect the airway during swallowing, and they regulate the tension on the vocal cords to allow phonation. The cricothyroids, posterior and lateral cricoarytenoids, and thyroarytenoids are paired muscles. The arytenoid muscle is unpaired. The actions of the intrinsic laryngeal muscles are summarized in [Table 18.1](#) and [Figure 18.4](#).

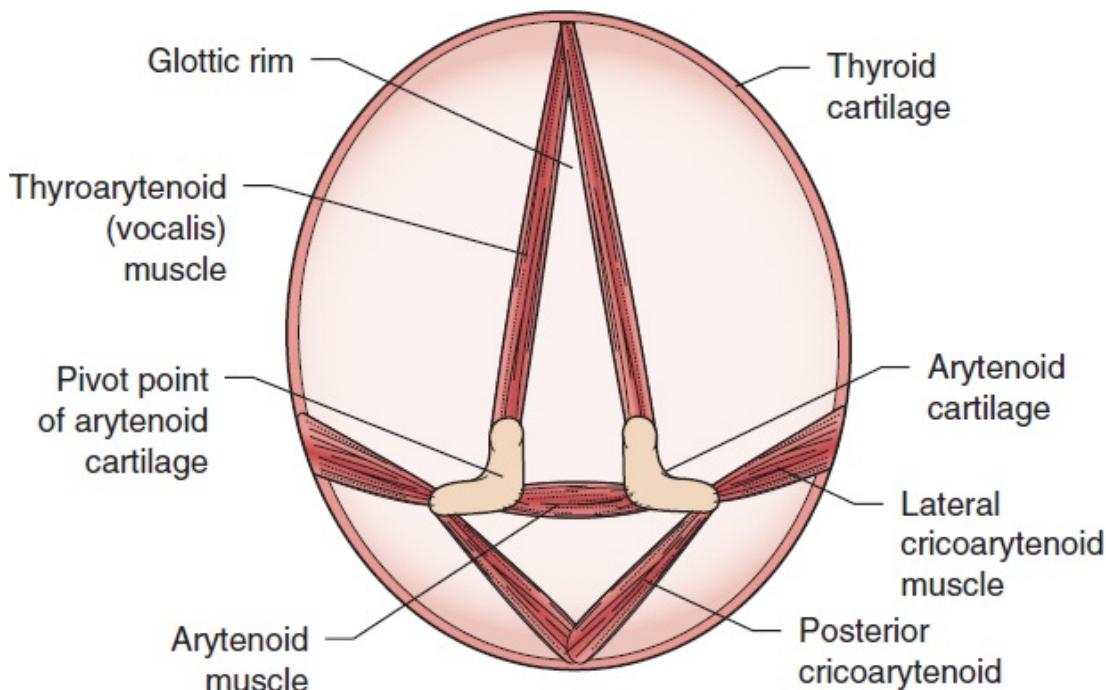


FIGURE 18.4 The cricothyroid muscles (not shown) tilt the thyroid cartilage forward on the cricoid cartilage, tensing the vocal cords. The thyroarytenoid muscles run from the thyroid cartilage to the arytenoid cartilages; contraction tenses the vocal cords. The other muscles attach to the cricoid cartilage. The paired arytenoids may either slide or pivot. Contraction of the arytenoid muscle pulls the arytenoid cartilages together, adducting the cords and closing the glottic rim. The lateral cricoarytenoid muscle causes the vocal process of the arytenoid to pivot medially, adducting the

cords. The posterior cricoarytenoid causes the vocal process to rotate laterally, abducting the cords.

Clinical Examination

Despite its size and importance, CN X is difficult to evaluate at the bedside. Formal autonomic function assessment can sometimes provide useful information.

Examination of the Motor Functions

The motor branches of CN X supply the soft palate, pharynx, and larynx in the same distribution as for CN IX and are examined in the same manner. The gag reflex is discussed in the section on CN IX.

The character of the voice and the ability to swallow provide information about the branchiomotor functions of the vagus. With acute unilateral lesions, the speech may have a nasal quality and dysphagia is often present; this is more marked for liquids than solids, with a tendency to nasal regurgitation because of velopharyngeal insufficiency. Examination of the soft palate includes observation of the position of the palate and uvula at rest and during quiet breathing and phonation. The median raphe of the palate rises in the midline on phonation. With a unilateral lesion of the vagus, there is weakness of the levator veli palatini and musculus uvulae, which causes a droop of the palate and flattening of the palatal arch ([Figure 18.5](#)). Preserved function of the tensor veli palatini (innervated by CN V) may prevent marked drooping of the palate. On phonation, the median raphe deviates toward the normal side. The palatal gag reflex may be lost on the involved side because of interruption of the motor rather than sensory path.

With bilateral vagus involvement, the palate cannot elevate on phonation; it may or may not droop, depending on the function of the tensor veli palatini. The palatal gag reflex is absent bilaterally. The tendency toward nasal speech and nasal regurgitation of liquids is pronounced. The speech is similar to that of a patient with cleft palate ([Chapter 9](#)).

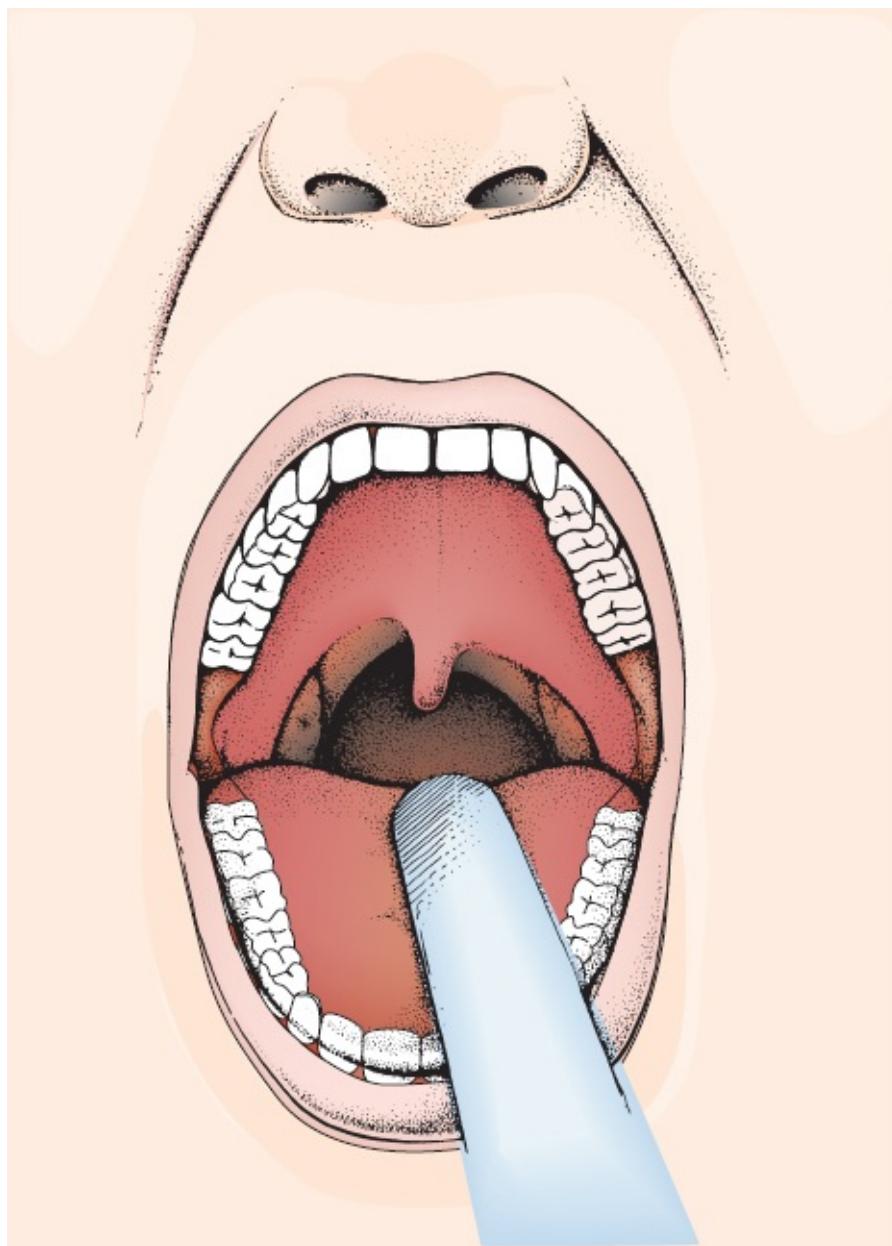


FIGURE 18.5 Unilateral paralysis of the soft palate.

Weakness of the pharynx may also produce abnormalities of speech and swallowing. With pharyngeal weakness, dysarthria is usually minimal unless there is also weakness of the soft palate or larynx. Spontaneous coughing and the cough reflex may be impaired. Dysphagia may occur but without the tendency to greater difficulty with liquids and to nasal regurgitation that occurs with palatal weakness. Dysphagia is marked only in acute unilateral or in bilateral lesions. Examination of the pharynx includes observation of the contraction of the pharyngeal muscles on phonation, notation of the elevation of the larynx on

swallowing, and testing the pharyngeal gag reflex. Unilateral weakness of the superior pharyngeal constrictor may cause a “curtain movement” (Vernet’s rideau phenomenon), with motion of the pharyngeal wall toward the nonparalyzed side on testing the gag reflex or at the beginning of phonation. The normal elevation of the larynx may be absent on one side in unilateral lesions and on both sides in bilateral lesions.

CN X innervates the vocal cords. Normal movement of the vocal cords is necessary for three vital functions: breathing, coughing, and talking. During inspiration and expiration, the cords abduct to allow for free airflow; when speaking, the cords adduct and vibrate to accomplish phonation. The cords are also adducted when coughing. Movements of the many small muscles that control the larynx are complex and have different effects on laryngeal function (Table 18.1). The effects of weakness of the different laryngeal muscles are summarized in Table 18.3. A unilateral lesion of the vagus may cause cord weakness or paralysis. Vocal cord dysfunction alters the character and quality of the voice and may produce abnormalities of articulation, difficulty with respiration, and impairment of coughing.

Spasmodic dysphonia is a common focal dystonia that involves the vocal cords and causes characteristic voice changes (Chapter 30; for video, see [Video Link 18.2](#)). Spasmodic dysphonia most often causes abnormal adduction spasms of both vocal cords, and the voice is strained and high-pitched. Abductor dysphonia is due to spasmodic contraction of the posterior cricoarytenoid, which causes a failure of normal adduction on phonation; the voice is breathy and hoarse. This type of spasmodic dysphonia is most likely to be confused with a lesion of CN X. Direct and indirect laryngoscopy and videostroboscopy are valuable adjuncts to the routine examination.

TABLE 18.3 The Effects of Weakness of Muscles of the Larynx

Muscle	Effect of Weakness
Cricothyroid	Loss of tension; elongation of the vocal cord in phonation; loss of high tones; voice deep, hoarse, and easily fatigued; inspiration normal with either dyspnea or stridor
Thyroarytenoid	Little difficulty with abduction, but adduction slightly impaired; with bilateral paralysis, the glottis has an

	oval instead of linear appearance on phonation; voice hoarse; no dyspnea or stridor
Arytenoid	Glottis closed only anteriorly; the larynx shows a small triangular slit posteriorly during phonation; inspiration is normal
Unilateral abductors	The cord lies close to midline; cannot be abducted on inspiration; voice hoarse, but phonation and coughing little affected (adduction is normal); dyspnea uncommon because normal cord abducts on inspiration, but inspiratory stridor may occur
Bilateral abductors	Both cords close to the midline and cannot be abducted; voice hoarse, but phonation little affected and coughing normal because adduction preserved; severe dyspnea with inspiratory stridor
Unilateral adductors	Paralysis of one lateral cricoarytenoid; hoarseness and impairment of coughing
Bilateral adductors	Cords not adducted on phonation and voice either lost or reduced to whisper; inspiration normal without stridor or dyspnea; coughing normal
Total unilateral palsy	Both adduction and abduction affected; involved cord lies in cadaveric position, motionless in midabduction; voice low-pitched and hoarse; difficulty coughing; little or no dyspnea; inspiratory stridor absent or present only with deep inspiration
Total bilateral palsy	Both cords in cadaveric position; phonation and coughing lost; marked dyspnea with stridor, especially on inspiration

The most common cause of vocal cord paralysis is a lesion of one recurrent laryngeal nerve. The paralysis may evolve from mild abduction impairment because of isolated involvement of the posterior cricoarytenoid to complete paralysis with the cord in the cadaveric position. With slight weakness of the

vocal cords or pharynx, hoarseness and dysphagia may be apparent only when the head is turned to either side. Occasionally, even severe weakness of a vocal cord causes little appreciable effect on the voice because of preserved movement of the normal cord.

Examination of the Autonomic Functions

The autonomic functions of CN X are summarized above and are discussed in more detail in [Chapter 45](#).

Examination of the Sensory Functions

The somatic sensory elements of CN X are discussed above. They are not clinically important and cannot be adequately tested.

Examination of the Reflexes

CN X plays a part in several autonomic, or visceral, reflexes; loss of these reflexes may follow a lesion of the tenth nerve. In some of these reflexes, such as the sternutatory, sucking, and yawning, the vagus plays a supportive role. The nasal, sneeze, or sternutatory reflex is discussed in [Chapter 15](#). Afferent impulses are carried over CN V to the reflex center in the brainstem and upper spinal cord, with efferent impulses primarily by CN VII with some overflow to CNs IX and X and the phrenic nerve. In other reflexes, such as swallowing, vomiting, and coughing, the vagus is central. These are discussed in [Box 18.1](#).

BOX 18.1

Vagally Mediated Reflexes

The oculocardiac reflex is bradycardia caused by pressure on the eyeball. It may also be induced by painful stimulation of the skin on the side of the neck. The afferent limb is carried by cranial nerve (CN) V and the efferent by CN X. The reflex is inconstant, unstandardized, and influenced by emotion. Usually, the pulse is not slowed more than 5 to 8 beats per minute. The slowing may be accompanied by extrasystoles. The oculocardiac reflex may be absent in lesions involving CN X. It is sometimes used to slow an

excessively rapid heart rate, as in tachyarrhythmias.

The vomiting reflex produces reverse peristalsis in the esophagus and stomach, with forceful ejection of material from the stomach. The reflex center is in the region of the dorsal efferent nucleus. Vomiting occurs for many reasons. Stimulation of the pharynx, palate, esophagus, stomach, duodenum, or lower gastrointestinal tract may activate the reflex. The afferent limb is carried by CN X, probably to the solitary tract; from there, the impulse is relayed to the dorsal efferent nucleus and also down the spinal cord to contract the diaphragm and abdominal muscles, relax the cardiac sphincter, and contract the pyloric sphincter. The swallowing reflex is caused by stimulation of the pharyngeal wall or back of the tongue. Afferent impulses travel through CNs V, IX, and X and efferent impulses through CNs IX, X, and XII. The cough reflex is activated by stimulation of the mucous membrane of the pharynx, larynx, trachea, or bronchial tree. Stimulation of the tympanic membrane or external auditory canal can also elicit a cough response (*mitempfindung*). The afferent limb of the reflex is carried through CNs IX and X to the solitary tract, and the efferent impulses descend to the pharyngeal muscles, tongue, palate, and larynx and to the diaphragm, chest, and abdominal muscles.

Hiccup (*singultus*) is a sudden reflex contraction of the diaphragm causing a forceful inspiration. Associated laryngeal spasm causes the glottis to snap shut, causing sudden arrest of the inspiration and the characteristic sound. The phrenic nerves are the major pathway, but CN X contributes. Yawning is a complex respiratory reflex with deep, prolonged inspiration, usually involuntary, through the open mouth. It typically occurs during sleepiness and fatigue but may also be brought on by suggestion or boredom. Yawning can occur in neurologic disease as well.

The carotid sinus reflex is produced by stimulation of the carotid sinus or the carotid body by pressure at the carotid bifurcation. It causes slowing of the heart rate, a fall in blood pressure, a decrease in cardiac output, and peripheral vasodilatation. When the response is exaggerated, there may be syncope. The afferent limb of the reflex is carried over CN IX and the efferent over CN X. The carotid sinus reflex is discussed further under CN IX.

Disorders of Function

A unilateral vagal lesion causes weakness of the soft palate, pharynx, and larynx. Acute lesions may produce difficulty swallowing both liquids and solids and hoarseness or a nasal quality to the voice. The only definite sensory change is anesthesia of the larynx because of involvement of the superior laryngeal nerve. It is seldom possible to demonstrate loss of sensation behind the pinna and in the external auditory canal. The gag reflex is absent on the involved side. Autonomic reflexes (vomiting, coughing, and sneezing) are not usually affected. Tachycardia and loss of the oculocardiac reflex on the involved side may occur, but usually there are no cardiac symptoms. Gastrointestinal disturbances are inconspicuous. Bilateral complete vagal paralysis is incompatible with life. It causes complete paralysis of the palate, pharynx, and larynx, with marked dysphagia and dysarthria; tachycardia; slow, irregular, respiration; vomiting; and gastrointestinal atonia. Lesions of individual vagal branches are rare except for involvement of the recurrent laryngeal nerve.

The primary effect of increased vagal activity is bradycardia. The term vasovagal refers to the effects of the vagus nerve on the blood vessels. Vasovagal attacks (fainting, syncope) are characterized by bradycardia, hypotension, peripheral vasoconstriction, and faintness, sometimes with loss of consciousness. Vasovagal attacks are typically induced by strong emotion or pain. The bradycardia and projectile vomiting that occur with increased intracranial pressure may be vagally mediated. Cheyne-Stokes, Biot, and Kussmaul breathing; respiratory tics; forced yawning; and other abnormalities of breathing may be vagally mediated as well. Spasm of pharyngeal muscles can occur in certain central nervous system disorders. Other conditions in which there is increased activity in the vagal system are seldom of primary neurologic origin.

Rhythmic movements of the palate (palatal myoclonus, palatal microtremor, or palatal nystagmus) can occur with a lesion of the brainstem, usually vascular ([Video 30.7](#)). The movements are mediated by CN X. Palatal myoclonus is discussed further in [Chapter 30](#). The very rare syndrome of superior laryngeal neuralgia causes lancinating pains that radiate from the larynx to the ear.

Unilateral supranuclear lesions generally cause no dysfunction because of bilateral innervation; dysphagia from a unilateral lesion can occur but is rare. Bilateral supranuclear lesions, as from pseudobulbar palsy, cause dysphagia and dysarthria ([Chapter 21](#)). Extrapyramidal disorders may produce difficulty with swallowing and talking. Patients with Parkinson's disease typically have a hypokinetic dysarthria ([Chapter 9](#)). Laryngeal spasm with stridor may occur in Parkinson's disease and other extrapyramidal disorders. The voice is commonly

affected by essential tremor.

Nuclear lesions of the nucleus ambiguus can occur with any intrinsic brainstem disease. A slowly progressive nuclear lesion, such as in bulbar ALS, syringomyelia, and some neoplasms, may cause fasciculations in the palatal, pharyngeal, and laryngeal muscles. The speech disturbances are discussed in [Chapter 9](#). Lesions of the nucleus ambiguus or intramedullary fibers of CNs IX and X commonly occur with vascular disease, for example, lateral medullary (Wallenberg) syndrome. Nuclear lesions are usually associated with involvement of other CN nuclei and long motor or sensory tracts. Because of the somatotopic organization, lesions limited to the rostral portion of the nucleus ambiguus may produce only weakness of the palate and pharynx, sparing laryngeal functions.

Infranuclear involvement may occur with lesions at the base of the brain, in the cerebellopontine angle, in the jugular foramen, or along the course of the vagus nerves. Extramedullary, intracranial involvement can occur in processes involving the meninges, extramedullary tumors, aneurysms, trauma, sarcoidosis, and skull fractures. Other lower CNs are usually involved as well ([Chapter 21](#)). Lesions at the jugular foramen or in the retroparotid space usually involve some combination of CNs IX, X, XI, and XII and the cervical sympathetics. These lower CN syndromes are discussed in [Chapter 21](#). Isolated or multiple lower CN palsies can be a manifestation of dissecting aneurysm of the cervical internal carotid artery or occur as a complication of carotid endarterectomy. Isolated CN IX palsy has been reported as a complication of traumatic internal maxillary artery dissection.

The main trunk of the vagus may be injured in the neck or thorax by trauma, carotid aneurysms, or other mass lesions. Vocal cord and diaphragmatic weakness occur in some forms of Charcot-Marie-Tooth disease. Individual vagal branches may be involved by disease processes in the neck, upper mediastinum, thorax, and abdomen. The recurrent laryngeal nerve is the most frequently affected; the left is more often damaged than the right because of its longer course. The recurrent laryngeals may be damaged by tumors in the neck, especially carcinoma of the thyroid, cervical adenopathy, metastatic lesions, Hodgkin disease, lymphosarcoma, aortic aneurysms, mitral stenosis with enlargement of the left atrium, pericarditis, mediastinal and apical tumors, stab wounds in the neck, or accidental trauma during a thyroidectomy or other surgical procedure. Recurrent laryngeal weakness causes a flaccid dysphonia with breathiness and mild inspiratory stridor; palatopharyngeal functions are preserved. Diplophonia may occur because of unbalanced vocal cord vibration

frequency. Compression of the left recurrent laryngeal nerve between the aorta and the pulmonary artery because of a variety of cardiovascular disorders may cause hoarseness (cardiovocal or Ortner's syndrome). Bilateral recurrent laryngeal palsies cause abduction impairment and leave the vocal cords approximating each other in the midline; the most common cause is thyroid surgery. This results in dyspnea and inspiratory stridor. The superior laryngeal and pharyngeal branches may be involved in trauma, or in neoplasms or abscesses in the neck, but clinical dysfunction is scant because of the primarily sensory function of the nerve; there may be mild hoarseness because of weakness of the cricothyroid muscle. Metastatic breast cancer infiltrating behind the carotid sheath at C6 has been reported to produce a combination of recurrent laryngeal and phrenic nerve dysfunction with an accompanying Horner syndrome. Hoarseness and voice fatigue because of laryngeal involvement may be prominent in rare patients with myasthenia gravis.

Syncope, sometimes associated with paroxysmal neck pain, may occur because of neoplasms involving the carotid sinus nerve. The mechanism is probably similar to that seen in syncope due to glossopharyngeal neuralgia. Swallow syncope results from dysfunction, usually because of metastatic disease, of CNs IX and X. The patient develops bradycardia and hypotension because of involvement of the baroreceptor nerves.

Video Links

Video Link 18.1. Palatal deviation. http://neurosigns.org/wiki/Palatal_deviation

Video Link 18.2. Spasmodic dysphonia.

http://neurosigns.org/wiki/Spasmodic_dysphonia

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CHAPTER 19

The Spinal Accessory Nerve

ANATOMY AND PHYSIOLOGY

The spinal accessory (SA) nerve, cranial nerve XI (CN XI), is actually two nerves that run together in a common bundle for a short distance. The smaller cranial portion (ramus internus) is a special visceral efferent (SVE) accessory to the vagus. Arising from cells within the caudal nucleus ambiguus, with some contribution from the dorsal motor nucleus of the vagus, it emerges from the medulla laterally as four or five rootlets caudal to the vagal filaments. The cranial root runs to the jugular foramen and unites with the spinal portion, traveling with it for only a few millimeters to form the main trunk of CN XI. The cranial root communicates with the jugular ganglion of the vagus and then exits through the jugular foramen separately from the spinal portion. It passes through the ganglion nodosum and then blends with the vagus ([Figure 19.1](#)). It is distributed principally with the recurrent laryngeal nerve to sixth branchial arch muscles in the larynx, and its contribution is indistinguishable from that of the vagus except there is no CN XI contribution to the cricothyroid muscle. A few fibers that originate in the dorsal motor nucleus may contribute parasympathetic fibers to the cardiac branches of the vagus. Lachman et al. have questioned whether the cranial root of the SA nerve even exists.

The major part of CN XI is the spinal portion (ramus externus). Its function is to innervate the sternocleidomastoid (SCM) and trapezius muscles. The fibers of the spinal root arise from SVE motor cells in the SA nuclei in the ventral horn from C2 to C5, or even C6. The cell column of the SA nucleus lies in a position analogous to the nucleus ambiguus in the medulla. The cell column making up the SA nucleus is somatotopically organized. The upper spinal cord portion innervates primarily the ipsilateral SCM; the lower spinal portion innervates primarily the ipsilateral trapezius. In keeping with the tendency of branchial

arch-related nerves to make internal loops, its axons arch posterolaterally through the lateral funiculus and emerge as a series of rootlets laterally between the anterior and posterior roots. These unite into a single trunk, which ascends between the denticulate ligaments and the posterior roots. The nerve enters the skull through the foramen magnum, ascends the clivus for a short distance, and then curves laterally. The spinal root joins the cranial root for a short distance, probably receiving one or two filaments from it. It exits through the jugular foramen in company with CNs IX and X.

CN XI emerges from the skull posteromedial to the styloid process and then descends in the neck near the internal jugular vein, behind the digastric and stylohyoid muscles, to enter the deep surface of the upper part of the SCM muscle. It passes through the SCM, sending filaments to it, and then emerges at its posterior border near the midpoint, coursing near the great auricular nerve. CN XI then runs obliquely across the posterior triangle of the neck on the surface of the levator scapula muscle, superficially and in close proximity to the lymph nodes of the posterior cervical triangle. About three fingerbreadths above the clavicle, the nerve enters the deep surface of the anterior border of the upper trapezius muscle. In the neck, the SA contributes fibers to the cervical plexus, rami trapezii, and then courses to the caudal aspect of the trapezius. Most of the communications with C2 through C4 are conveying proprioceptive information from CN XI, which will enter the spinal cord in the upper cervical segments. The innervation of the SCM may be more complex than is to be found in most anatomical texts, possibly including fibers from CN X. Over half of the patients undergoing division of the SA nerve and the upper cervical motor roots as treatment for cervical dystonia had residual SCM activity of sufficient magnitude to make further surgery necessary before the muscle was effectively paralyzed.

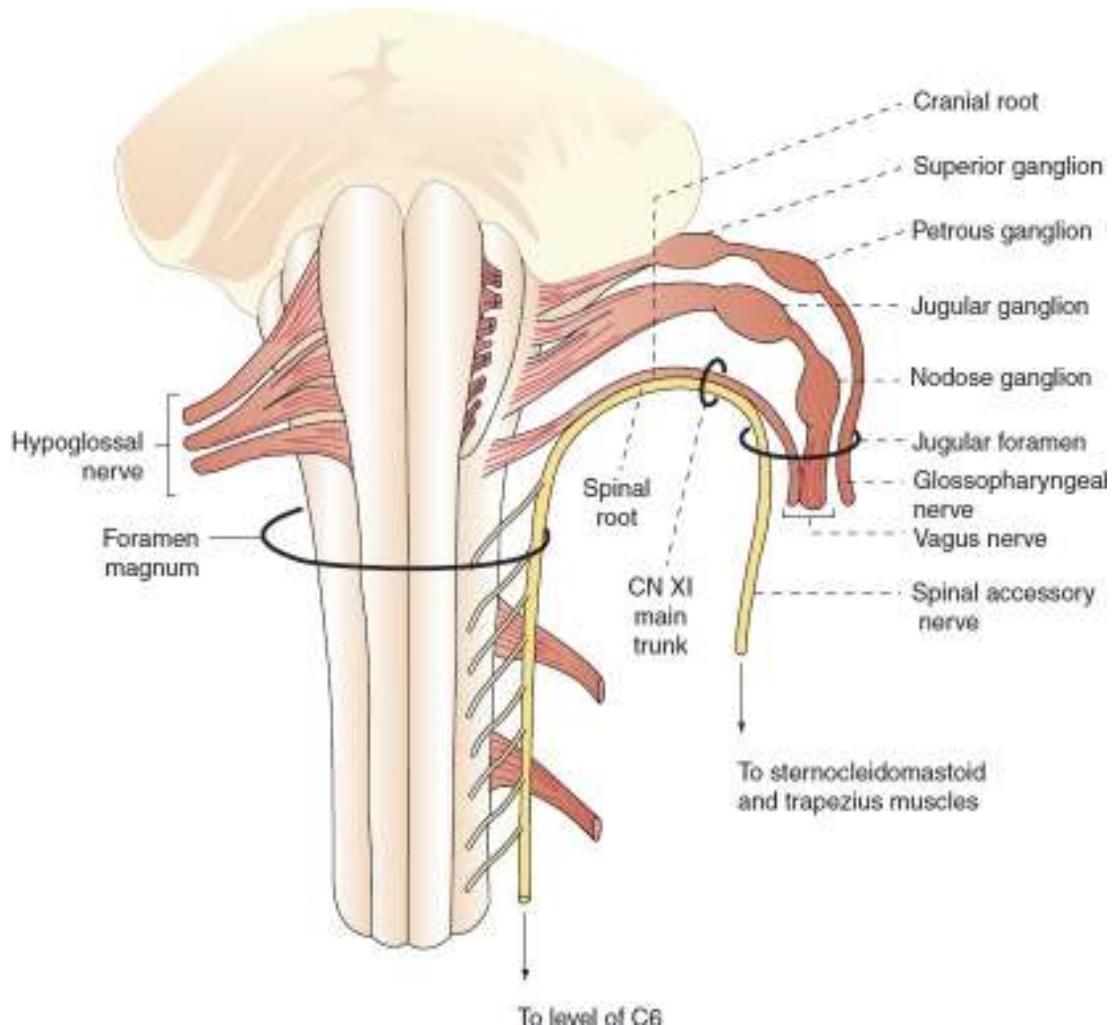


FIGURE 19.1 Relationship of the cranial and spinal portions of the accessory nerve to the vagus and glossopharyngeal nerves.

The innervation of the trapezius shows some individual variability. The SA nerve is the primary innervation to the upper trapezius, but Soo et al. have shown that the cervical plexus may contribute motor fibers, especially to the middle and lower trapezius. The neurons of the spinal portion of XI communicate with the oculomotor, trochlear, abducens, and vestibular nuclei through the medial longitudinal fasciculus. These connections are important in controlling conjugate deviation of the head and eyes in response to auditory, vestibular, and other stimuli.

The supranuclear innervation of CN XI arises from the lower portion of the precentral gyrus. Fibers from the lateral corticospinal tract in the cervical spinal cord communicate with the SA nucleus. There is some controversy, but the bulk of current evidence indicates that both the SCM and trapezius receive bilateral

supranuclear innervation. However, the input to the SCM motor neuron pool is predominantly ipsilateral and that to the trapezius motor neuron pool is predominantly contralateral (Box 19.1). The SCM turns the head to the opposite side, and its supranuclear innervation is ipsilateral. Therefore, the right cerebral hemisphere turns the head to the left.

The SCM muscles function with the other cervical muscles to flex the head and turn it from side to side. When one SCM contracts, the head is drawn toward the ipsilateral shoulder and rotates so that the occiput is pulled toward the ipsilateral shoulder, while the face turns in the opposite direction and upward. Acting together, the two muscles flex the neck and bring the head forward and downward. With the head fixed, the two muscles assist in elevating the thorax in forced inspiration.

The trapezius retracts the head and draws it ipsilaterally. It also elevates, retracts, and rotates the scapula and assists in abducting the arm above horizontal. When one trapezius contracts with the shoulder fixed, the head is drawn to that side. When both contract, the head is drawn backward and the face deviated upward. When the head is fixed, the upper and middle fibers of the trapezius elevate, rotate, and retract the scapula and shorten the distance between the occiput and the acromion. The lower fibers depress the scapula and draw it toward the midline. The SCM and trapezius muscles thus act together to rotate the head from side to side and to flex and extend the neck.

BOX 19.1

Cortical Innervation of the Sternocleidomastoid Muscle

The sternocleidomastoid (SCM) may be an exception to the general scheme of contralateral hemispheric innervation. Authorities debate whether the SCMs receive ipsilateral, contralateral, or bilateral cortical innervation. Studying the function of the SCM muscles during intracarotid injection of amytal (Wada testing), DeToledo et al. demonstrated weakness of the right SCM after injection into the right internal carotid artery in some patients and little to no weakness in others. This suggested that the SCMs receive bilateral hemispheric innervation with the maximal input from the ipsilateral hemisphere. They proposed that the SA nucleus has rostral and caudal portions and that the rostral (SCM) portion receives bihemispheric projections, but the innervation of the caudal (trapezius) portion is

predominantly contralateral. This would be analogous to the supranuclear innervation of the facial nerve nucleus, bilateral to the rostral portions but contralateral to the caudal portions. Transcranial stimulation studies concluded projections to the SCM were bilateral but predominantly contralateral, and those to the trapezius exclusively contralateral. Some have contended the nerve double decussates, but this remains unproven.

CLINICAL EXAMINATION

The functions of the cranial portion of CN XI cannot be distinguished from those of CN X, and examination is limited to evaluation of the functions of the spinal portion. A complex array of many muscles is involved in moving the head, including the scaleni, splenii and obliqui capitis, recti capitis, and longi capitis and colli. With bilateral paralysis of CN XI–innervated muscles, there is diminished but not absent neck rotation, and the head may droop or even fall backward or forward, depending upon whether the SCMs or the trapezii are more involved.

One SCM acts to turn the head to the opposite side or to tilt it to the same side. Acting together, the SCMs thrust the head forward and flex the neck. The muscles should be inspected and palpated to determine their tone and volume. The contours are distinct even at rest. With a nuclear or infranuclear lesion, there may be atrophy or fasciculations.



FIGURE 19.2 Examination of the sternocleidomastoid (SCM) muscle. When the patient turns his head to the right against resistance, the contracting muscle can be seen and palpated.

To assess SCM power, have the patient turn the head fully to one side and hold it there, and then try to turn the head back to midline, avoiding any tilting or leaning motion. The muscle usually stands out well, and its contraction can be seen and felt (Figure 19.2). Significant weakness of rotation can be detected if the patient tries to counteract firm resistance. Unilateral SCM paresis causes little change in the resting position of the head. Even with complete paralysis, other cervical muscles can perform some degree of rotation and flexion; only occasionally is there a noticeable head turn. The two SCM muscles can be examined simultaneously by having the patient flex his neck while the examiner exerts pressure on the forehead or by having the patient turn the head from side to side. Flexion of the head against resistance may cause deviation of the head toward the paralyzed side. With unilateral paralysis, the involved muscle is flat and does not contract or become tense when attempting to turn the head contralaterally or to flex the neck against resistance. Weakness of both SCMs causes difficulty in anteroflexion of the neck, and the head may assume an extended position. The SCM reflex may be elicited by tapping the muscle at its clavicular origin. Usually, there is a prompt contraction. The reflex is mediated

by the accessory and upper cervical nerves, but has little significance in neurologic diagnosis.



FIGURE 19.3 Paralysis of the left trapezius muscle. There is a depression in the shoulder contour with downward and lateral displacement of the scapula. (Reprinted with permission from Kelley MJ, Kane TE, Leggin BG. Spinal accessory nerve palsy: associated signs and symptoms. *J Orthop Sports Phys Ther* 2008;38(2):78–86. <https://doi.org/10.2519/jospt.2008.2454>. Copyright © Journal of Orthopaedic & Sports Physical Therapy®.)

With trapezius atrophy, the outline of the neck changes, with depression or drooping of the shoulder contour and flattening of the trapezius ridge (Figure 19.3). Severe trapezius weakness causes sagging of the shoulder, and the resting position of the scapula shifts downward. The upper portion of the scapula tends to fall laterally, while the inferior angle moves inward. This scapular rotation and displacement are more obvious with arm abduction.

The strength of the trapezius is traditionally tested by having the patient shrug the shoulders against resistance (Figure 19.4). However, much of shoulder shrugging is due to the action of the levator scapulae. A better test of the upper trapezius is resisting the patient's attempt to approximate the occiput to the acromion. The movement may be observed and the contraction seen and palpated. To examine the middle and lower trapezius, place the patient's

abducted arm horizontally, palm up, and attempt to push the elbow forward. Muscle power should be compared on the two sides. In unilateral weakness of the trapezius, these movements are impaired.



FIGURE 19.4 Examination of the trapezius muscle. **A.** Examiner pressing the shoulder down against patient's resistance. **B.** Patient attempting to elevate shoulder against examiner's resistance.

The trapezius is one of several muscles that act to stabilize the scapula and create a platform for movements of the humerus. The serratus anterior protracts the scapula, moving it forward as in a boxing jab. The trapezius is a synergist to the main mover, the rhomboids, in retracting the scapula. The trapezius and serratus anterior act in concert to rotate the scapula when the arm is abducting. The trapezius brings the glenoid fossa progressively more cephalad so that the abduction motion is unrestricted. In addition, contraction of the upper trapezius adds the final few degrees of abduction, after the glenohumeral and acromioclavicular ranges of motion are exhausted, so that the arm can be brought directly overhead ([Figure 27.4](#)).

Weakness of the trapezius disrupts the normal scapulohumeral rhythm and impairs arm abduction. Impairment of upper trapezius function causes weakness of abduction beyond 90 degrees. Weakness of the middle trapezius muscle causes winging of the scapula. The winging because of trapezius weakness is more apparent on lateral abduction in contrast to the winging due to serratus anterior weakness, which is greatest with the arm held in front. In fact, with winging due to trapezius weakness, the jutting of the inferior angle lessens when the arm is raised anteriorly; in winging due to serratus anterior weakness, it

worsens. Scapular winging is discussed further in [Chapter 27](#). For videos of scapular winging, see [Video Links 19.1](#) and [19.2](#).

When the trapezius is weak, the arm hangs lower on the affected side, and the fingertips touch the thigh at a lower level than on the normal side. Placing the palms together with the arms extended anteriorly and slightly below horizontal shows the fingers on the affected side extending beyond those of the normal side. The drooping of the arm and shoulder caused by trapezius weakness may lead to pain and subjective sensory complaints in the extremity because of traction on musculoligamentous structures and possibly sensory nerves. Loss of shoulder mobility may result in a secondary adhesive capsulitis, which further restricts motion.

The two trapezius muscles can be examined simultaneously by having the patient extend his neck against resistance. Bilateral paralysis causes weakness of neck extension. The patient cannot raise his chin, and the head may tend to fall forward (Dropped Head Syndrome, see below). The shoulders look square or have a drooping, sagging appearance because of atrophy of both muscles. The relationship of the trapezius muscle to the movements of the shoulder girdle and the examination of the functions of its lower fibers are discussed in [Chapter 27](#).

DISORDERS OF FUNCTION

Weakness of the muscles supplied by CN XI may be caused by supranuclear, nuclear, or infranuclear lesions. Supranuclear involvement usually causes at worst moderate loss of function because innervation is at least partially bilateral in most patients. In hemiplegia, there is usually no head deviation, but testing may reveal slight, rarely marked, weakness of the SCM, with difficulty turning the face toward the involved limbs. When significant SCM paresis is present, the head may be turned away from the weak limbs, indicating weakness of the SCM ipsilateral to the lesion with the preserved SCM turning the head toward the lesion. This occurs with lesions involving the corticobulbar fibers at any level from the cortex to the brainstem. There may be depression of the shoulder resulting from trapezius weakness on the affected side.

Irritative supranuclear lesions may cause head turning away from the discharging hemisphere. This turning of the head (or head and eyes) may occur as part of a contraversive, ipsiversive, or jacksonian seizure and is often the first manifestation of the seizure. Extrapyramidal lesions may also involve the SCM

and trapezius muscles, causing rigidity, akinesia, or hyperkinesis ([Chapter 30](#)). Abnormal involuntary movements of the head and neck are seen in chorea, athetosis, dystonia musculorum deformans, and other dyskinesias. The SCM and trapezius are frequently involved in cervical dystonia, a common focal dystonia causing torticollis, anterocollis, or retrocollis ([Chapter 30](#)). Cervical dystonia occasionally causes hypertrophy of the SCM ([Figure 19.5](#)).

Lesions of the lower brainstem or upper cervical spinal cord may cause dissociated weakness of the SCM and trapezius muscles depending on the exact location. Nuclear involvement of the SA nerve may occur in motor neuron disease, syringobulbia, and syringomyelia. In nuclear lesions, the weakness is frequently accompanied by atrophy and fasciculations.

Infranuclear or peripheral lesions—either extramedullary but within the skull, in the jugular foramen, or in the neck—are the most common causes of impairment of function of the SA nerve. Tumors in the foramen magnum or along the clivus can compress CN XI, usually with concomitant CNs IX and X involvement. Lesions of the cerebellopontine angle occasionally extend caudal toward the foramen magnum and involve CN XI. Tumors more caudal may extend upward; most common are neurinomas of the hypoglossal nerve. Neurinomas involving CN IX or X may extend to involve CN XI. Other intracranial, extramedullary neoplasms include meningiomas and neurofibromas, which may extend through the jugular foramen in dumbbell fashion. Basal skull fractures, meningitis, or processes at or just distal to the skull base give rise to a number of syndromes reflecting involvement of the lower CNs ([Chapter 21](#)). The most common is the jugular foramen syndrome, in which the SA nerve is involved along with CNs IX and X ([Chapter 21](#)). Such conditions affect both the SCM and the trapezius.

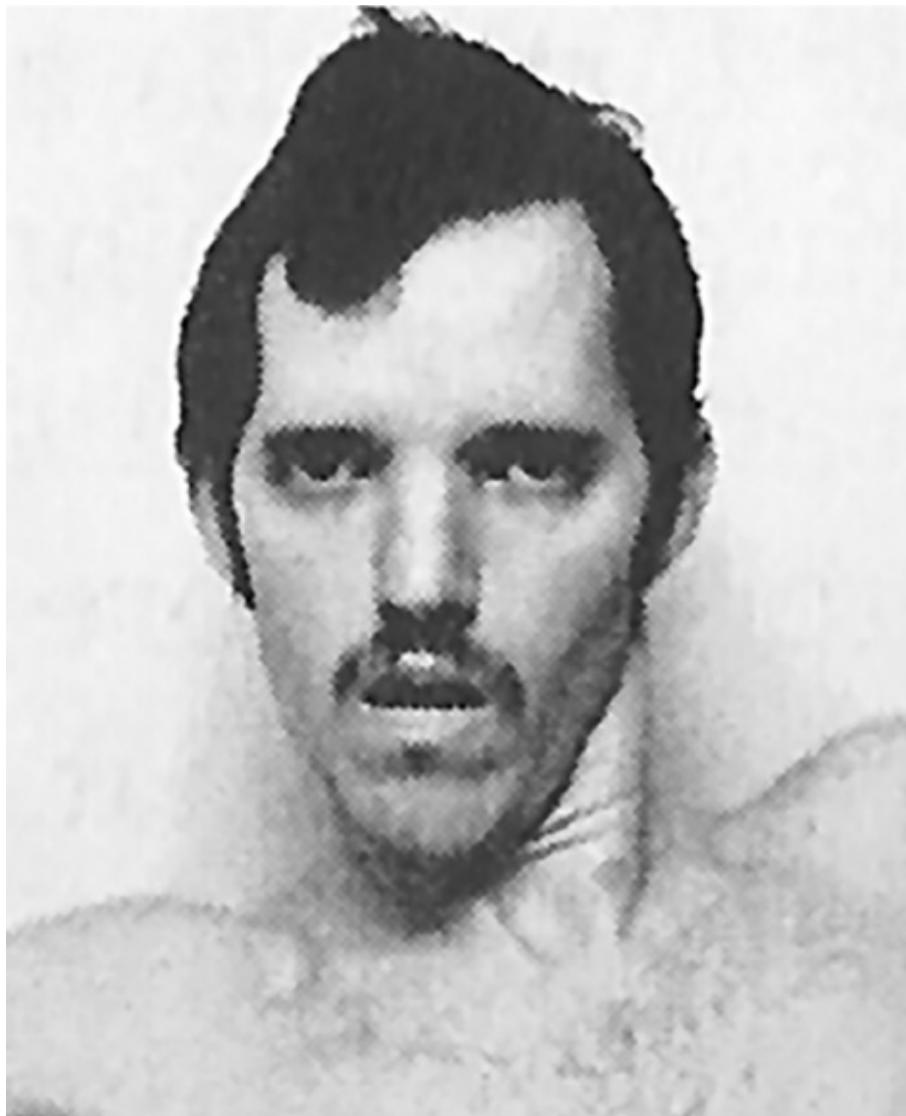


FIGURE 19.5 Marked hypertrophy of the left sternocleidomastoid because of cervical dystonia. (Modified from Jankovic J, Tolosa E. *Parkinson's Disease & Movement Disorders*. 6th ed. Philadelphia: Wolters Kluwer, 2015, with permission.)

In the posterior triangle of the neck, the SA nerve is very vulnerable, because it lies superficially, covered only by skin and subcutaneous tissue. The nerve may be affected by severe cervical adenopathy, neoplasms, trauma, or abscesses. These lesions are generally distal to the SCM and affect only trapezius function. The most common cause of SA neuropathy in the posterior triangle is trauma, often iatrogenic. Surgical trauma may be unavoidable, as in radical neck dissection, or inadvertent, as in lymph node biopsy. The procedures most commonly implicated are lymph node biopsy and carotid endarterectomy. Intraoperative traction on the SCM may stretch the branch to the trapezius.

Intraoperative monitoring may decrease the likelihood of injury. In one series of 111 patients with SA injury, 93% were iatrogenic and 80% of those injuries were from lymph node biopsy.

Traction injury may occur when the shoulder is pulled down and the head turned in the opposite direction. Carrying heavy loads on the shoulder may cause SA injury because of local trauma or stretch. Other causes of SA neuropathy include jugular vein cannulation, upper cervical spine hyperextension injury, cervical internal carotid artery dissection, neuralgic amyotrophy (Parsonage-Turner syndrome), radiotherapy, coronary artery bypass surgery, human bites to the neck, shoulder dislocation, attempted hanging, mononeuritis multiplex, and nerve tumors such as schwannoma or neurinoma.

Spontaneous, idiopathic cases of isolated SA palsy, often benign and self-limited, are likely comparable to similar focal neuropathies, such as Bell's palsy or long thoracic nerve palsy, or may represent a restricted type of neuralgic amyotrophy. In these cases, the onset is typically sudden with pain in the posterior triangle, which resolves and is followed by SA palsy.

Neuromuscular disorders that affect the SCM and trapezius muscles include anterior horn cell disease, myasthenia gravis, inflammatory myopathies, and facioscapulohumeral dystrophy. Atrophy and weakness of both SCM muscles is a prominent feature of myotonic dystrophy ([Figure 19.6](#)). The “dropped head syndrome,” characterized by severe neck extensor weakness and an inability to hold the head up, occurs in a variety of neuromuscular disorders ([Box 19.2](#), [Figure 19.7](#)).

Patients with traumatic SA neuropathies generally have poorer long-term outcomes than those with neuropathies of other etiologies. Dominant limb involvement, impaired arm abduction, and scapular winging are all associated with a poor outcome. Trapezius weakness may lead to drooping of the shoulder with resultant compression of the neurovascular bundle at the thoracic outlet.

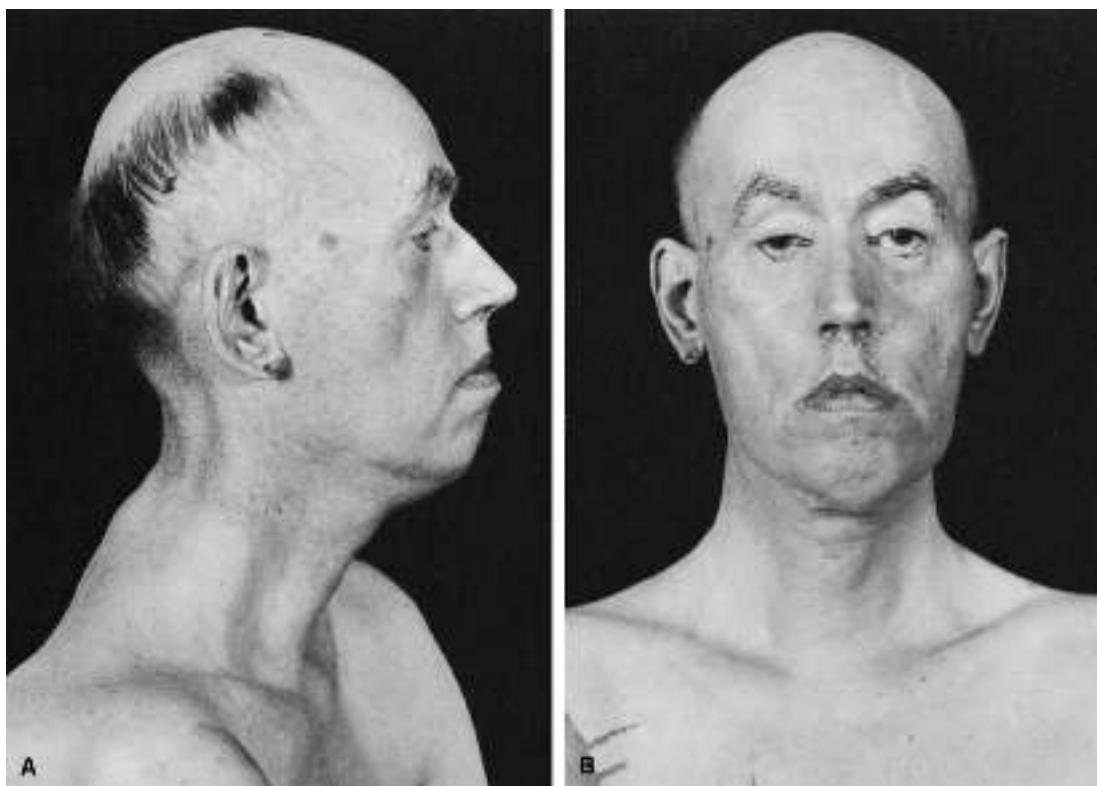


FIGURE 19.6 A patient with myotonic dystrophy. There is atrophy of the SCM muscles.

BOX 19.2

Dropped Head Syndrome

Severe weakness of the neck extensors leads to an inability to hold the head up. The most common causes of the dropped head syndrome (head ptosis, floppy head, camptocormia) are inflammatory myopathy, ALS, and myasthenia gravis. In these conditions, posterior paraspinal muscle weakness can occur early and selectively, and head drop may be the presenting manifestation of the disease. It is common in the later stages of facioscapulohumeral dystrophy and some forms of spinal muscular atrophy. Some cases are due to a relatively benign isolated neck extensor myopathy, an idiopathic restricted noninflammatory myopathy. The “bent spine syndrome,” related to thoracic paraspinal weakness, may cause a similar head posture.

Rare causes include adult-onset acid maltase deficiency, chronic inflammatory demyelinating polyneuropathy, desmin myopathy, nemaline

myopathy, mitochondrial myopathy, hypothyroid myopathy, hyperparathyroidism, Lambert-Eaton syndrome, myasthenia gravis, and myotonic dystrophy. Dropped head syndrome from neck extensor weakness may be confused with anterocollis because of cervical dystonia. This flexed neck posture is also common in Parkinson's disease, but neck extension strength is unimpaired. Dropped head syndrome has also been reported in syringomyelia.



FIGURE 19.7 Dropped head syndrome due to isolated neck extensor myopathy. (From Katz JS, Wolfe GI, Burns DK, et al. Isolated neck extensor myopathy: a common cause of dropped head syndrome. *Neurology* 1996;46[4]:917–921.)

Video Links

Video Link 19.1. Scapular winging. <http://www.youtube.com/watch?v=dfTe0nPclDE>

Video Link 19.2. Scapular winging. http://neurosigns.org/wiki/Scapular_winging

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CHAPTER 20

The Hypoglossal Nerve

ANATOMY AND PHYSIOLOGY

The hypoglossal nerve (CN XII) is a purely motor nerve, supplying the tongue. Its cells of origin are in the hypoglossal nuclei, which are upward extensions of the anterior gray columns of the spinal cord; they consist of large, multipolar cells, similar to the anterior horn motoneurons. The paired nuclei extend almost the entire length of the medulla just beneath the floor of the fourth ventricle, close to the midline, under the medial aspect of the hypoglossal trigone ([Figure 20.1](#)). The nucleus is somatotopically organized, with different cell groups innervating different tongue muscles. From rostral to caudal, the innervation is intrinsic tongue muscles, then genioglossus, hyoglossus, and styloglossus. Numerous fibers connect the nuclei of the two sides. The axons stream ventrolaterally through the reticular formation, just lateral to the medial longitudinal fasciculus and medial lemniscuses, and the nerve emerges from the medulla in the sulcus between the pyramid and inferior olive (preolivary or ventrolateral sulcus) as a series of 10 to 15 rootlets on each side, anterior to the rootlets of CNs IX, X, and XI (see [Figures 11.3](#) and [11.11](#)).

The hypoglossal fibers gather into two bundles, which perforate the dura mater separately, pass through the hypoglossal canal, and then unite. The nerve descends through the neck to the level of the angle of the mandible and then passes forward under the tongue (hence its name) to supply its extrinsic and intrinsic muscles ([Figure 20.2](#)). In the upper portion of its course, the nerve lies beneath the internal carotid artery and internal jugular vein and near the vagus nerve. It passes between the artery and vein, runs forward above the hyoid bone, between the mylohyoid and hypoglossus muscles, and breaks up into a number of fibers to supply the various tongue muscles. The nerve sends communicating branches to the inferior vagal ganglion and to the pharyngeal plexus. At the base

of the tongue, it lies near the lingual branch of the mandibular nerve, which provides touch sensation to the anterior two-thirds of the tongue.

The branches of the hypoglossal nerve are the meningeal, descending, thyrohyoid, and muscular. The meningeal branches send filaments derived from communicating branches with C1 and C2 to the dura of the posterior fossa. The descending ramus joins with fibers from C1, sends a branch to the omohyoid, and then joins a descending communicating branch from C2 to C3 to form the ansa cervicalis ([Figure 20.2](#)), which supplies the omohyoid, sternohyoid, and sternothyroid muscles. The thyrohyoid branch supplies the thyrohyoid muscle. The descending and thyrohyoid branches carry hypoglossal fibers but are derived mainly from the cervical plexus.

The muscular, or lingual, branches constitute the real distribution of the hypoglossal nerve. The tongue has extrinsic and intrinsic muscles. CN XII supplies the intrinsic muscles, and all of the extrinsic muscles of the tongue except the palatoglossus, and possibly the geniohyoid muscle. The paired extrinsic muscles (genioglossus, styloglossus, hyoglossus, and chondroglossus) pass from the skull or hyoid bone to the tongue. The genioglossus is the largest and most important of the extrinsic tongue muscles. It originates from the chin (Gr. geneion “chin”) and inserts into the tongue. The intrinsic muscles (superior and inferior longitudinales, transversus, and verticalis) arise and end within the tongue. The extrinsic muscles protract and retract the tongue and move the root up and down. The intrinsic muscles change the length, the width, and the curvature of the dorsal surface and turn the nonprotruded tip from side to side. The actions of the tongue muscles are summarized in [Table 20.1](#).

The cerebral center regulating tongue movements lies in the lower portion of the precentral gyrus near and within the sylvian fissure. The cortical representation of the tongue in humans is huge compared with other mammals and even other primates. In a patient with a small cortical lesion causing obvious tongue deviation, the lesion by magnetic resonance imaging (MRI) was located lateral to the precentral knob, a reliable anatomical landmark for the motor hand area. Therefore, the lesion involved the most lateral part of the precentral gyrus, lateral to the precentral knob.

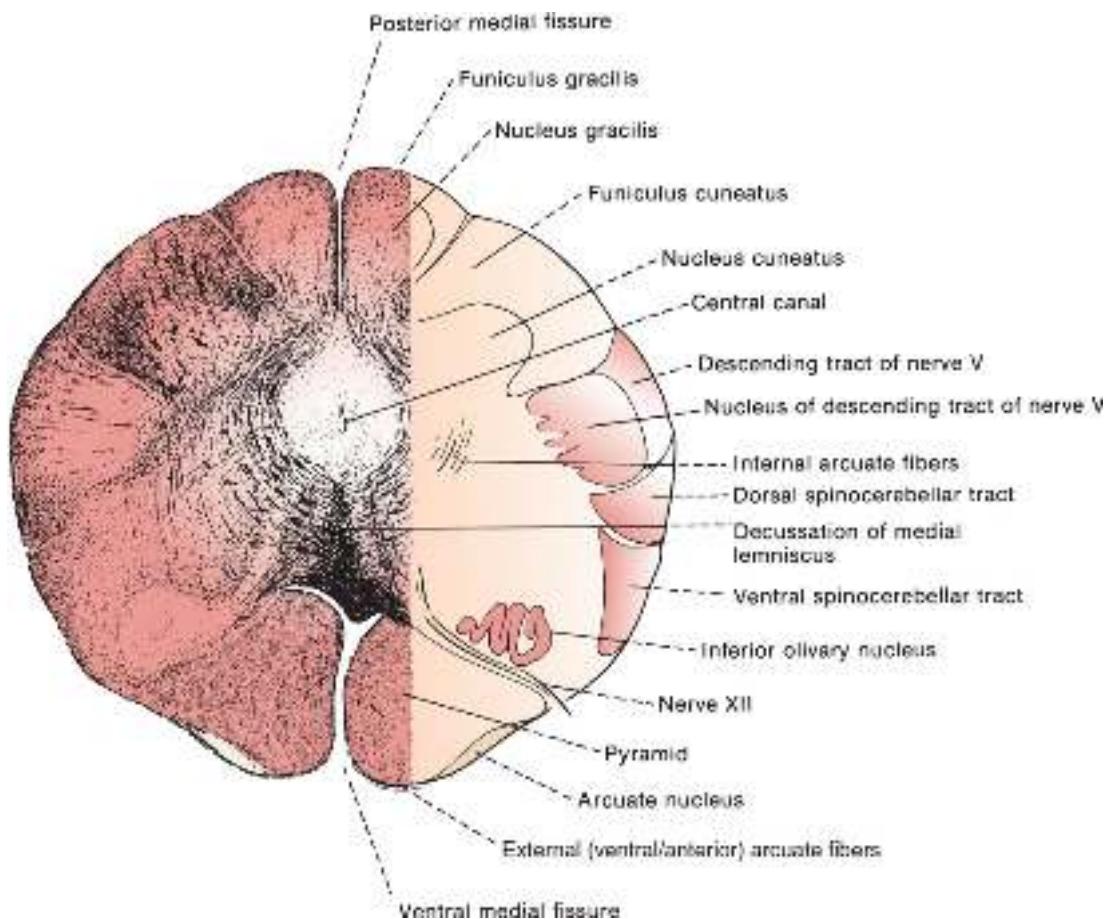


FIGURE 20.1 Section through the medulla at the level of the decussation of the medial lemniscus.

The supranuclear fibers run in the corticobulbar tract through the genu of the internal capsule and through the cerebral peduncle. Some corticolingual fibers shift to the medial lemniscus in the pons. Other fibers leave the main ventral pyramidal tract and cross the midline at the pontomedullary junction to enter the hypoglossal nucleus from the lateral aspect. Supranuclear control to the genioglossus muscle is primarily crossed; supply to the other muscles is bilateral but predominantly crossed. Some authorities feel the entire supranuclear pathway is crossed.

The suprathyroid muscles also influence tongue movement by changing the position of the hyoid bone. The geniohyoid is supplied by C1 fibers traveling in the hypoglossal nerve. The other suprathyroid muscles are the mylohyoid and anterior belly of the digastric, innervated by CN V, and the stylohyoid and posterior belly of the digastric, innervated by CN VII.

Afferents in the hypoglossal nerve are primarily proprioceptive, but there may

be some lingual somatic afferents present as well. The neck-tongue syndrome, consisting of pain in the neck and numbness or tingling in the ipsilateral half of the tongue on sharp rotation of the head, has been attributed to damage to lingual afferent fibers traveling in the hypoglossal nerve to the C2 spinal roots through the atlantoaxial space.

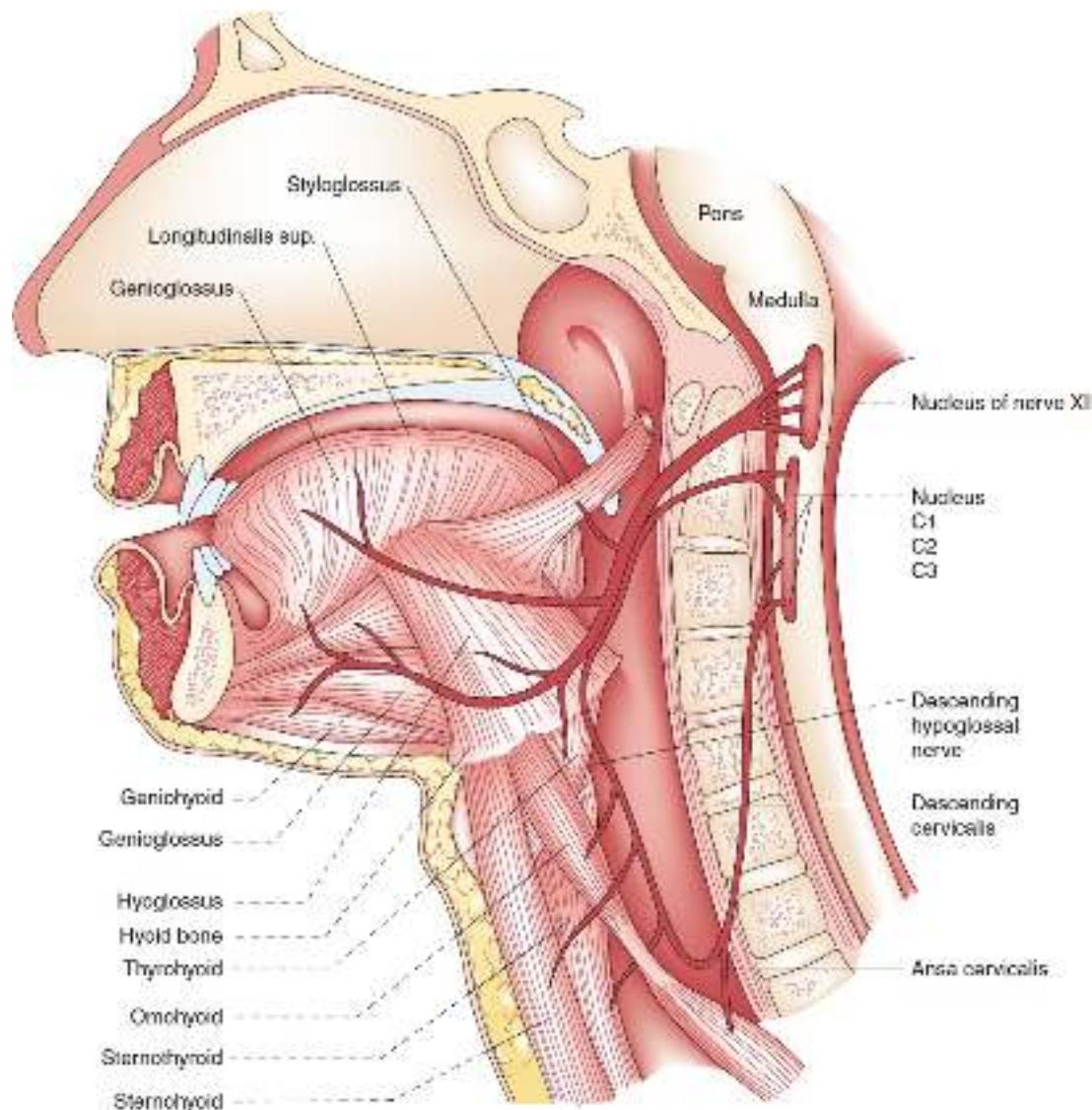


FIGURE 20.2 Ansa cervicalis (hypoglossi) and muscles supplied by the hypoglossal nerve.

CLINICAL EXAMINATION

The clinical examination of hypoglossal nerve function consists of evaluating the

strength, bulk, and dexterity of the tongue—looking especially for weakness, atrophy, abnormal movements (particularly fasciculations), and impairment of rapid movements. For a video of tongue fasciculations from the NEJM, see [Video Link 20.1](#). After noting the position and appearance of the tongue at rest in the mouth, the patient is asked to protrude it, move it in and out, from side to side, and upward and downward, both slowly and rapidly. Tongue dexterity can be tested by having repeat lingual sounds, as in la-la-la, or use words with the t or d phoneme. For a demonstration of slow tongue movements and difficulty with labials in a case of pseudobulbar palsy, see [Video Link 20.2](#). Motor power can be tested by having the patient press the tip against each cheek as the examiner tries to dislodge it with finger pressure. The normal tongue is powerful and cannot be moved. For more precise testing, press firmly with a tongue blade against the side of the protruded tongue, comparing the strength on the two sides.

**TABLE
20.1**

Actions of the Extrinsic and Intrinsic Tongue Muscles

Muscle	Action
Genioglossi	Posterior fibers draw root of the tongue forward and protrude the tip; anterior fibers depress and retract the tongue and draw it back into the mouth; anterior and posterior fibers together draw the tongue downward and make its superior surface concave from side to side; posterior fibers on one side push the tongue toward the opposite side
Hypoglossi	Retract the tongue and depress its sides; make the superior surface convex
Chondroglossi	Depressor and retractor, sometimes described as part of hypoglossi
Styloglossi	Aids in drawing root of the tongue upward; may be classified as an extrinsic tongue muscle but is more closely related to the muscles of the soft palate; innervated by the vagus nerve

Intrinsic muscles (superior and inferior longitudinales, transversus, verticalis)	Mainly concerned with altering the tongue's shape; causing it to shorten, narrow, or curve in different directions. Both longitudinales shorten the tongue; superior longitudinalis turns the tip, pulls the tip up, and makes the dorsum concave; inferior longitudinalis pulls the tip down and makes the dorsum convex; transversus narrows and elongates the tongue; verticalis flattens and broadens it
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When unilateral weakness is present, the tongue deviates toward the weak side on protrusion because of the action of the normal genioglossus, which protrudes the tongue by drawing the root forward ([Figure 20.3](#)). The tongue always deviates toward the weak side (see [Video Link 20.3](#)). Whether this is toward or away from the side of the lesion depends on the specifics of the lesion. There is impairment of the ability to deviate the protruded tongue toward the opposite side. The patient cannot push the tongue against the cheek on the normal side but is able to push it against the cheek on the side toward which it deviates. At rest, it may deviate or curl slightly toward the healthy side because of unopposed action of the styloglossus, which draws the tongue upward and backward. There is impairment of the ability to deviate the protruded tongue toward the nonparetic side and of the ability to push it against the cheek on the sound side, but the patient is able to push it against the cheek on the paralyzed side. Lateral movements of the tip of the nonprotruded tongue, controlled by the intrinsic tongue muscles, may be preserved. Because of the extensive interlacing of muscle fibers from side to side, the functional deficit with unilateral tongue weakness may be minimal except for difficulty manipulating food in the mouth and an inability to remove food from between the teeth and the cheeks on either side. Either weakness or incoordination may impair rapid tongue movements.

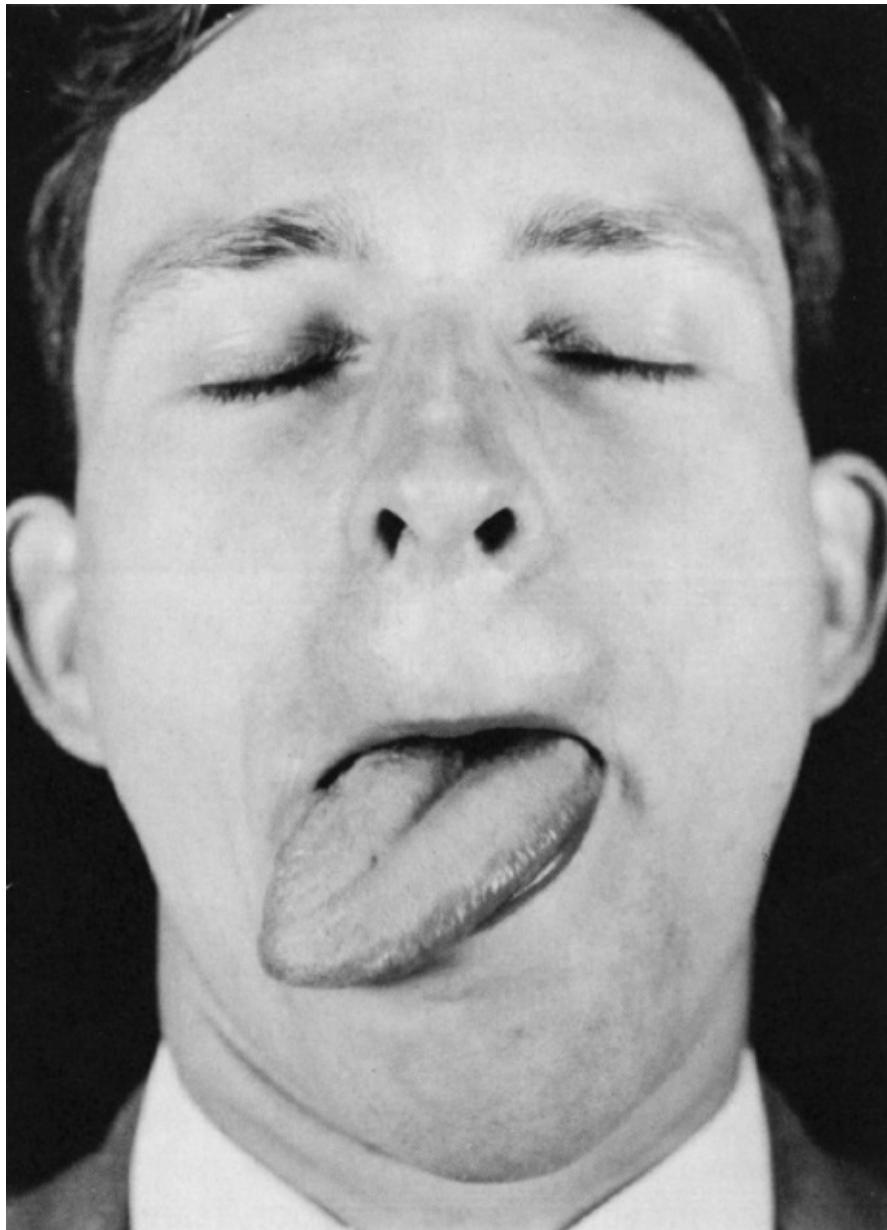


FIGURE 20.3 Infranuclear paralysis of muscles supplied by the hypoglossal nerve: unilateral atrophy and deviation of the tongue following a lesion of the right hypoglossal nerve. (Modified from: https://library.med.utah.edu/neurologicexam/html/cranialnerve_abnormal.html#25, by Dr. Paul D. Larsen.)

Facial muscle weakness or jaw deviation makes it difficult to evaluate deviation of the tongue. Patients with significant lower facial weakness often have distortion of the normal facial appearance that can produce the appearance of tongue deviation when none is present. Protruding the tongue may cause an appearance of deviation toward the side of the facial weakness. Because of the

lack of facial mobility, the corner of the mouth does not move out of the way and the protruded tongue lies tight against it, making it look as though the tongue has deviated. Manually pulling up the weak side of the face eliminates the “deviation.” It may help to gauge tongue position in relation to the tip of the nose or the notch between the upper incisors.

If the paralysis is not accompanied by atrophy, the tongue may appear to bulge slightly and to be higher and more voluminous on the paralyzed side. When atrophy supervenes, the loss of bulk is first apparent along the borders or at the tip, and the tongue may take on a scalloped appearance ([Figure 20.4](#)). The normal slight midline groove may become accentuated. With advanced atrophy, the tongue is wrinkled, furrowed, and obviously smaller. The epithelium and mucous membrane on the affected side are thrown into folds. As the paralyzed side becomes wasted, the protruded tongue may curve strikingly toward the atrophic side, assuming a sickle shape. In bilateral paralysis, the patient can protrude the tongue only slightly or not at all. Unilateral tongue atrophy can sometimes be confirmed by palpation.

Progressive bulbar palsy and advanced amyotrophic lateral sclerosis (ALS) may cause atrophy so severe the tongue cannot be protruded and lies inert on the floor of the mouth (glossoplegia). Atrophy may be accompanied by fasciculations, especially in motor neuron disease. In long-standing myasthenia gravis (MG), tongue atrophy may develop and lead to a triple furrowed appearance with grooves paralleling the median sulcus on each side (trident tongue, see [Video Link 20.4](#)). With bilateral suprasegmental lesions, for example, primary lateral sclerosis, the tongue may be of normal bulk but move slowly. In some patients, the tongue is tremulous, and it may be difficult to distinguish these fine, rapid tremors from fasciculations, especially when the tongue is protruded. Tremors will usually disappear when the tongue is lying at rest in the mouth, whereas fasciculations persist. Profuse fasciculations may cause the tongue to have a “bag of worms” appearance.



FIGURE 20.4 Tongue atrophy in ALS. (Reprinted from Louis ED, Mayer SA, Rowland LP. *Merritt's Neurology*. 13th ed. Philadelphia: Wolters Kluwer, 2016, with permission.)

In addition to fasciculations, other abnormal movements of the tongue sometimes occur. Tremors are usually accentuated by protrusion of the tongue or by talking. Coarse tremors of the tongue can occur in parkinsonism, alcoholism, and general paresis; a fine tremor can occur in thyrotoxicosis. Chorea may cause irregular, jerky movements of the tongue, and often the patient is unable to keep the tongue protruded (snake, trombone, or fly-catcher tongue). Athetosis, dystonia, habit spasms, and tics may involve the tongue; lingual spasm has been described in tetanus. The tongue is often prominently involved in orofacial or buccolingual dyskinesias, which usually occur as a type of tardive dyskinesia following the use of phenothiazines and other psychotropic drugs. Similar dyskinesias may also occur in patients with Parkinson's disease related to the use of levodopa and dopamine agonists and in Meige's syndrome. The bonbon sign is a dystonic or dyskinetic movement of the tongue characterized by protrusion or lateral tongue movements within the mouth producing a bulge in the cheek as if the patient were storing a piece of candy there. It is reportedly helpful in distinguishing tardive dyskinesias, where it is present, from chorea, where it is not.

Morphologic changes in the tongue may be of diagnostic significance in many medical conditions. Some disorders of neurologic interest include the following. Ankyloglossia (tongue-tie) may simulate paresis. A neoplasm involving one side of the tongue may hinder muscle contraction and cause the

tongue to deviate. Macroglossia may occur in hypothyroidism, Down's syndrome, amyloidosis, acromegaly, neurofibromatosis, sarcoidosis, GM1 gangliosidosis, glycogen storage diseases, Duchenne's muscular dystrophy, some forms of limb girdle muscular dystrophy, polymyositis, mucopolysaccharidosis, and with local conditions involving the tongue, such as angioma, hamartomas, and lymphoma. Macroglossia can also occur in posterior fossa disease and after posterior fossa surgery. Rarely, ALS may cause macroglossia because of fatty infiltration. Tongue hypertrophy can result from conditions causing excessive movement, such as lingual dyskinesias. Tongue pseudohypertrophy because of denervation has been reported.

The term atrophic glossitis refers to atrophy of the epithelium and papillae, causing a smooth, glistening, often reddened tongue. There may be punctate, erythematous lesions from atrophic, hyperemic papillae. There is no neurogenic atrophy of the musculature. When advanced, atrophic glossitis may cause pain and swelling. Atrophic glossitis occurs in certain deficiency states, especially vitamin B₁₂, folate, other B vitamins, and iron. In pernicious anemia, the tongue is smooth, slick, and translucent, with atrophy of the fungiform and filiform papillae. In some stages, the tongue is pale; in others, it is red. In pellagra and niacin deficiency, the tongue is smooth and atrophic; acutely, it is scarlet red and swollen and may have ulcerations. In riboflavin deficiency, the tongue may be a purplish or magenta hue, with prominent, edematous fungiform and filiform papillae that resemble cobblestones.

Fusion and atrophy of the papillae and fissuring may cause a geographic, or scrotal, tongue. Melkersson-Rosenthal syndrome causes facial nerve palsy and scrotal tongue. Geographic tongue also occurs as a benign curiosity of unknown etiology. Burning tongue (glossodynia, glossalgia) with no visible lesions may occur from early glossitis, tobacco abuse, heavy metal intoxication, as a menopausal symptom, and in pellagra. Xerostomia and local irradiation may make the tongue dry and sore. Longitudinal lingual fissuring occurs in syphilitic glossitis. Ulcerations of the tongue may be seen in primary syphilis (lingual chancre) and in Behcet's disease. The tongue is often bitten during generalized tonic-clonic seizures.

DISORDERS OF FUNCTION

Lesions of CN XII or its central connections may cause weakness of the tongue.

There are no sensory changes. Unilateral weakness may cause few symptoms; speech and swallowing are little affected. With severe bilateral weakness, the tongue cannot be protruded or moved laterally; the first stage of swallowing is impaired; and there is difficulty with articulation, especially for linguals. Rarely, the tongue tending to slip back into the throat may cause respiratory difficulty.

Tongue weakness may result from a supranuclear, nuclear, or infranuclear lesion. Supranuclear lesions cause weakness but no atrophy, and the weakness is rarely severe. Because the genioglossus—the principal protractor of the tongue—has mainly crossed supranuclear innervation, the tongue protrudes toward the weak side but to the side opposite the supranuclear lesion. Supranuclear tongue weakness may occur with a destructive lesion of the cerebral cortex or the corticobulbar tract in the internal capsule, cerebral peduncle, or pons. Pontine lesions may cause supranuclear tongue weakness depending on the relationship to the decussating corticolingual fibers. Medial pontine lesions tend to cause contralateral tongue weakness, whereas lateral pontine lesions cause ipsilateral tongue weakness. Medullary lesions may interrupt ipsilateral corticolingual fibers. In a large series of patients with acute unilateral ischemic strokes above the lower brainstem, tongue deviation occurred in 29%, always toward the side of limb weakness; it occurred most commonly in patients with cortical or large subcortical infarctions who also had facial and prominent upper extremity weakness.

Supranuclear lesions may cause dysarthria because of tongue weakness and incoordination (spastic tongue). The dysarthria is spastic and tongue movements are slow and irregular. Isolated dysarthria has been reported as a manifestation of lacunar infarction involving the supranuclear corticolingual pathways. Pseudobulbar palsy because of bilateral upper motor neuron disease may cause bilateral tongue weakness; the tongue may appear small and the patient may be unable to protrude it beyond the teeth. Patients with hemispheric lesions may have apraxia of tongue movements and are often unable to protrude it on command. Extrapyramidal disorders may cause slowing of tongue movements, with thickness of speech and difficulty in protrusion.

In addition to weakness, nuclear and infranuclear lesions cause atrophy of the involved side. The tongue protrudes toward the weak side, which is also the side of the lesion. Progressive nuclear lesions, such as motor neuron disease, often cause fasciculations in addition to weakness. Any accompanying dysarthria is flaccid with particular difficulty with lingual consonants. Common disorders that may involve the hypoglossal nucleus include neoplasms, vascular lesions, and

motor neuron disease. Rare disorders include syringobulbia, abscess, granuloma, syphilis, polioencephalitis or postpolio syndrome, and infectious mononucleosis. Nuclear lesions may involve contiguous structures, such as the ascending sensory or descending motor pathways. Progressive bulbar palsy is a form of motor neuron disease where the disease begins in the bulbar motor nuclei; hypoglossal involvement is common. In X-linked bulbospinal muscular atrophy (Kennedy's disease), the bulbar muscles are prominently affected. There are rare forms of bulbar motor neuron disease in childhood (e.g., Fazio-Londe disease).

Intranuclear lesions may involve the intramedullary fibers between the nucleus and the point of exit. Except for motor neuron disease and similar conditions, causes are generally the same as for nuclear lesions. In the medial medullary (Dejerine's, anterior bulbar) syndrome, or inferior alternating hemiplegia, the lesion involves the exiting hypoglossal fibers and the neighboring medullary pyramid, causing tongue weakness and contralateral hemiparesis ([Chapter 21](#), [Box 21.1](#)). A patient has been reported with contralateral glossoplegia due to a ventromedial lesion of the upper medulla. Lesions of the medullary tegmentum may involve CNs X, XI, and XII (Jackson's syndrome [[Chapter 21](#)]). In Keane's series of 578 cases with bilateral involvement of a single CN, hypoglossal palsy accounted for only 5 (0.9%); of these, 2 were due to tumor, 1 was vascular, and 1 was due to infection. But in a series of 100 cases of hypoglossal palsy, the nerve was involved bilaterally in one-third; tumor and trauma accounted for the majority.

Processes involving the extramedullary, intracranial course of the nerve include disorders involving the meninges, such as infectious and neoplastic meningitis, subarachnoid hemorrhage, neoplasms and other mass lesions (e.g., schwannoma), inflammation, and trauma. Processes involving the skull base—such as basal skull fractures, basilar impression, platybasia, Chiari malformation, impaction of the medulla into the foramen magnum by increased intracranial pressure, or dislocation of the upper cervical vertebrae—may affect the nerve before it leaves the skull. Lesions along the clivus may cause bilateral hypoglossal palsies. Combined CN VI and XII palsies are usually due to a lesion of the clivus, typically malignant, or to nasopharyngeal carcinoma. Lesions within the hypoglossal canal are rare. Inflammatory, neoplastic or traumatic lesions in the region of the occipital condyle may cause isolated hypoglossal palsy and a characteristic pain pattern (occipital condyle syndrome); it is most often due to metastatic disease to the skull base. Bilateral hypoglossal nerve injury may occur with occipital condylar fracture.

Processes involving the extracranial course of the nerve include trauma of various types, especially penetrating wounds (including surgery on the neck, mouth, or tongue), carotid aneurysms (especially dissections), vascular entrapment by the vertebral artery, tumors or infections in the retroparotid or retropharyngeal spaces, deep cervical adenopathy, cranial irradiation, and tumors involving the neck, tongue base, or salivary glands. Hypoglossal nerve palsy can also occur as an idiopathic, benign syndrome that resolves spontaneously. Mechanical lesions may result in aberrant regeneration, which causes progressive difficulty with coordinated tongue movements. Rarely, primary neural tumors involve CN XII extracranially. CN XII may be involved with other lower CNs and the cervical sympathetics in lesions in the retroparotid space (Collet-Sicard or Villaret syndromes, [Chapter 21](#)). CN XII may be involved unilaterally or bilaterally in Guillain-Barré syndrome, hereditary neuropathy with liability to pressure palsies, and related polyneuropathies. Tongue involvement can occur in Lewis-Sumner syndrome and multifocal motor neuropathy, causing confusion with ALS.

Except for MG, neuromuscular junction disorders and myopathies rarely involve the tongue to any clinically significant degree. Tongue weakness and fatigability may occur in MG but generally only with severe involvement. The triple furrowed appearance is characteristic (see above). It is often difficult to separate bulbar weakness because of MG from that due to early motor neuron disease.

The tongue may be involved in myotonic disorders, although it rarely causes any symptoms. One way to test for myotonia is to place the edge of a tongue blade across the tongue and then percuss it sharply. Myotonia may cause a temporary focal contraction along the line of percussion, causing the tongue to narrow sharply at that point (see [Video Link 20.5](#)). The appearance of the resulting constriction has been referred to as the napkin ring sign.

Seizures may involve the tongue, either as part of a jacksonian seizure or rarely in isolation. Paroxysmal, rhythmic tongue movements have been described as a manifestation of subcortical seizures. The tongue may participate in the rhythmic movements of palatal myoclonus. Unusual episodic, rhythmic tongue movements may occur after head and neck trauma (galloping tongue). Serpentine tongue refers to a dyskinesia producing incessant writhing movements (see Sheehy et al. for video). Tongue myokymia may follow cranial radiotherapy (see Rison and Beydoun for video).