CHAPTER 10

The Trigeminal Nerve

Sashank Prasad and Steven Galetta

HISTORY AND DEFINITIONS

The *trigeminal nerve*, or cranial nerve V, contains both sensory and motor components and thus subserves and controls ipsilateral facial sensation and masticatory movements. Pain, thermal, tactile, and kinesthetic sensory stimuli are received from the facial skin, oropharynx, nasal mucous membranes, sinuses, teeth, palate, dura, and masticatory muscles. Motor fibers extend to the muscles of mastication as well as the tensor tympani and tensor veli palatini. The trigeminal brain stem nuclei are the *spinal trigeminal nucleus* and *tract*, the *main* (or principal) *sensory nucleus*, the *mesencephalic nucleus*, and the *motor trigeminal nucleus*. The nerve splits into three divisions: V1 (the *ophthalmic* branch), V2 (the *maxillary* branch), and V3 (the *mandibular* branch). The neurons of these branches have their cell bodies in the *gasserian* (or semilunar) ganglion (with the exception of jaw proprioceptive fibers). The gasserian ganglion resides in *Meckel's cave* in the temporal bone.

The first adequate clinical description of the condition *trigeminal neuralgia* was made by Fothergill in 1773. Thereafter, Charles Bell (1829) demonstrated that the trigeminal nerve subserved sensation to the face. The trigeminal ganglion was excised in the late 19th century by Rose (1890), and the celebrated surgeon Horsley first sectioned cranial nerve V through an intradural middle fossa approach in 1891. Early 20th-century studies focused primarily on physiology, and more modern research has integrated neurochemistry, neuropharmacology, and microsurgical interventions in the treatment of trigeminal lesions. In 1962, Blom first reported the successful treatment of trigeminal neuralgia with carbamazepine, a new antiepileptic agent at that time.[1]

CLINICAL HISTORY

When interviewing a patient with complaints referable to the trigeminal system, there are several key considerations to address. First is the nature of the patient's complaint (i.e., pain, sensory changes, sensory loss, or motor difficulty) because the characteristic clinical features are critical to making an appropriate neurological diagnosis. For example, a description of excruciating and lancinating pain, or else tolerable yet disturbing paresthesias, may suggest distinct clinical syndromes. Determination of whether the symptoms are intermittent, paroxysmal, or chronic and the temporal profile of symptom development (i.e., whether symptoms began in an acute, subacute, or indolent fashion) also provides diagnostic clues. Thus, sudden complaints of sensory loss, paresthesias, or motor dysfunction in the face are consistent with vascular or traumatic processes, whereas similar complaints developing over weeks more often reflect neoplastic or inflammatory etiologies. Inquiries regarding a family history of neurological disorders that may have a possible genetic link, such as multiple sclerosis, stroke, brain tumor, or aneurysm, should be made. Possible precipitating elements, such as recent trauma, toxic exposures, illicit drug abuse, and medication usage, should be identified. It is also important to elicit other neurological symptoms, such as autonomic, visual, ocular, or facial motor dysfunction, which may help to localize the lesion. Specifically, patients should be questioned regarding changes in facial sweating; recurrent corneal irritation or abrasions; and difficulty blinking, swallowing, or speaking. Specific trigger points of facial pain, or associated oropharyngeal or jaw pain, may be useful historical details. It is imperative to identify past or concurrent medical or neurological disorders that may be related etiologically to a patient's complaints of trigeminal dysfunction. Specifically, a history of collagen vascular diseases, prior strokes, diabetes, neoplasms, granulomatous diseases, bleeding disorders, or recent and recurrent infections may prove helpful.

ANATOMY OF CRANIAL NERVE V (Table 10-1)

Overview

The trigeminal nerve is a mixed cranial nerve, and the afferent and efferent projections of cranial nerve V provide sensorimotor inputs and outputs to the face (see Table 10-1).[2]

TABLE 10-1

Parasympathetic (Visceromotor) Cranial Nerve Innervation, with Associated Trigeminal Nerve Branches

CRANIAL NERVE	SOURCE DESTINATION	SYNAPSE	VIA	DESTINATION
III	Edinger-Westphal nucleus	Ciliary ganglion	—	Sphincter pupillae Ciliary body
VII	Superior salivatory nucleus	Pterygopalatine ganglion Submandibular ganglion	V1 V2	Lacrimal gland Submandibular gland Sublingual gland
IX	Inferior salivatory nucleus	Otic ganglion	V3	Parotid gland
X	Dorsal motor nucleus of X Nucleus ambiguus	Body organs	—	Chest and abdomen

The multimodal sensory components (pain, temperature, position, and light touch) of the trigeminal system send projections via the thalamus to primary sensory cortices (Brodmann areas 3, 1, and 2). The three primary sensory nerves of the trigeminal system are named for the facial regions they innervate (e.g., ophthalmic [V1], maxillary [V2], and mandibular [V3]) (Fig. 10-1A). The unilateral cutaneous sensory distributions of these nerves overlap slightly in the facial midline. First-order motor efferents originate in primary motor cortex (area 4) and project bilaterally to the pontine trigeminal motor nucleus. Axon collaterals extend to the thalamus and cerebellum. The motor projections innervate the muscles of mastication, including the masseter, medial and lateral pterygoid, temporalis, mylohyoid, and anterior belly of the digastric muscles, as well as the tensors tympani and vela palatini. The motor portion of the trigeminal nerve runs with the mandibular sensory branch (V3) in the face.

Sensory Portion

Receptors

Cutaneous receptors for the trigeminal nerve are primarily mechano-, thermo-, and nociceptive endings. These include pacinian corpuscles, free nerve endings, Merkel's discs, and Ruffini's endings. Although these are often associated with facial hairs, areas of particularly dense innervation include the lips, buccal and gingival surfaces, and the cornea. Some sensory nociceptive afferents are not myelinated, whereas others, and tactile and mechanical afferents, are heavily so. In addition, muscle spindles and Golgi tendon organs exist within facial muscles and extend via type Ia and Ib fibers to the pons.

First-Order Neurons

Primary sensory neuron cell bodies for the afferent trigeminal fibers (V1-V3) are within the trigeminal (gasserian or semilunar) ganglion, which is embedded in the petrous portion of the temporal bone.[3,4] In this area is Meckel's cave, a dural-lined cavity in the middle cranial fossa adjacent to the petrous apex, which houses the gasserian ganglion and its branches as they exit into the petrous temporal bone. A single large trigeminal sensorimotor root passes into the gasserian ganglion and then emits the three trigeminal divisions that exit the skull base via distinct foramina: V1 exits via the superior orbital fissure, V2 via the foramen rotundum, and V3 via the foramen ovale.

The ophthalmic division of the trigeminal nerve (V1) is entirely sensory (all modalities) and innervates the eye, orbit, and nose. V1 passes within the cavernous sinus, where it lies inferolateral to the oculomotor, trochlear, and abducens nerves. From the cavernous sinus, V1 extends through the superior orbital fissure, still in association with cranial nerves III, IV, and VI, before dividing into the lacrimal, frontal, and nasociliary nerves. The lacrimal branches innervate the orbit and eye, the frontal branches innervate the upper eyelid and forehead, and the nasociliary branches innervate the nasal cavity and nasal sinuses. Cutaneous fibers reach the skin via the supraorbital foramen along the ridge of the brow. Smaller tentorial and dural branches innervate the tentorium cerebelli and dura mater.[5] Vasomotor fibers from the trigeminal system (trigeminovascular innervation) provide autonomic inputs to intracranial blood vessels, modulating increases in blood flow. Finally, autonomic fibers from the facial nerve (CN VII) "piggyback" on V1, providing parasympathetic innervation to the lacrimal gland (Table 10-2).

The maxillary division (V2) is also completely sensory; it innervates the skin of the cheek, nose, lower eyelid, upper lip, nasopharynx, soft and hard palate, maxillary sinus, and upper teeth. A small meningeal branch follows the middle meningeal artery and supplies the dura.[5] V2 fibers leave the gasserian ganglion, exit the foramen rotundum, and run inferiorly within the cavernous sinus. V2 axons pass through the pterygopalatine fossa to exit the infraorbital foramen. These cutaneous branches include the zygomaticotemporal, zygomaticofacial, and infraorbital nerves, whereas branches innervating the nasopharynx and maxillary sinuses include the greater and lesser palatine nerves, nasopalatine nerve, and pharyngeal nerve. V2 innervation of the upper teeth, maxillary sinuses, and palate is via the anterior, middle, and posterior superior alveolar nerves, respectively. Autonomic fibers that originate from the superior salivatory nuclei of the facial nerve (CN VII) accompany V2 branches and comprise the superficial petrosal nerve (see Table 10-2). These fibers synapse within the pterygopalatine ganglion, and the postganglionic fibers provide parasympathetic input to the lacrimal, nasal, and palatine glands.

The mandibular division (V3) carries both sensory and motor fibers to the lower face. In addition, it mediates pain and touch sensation (but not taste) from the anterior two-thirds of the tongue. V3 axons leave the gasserian ganglion to exit the skull base via the foramen ovale. The fibers

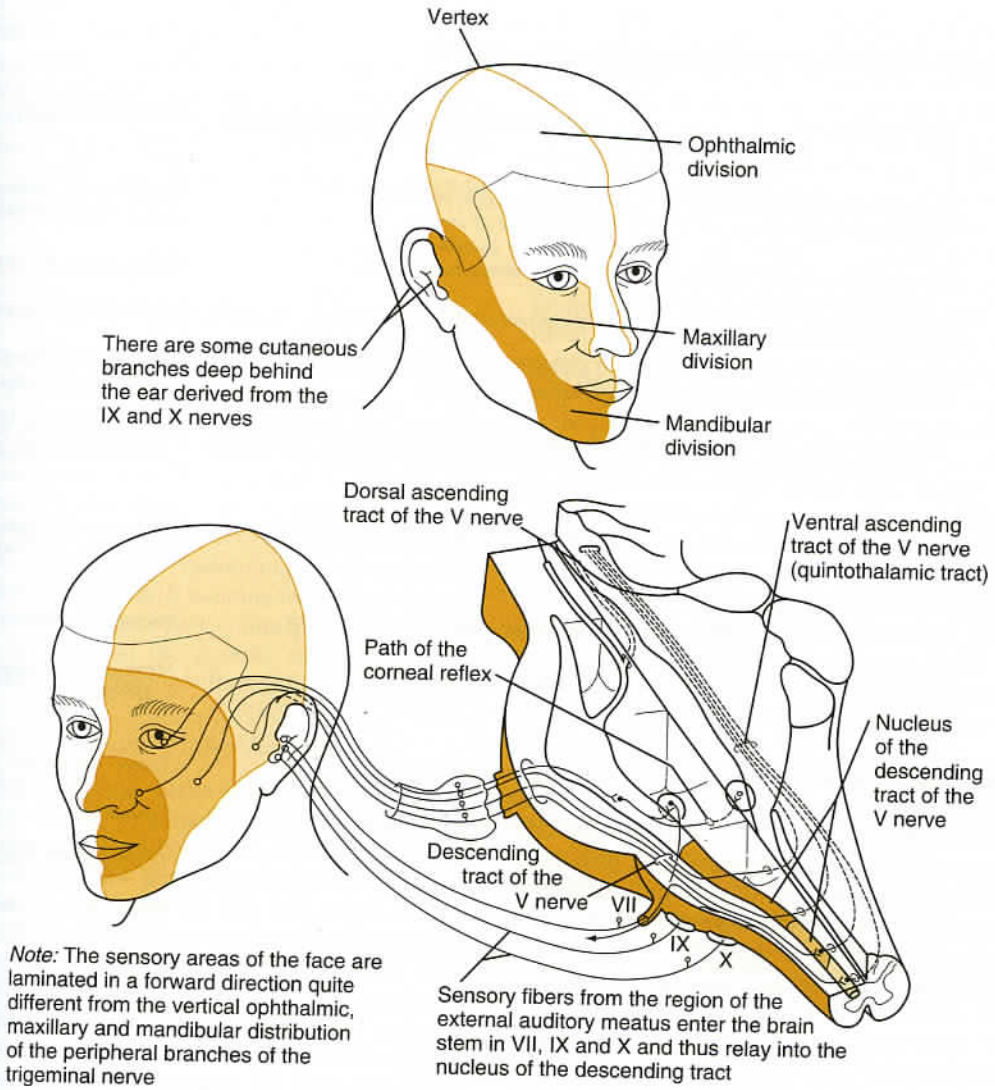


Figure 10-1. *Top,* Cutaneous distribution and facial innervation of V1-V3. *Bottom,* Anatomical relationship between cutaneous trigeminal fibers, the gasserian ganglion, and brain stem trigeminal nuclei and pathways. Note termination of afferent fibers via the descending (spinal) trigeminal tract into the spinal (descending) nucleus. The anterior innervation of the nose and mouth blends laterally with maxillary and preauricular innervation in a characteristic onion skin pattern. (From Patten JP: Neurological Differential Diagnosis: An Illustrated Approach, 2nd ed. Copyright 1995 Springer-Verlag, Berlin, Heidelberg. Used by permission of the publisher.)

ramify through the deep face lateral to the medial pterygoid muscles and then divide into branches that provide sensation to the skin around the mandible, chin, and ear (lingual, auriculotemporal, and mental branches) and mucosa around the inner cheek (buccal branch), lower teeth (inferior alveolar nerves), and dura (meningeal branch). Parasympathetic fibers from CN VII and CN IX synapse within the submandibular and otic ganglia and project via V3 branches to the submandibular and parotid glands, respectively (see Table 10-2).

Sensory axons from V1- to V3-innervated regions of the face reach the trigeminal ganglion, where cell bodies of these peripheral axons send central axons in a solitary sensory root into the midpons. Within the brain stem, these axon bundles bifurcate into fascicles that terminate rostrally or caudally.[6] Synapses occur in the brain stem in three sensory subnuclei that extend from the upper cervical spine to the pontomesencephalic junction. These include the spinal (descending) trigeminal tract and nucleus, the principal sensory nucleus, and the mesencephalic nucleus, each of which subserves a distinct trigeminal function.

Fibers entering the spinal trigeminal tract pass caudally to the spinal nucleus in an inverted somatotopic organization (V1 ventrally, V2 medially, and V3 dorsally) and convey most of the nociceptive and cutaneous inputs mediated by the trigeminal system. The spinal trigeminal tract extends into the upper cervical spinal cord, and afferents synapse on the immediately adjacent spinal nucleus. The spinal trigeminal nucleus may be divided cytoarchitecturally into a pars oralis, which receives sensory inputs from the oral and nasal regions, and the pars interpolaris and pars caudalis, which receive afferents from cutaneous portions of the face. Within the pars caudalis, four somatotopically organized laminae (I-IV) similar to the central gray area of the spinal cord parcel sensory inputs into pain and tactile stimuli. Two somatotopic homunculi for facial

TABLE 10-2

Clinico-anatomical Correlation of Localization of Lesions of CN V

ANATOMICAL SITE OF DAMAGE	CN V FINDING	OTHER NEUROLOGICAL AND MEDICAL FINDINGS	COMMON ETIOLOGIES
Supranuclear			
Sensory cortex	Facial numbness, paresthesias	Neglect, apraxia, aphasia	Stroke, tumor, hemorrhage
Internal capsule	Hemifacial sensory loss	Hemiparesis of arm	Stroke, tumor, hemorrhage, MS
Corona radiata		Central 7th paresis	
VPM thalamus	Facial numbness, paresthesias, pain, cheiro-oral syndrome	Anornia, hemisensory deficit	Stroke, tumor, hemorrhage
Midbrain	Facial numbness, paresthesias, pain	Ophthalmoparesis	Stroke, MS, tumor, aneurysm
Nuclear			
Pons	Facial numbness, paresthesias, pain, trigeminal neuralgia, facial weakness	Ophthalmoparesis, CN VI, VII, VIII, Horner's syndrome	Stroke, tumor, hemorrhage, MS, syringobulbia, abscess, trauma
Medulla	Facial numbness, paresthesias, pain, trigeminal neuralgia	Ataxia, CN X, ophthalmoparesis, nystagmus, Horner's syndrome, Wallenberg's syndrome	Stroke, MS, tumor, aneurysm, abscess, vasculopathy
Preganglionic			
Cerebellopontine angle	Facial numbness	CN VII, VIII, headache, cerebellar dysergia	Neuroma, meningioma, meningitis (bacterial, TB, cancer), aneurysm, trauma
Middle cranial fossa			
Gasserian ganglion	Facial numbness, facial weakness	Gradenigo's syndrome, CN VI, VII	Tumor, infection, trauma
Skull base	Facial numbness, facial weakness	Headache, meningismus	Meningitis (bacterial, TB, cancer, sarcoid)
Trigeminal nerve branches V1			
Cavernous sinus	Facial numbness, pain	Headache, ophthalmoparesis, Horner's syndrome	Tumor, thrombosis, infection, trauma
Carotid–cavernous fistula	Facial numbness	Proptosis, bruit, ophthalmoparesis	Trauma
V2:Maxillary region	Facial numbness, numb cheek syndrome		Tumor, infarct, vasculopathy, trauma
V3:Mandibular region	Weakness of mastication, numb chin syndrome		Tumor, trauma, infarct

CN, cranial nerve; MS, multiple sclerosis; TB, tuberculosis; VPM, ventroposteromedial.

representation of pain are proposed within the spinal trigeminal nucleus. First, there is a rostrocaudal representation of facial innervation such that mandibular regions terminate more rostrally, followed by maxillary and ophthalmic regions more caudally extending into the cervical cord. This facial representation is distinct from a second homuncular pattern, the so-called "onion skin" pattern, in which the mouth and nose (central regions) are represented rostrally in the brain stem, whereas the cheeks, eyes, and ears (more peripheral facial areas) are represented more caudally (Fig. 10-1B).

The second brain stem nucleus, the principal sensory nucleus, receives tactile and pressure sense fibers that have entered the midpons and extended rostrally. These inputs are somatotopically organized similar to the spinal trigeminal tract. Cells within the principal sensory nucleus have large receptive fields; they respond to various tactile and pressure stimuli applied to the skin, mucous membranes, palate, orbit, and teeth.

The third nucleus, the mesencephalic nucleus, is located dorsolaterally above the middle cerebellar peduncle near the pontomesencephalic junction and adjacent to the fourth ventricle. Afferent fibers to the mesencephalic nucleus travel within the motor root of the trigeminal nerve and convey primarily kinesthetic sensation from the teeth, oropharynx, and jaws from stretch receptors in masticatory muscles and function as the afferent portion of the jaw jerk reflex. The cell bodies of these neurons are within the mesencephalic nucleus.

Second- and Third-Order Sensory Neurons

The second-order sensory neurons located within the spinal trigeminal, main sensory, and mesencephalic nuclei send projections rostrally via the trigeminothalamic tract and trigeminal lemniscus.[7,8] Neurons within the pars oralis and caudalis of the spinal trigeminal nucleus and cell bodies from the mesencephalic and principal nuclei project medially into the pontine reticular formation, cross within the median raphe, and ascend contralaterally within the trigeminothalamic tract closely adjacent to the medial lemniscus.

Axons from the second-order neurons terminate somatotopically within the venteroposteromedial nucleus (VPM) of the thalamus contralateral to their nucleus.[2,7,8] A smaller proportion of fibers terminate within the intralaminar nuclei. In contrast, a small fascicle of ipsilateral projections extend rostrally via the dorsal trigeminal tract to terminate in the VPM. Trigeminocerebellar fibers project bilaterally from the mesencephalic and motor trigeminal nuclei.

Third-order thalamocortical projections from the VPM travel in the anterior limb of the internal capsule and terminate primarily in sensory cortex, Brodmann areas 3, 1, and 2.[7] Less dense projections reach the parietal lobule and the precentral gyrus. The presence of some sensory afferents in the cortical motor region explains why sensory abnormalities may be reported by patients with lesions affecting only the precentral gyrus.

Motor Portion

Supranuclear Control and Upper Motor Neurons

Corticobulbar projections to the trigeminal motor nucleus (upper motor neurons) extend from facial regions of the precentral gyrus (first-order neurons in primary and supplementary motor cortices, areas 4 and 6) via the corticobulbar tract to terminate directly on neurons within the pontine trigeminal motor nucleus or on adjacent pontine reticular interneurons, which project to motor nuclear cells. The pattern of bilateral innervation makes contralateral weakness unlikely following a supranuclear lesion; however, a second supranuclear event contralateral to the first may eliminate all input to the pontine trigeminal motor nuclei and present as a "pseudobulbar palsy."[9]

Pontine Nucleus and Lower Motor Nucleus

The motor nucleus of cranial nerve V is located in the rostral pons medial to the principal sensory nucleus. The motor nucleus also receives fibers from the mesencephalic nucleus, which receives jaw proprioceptive information, to mediate the efferent portion of the jaw jerk reflex. Motor axons extend from the motor trigeminal nucleus in the pons and travel along the petrous portion of the temporal bone through Meckel's cave. Motor efferents pass through the gasserian ganglion, join sensory V3 fibers, and exit the skull base via the foramen ovale. Motor efferents in the face travel in association with sensory V3 fibers and reach the masticatory muscles via the medial and lateral pterygoid, deep temporal, masseteric, and mylohyoid nerves. These muscles serve to open (lateral pterygoids, digastric, and mylohyoid) and close (masseter, temporalis, and medial pterygoids) the jaw and provide medial and lateral jaw movements necessary for effective mastication. Small motor branches also extend to the tensor veli palatini and tensor tympani muscles. The tensor veli palatini in the posterior pharynx is active during swallowing and tenses the soft palate against the tongue. The tensor tympani is a small muscle in the middle ear recruited during continuous loud sound; it serves to draw the malleus and tympanic membrane toward the medial wall of the middle ear to dampen the vibrations of the tympanic membrane.

EXAMINATION OF THE TRIGEMINAL NERVE

Directed Neurological Examination

Sensory Function of Cranial Nerve V

When assessing the trigeminal system, it is important to perform a directed and assiduous neurological examination because subtle alterations in function may provide clues to detect potentially serious neurological disease. Sensory and motor components should be tested separately, comparing right and left sides, and light touch, pinprick, and temperature sensation should be tested individually in V1 to V3. The cornea and sclera should be inspected for evidence of keratitis, which may be suggestive of diminished corneal (trigeminal) sensation or lacrimation, as well as the facial skin, oropharynx, teeth, gums, and nares for evidence of inflammatory, infectious, or neoplastic disorders. When considering trigeminal neuralgia or, less often, post-herpetic neuralgia, trigger points that elicit pain should be identified. Localizing signs from involvement of the neuraxis in close proximity to the affected trigeminal region may be helpful. For example, associated cranial neuropathies such as ocular motor dysfunction or facial weakness and Horner's syndrome may provide clues as to the lesion locus. In general, lesions that affect branches of V1 to V3 distal to the gasserian ganglion result in highly focal, circumscribed sensory loss within one division or subdivision of the trigeminal nerve. In contrast, pathological processes affecting the ganglion typically cause hemifacial sensory dysfunction. Lesions within the brain stem that affect the individual trigeminal nuclei may give a distinct picture of dissociated sensory loss in which pinprick, temperature, and light touch sensory modalities are differentially affected.

Sensory examination should assess pain, temperature, light touch, and vibration as well as checking the corneal and jaw jerk reflexes. Painful stimuli can reliably be delivered with a nonreusable pin applied evenly and gently to the skin (Fig. 10-2). Two-point discrimination testing, especially on the lips, can be useful. Although temperature discrimination can best be assessed with glass tubes of hot or cold water, in clinical practice, touching the face with a tuning fork and asking if it feels cold is effective. Light touch can be tested with a cotton wisp or tissue paper stroked gently against the skin. Vibration may be assessed with a 125-Hz tuning fork held against the frontal bones, maxilla, and mandible. It is especially important to pay attention to upper cervical dermatomal distributions when assessing sensation along the angle of the jaw because there may be overlap between the sensory loss from a lesion affecting V3 and the cervical spinal nerves of C2 to C3. Typically, the sensation along the angle of the jaw is in the C2 to C3 distribution and not the V3 distribution.

When performing a sensory examination, one should avoid suggesting or directing the patient into desired responses and be vigilant for the malingering or hysterical patient. Thus, a conservative way to test sensation is to ask the patient to respond "yes" if present or "no" if not and then to determine a more subjective difference between the two responses. The sensory fibers of V1 to V3 cross the midline to a small degree on each side; therefore, in patients complaining of a subtle gradation of loss across the midline, organic causes must be carefully considered. However, if hemifacial sensory loss begins abruptly at the midline, nonorganic causes should be suspected. In addition, because the sensory fibers to the upper face and the scalp merge near the vertex with fibers of the greater occipital nerve, innervating the posterior scalp, loss of sensation on the forehead that ends abruptly at the hairline may suggest a nonorganic etiology. Facial sensory loss

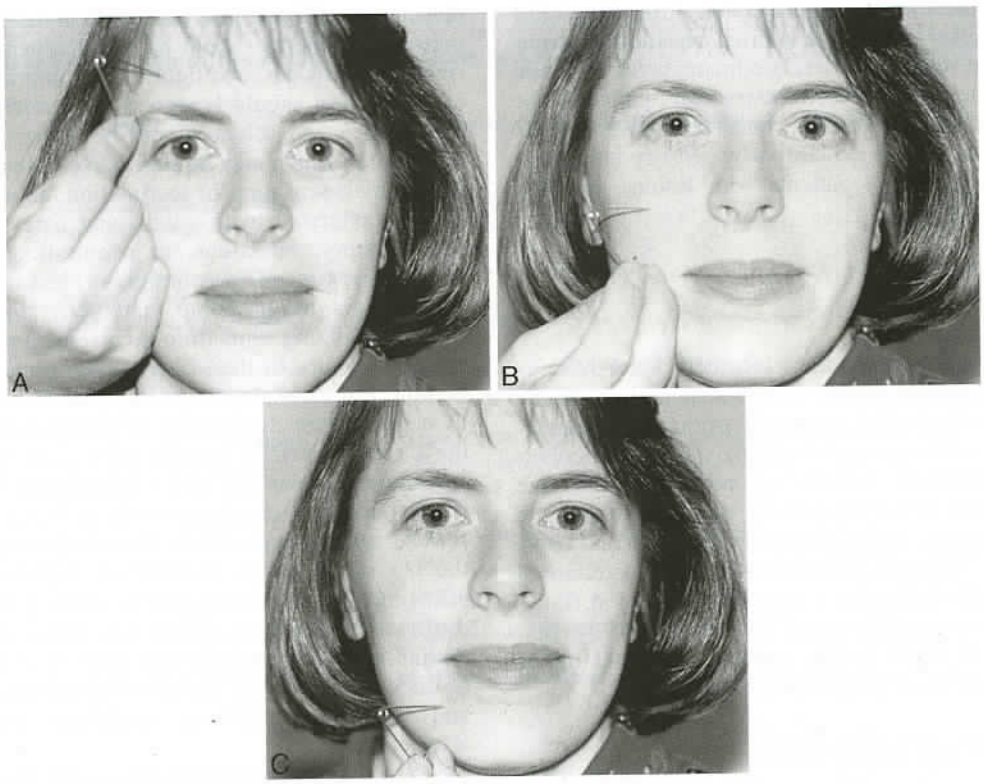


Figure 10-2. Sensory examination of the trigeminal nerve. Testing pain sensation in the cutaneous distribution of V1 (**A**), V2 (**B**), and V3 (**C**) by lightly touching the skin with a pin. Light touch and temperature modalities should also be assessed in the same distributions.

from leprosy, however, affects facial cutaneous regions, which have a cooler temperature, but spares fibers at the hairline where the skin is warmer. Finally, by testing vibratory sensation on the frontal bone, malingering or hysterical patients can often be identified as those who report a difference in sensation despite the physiological impossibility of detecting differences in vibratory sensation when applying the tuning fork to the same albeit "right" or "left" frontal bone.

Motor Function of Cranial Nerve V

Proper evaluation of the trigeminal nerve includes assessment of the integrity of its motor function. Evidence of trigeminal motor involvement may be present, such as muscle atrophy, spasm, or fasciculations; jaw deviation; difficulty chewing; and hyperacusis. Atrophy of the temporalis is often easy to observe. To assess muscle bulk, the masseter may be pinched between the fingertips and the temporalis muscle should be palpated as the patient opens and closes the mouth (Fig. 10-3A). The strength of jaw opening (Fig. 10-3B), closure, and lateral deviation should be assessed because jaw closure is very strong and difficult to evaluate clinically, and subtle changes may not be easily detected.

If it is difficult for the patient to open the mouth against resistance, some degree of motor weakness is likely to be present. Weakness of the pterygoids resulting from nuclear or nerve lesions may produce ipsilateral jaw deviation (see Fig. 10-3). Lower motor neuron processes involving the trigeminal motor nucleus such as motor neuron disease may produce fasciculations in association with muscle weakness and atrophy. Masseteric spasm and contracture, in association with ipsilateral hearing loss, facial numbness, diminished corneal reflex, and paretic facial muscles, is a useful sign in the diagnosis of tumors infiltrating the dorsal pontine tegmentum.[10,11]

Trigeminal Reflexes

The corneal reflex is a reliable measure of afferent trigeminal V1 and efferent facial nerve VII fibers (a V-VII reflex) and is present at infancy. Lightly touching the cornea with a tissue or cotton swab induces a rapid bilateral blink reflex (Fig. 10-4A). Touching the sclera or eyelashes, tapping the glabellar regions (glabellar blink reflex), presenting a light flash, or stimulating the supraorbital nerve induce a less rapid but still reliable response. Anatomically, afferent corneal V1 fibers may synapse within the spinal trigeminal nucleus as well as the main sensory nucleus. Neurons project bilaterally to the facial nuclear neurons, which in turn provide input to the orbicularis oculi muscles (see Fig. 10-1B). The corneal reflex may be slowed in various disorders affecting the trigeminal nerve, ganglion, or brain stem nuclei; these include posterior fossa and cerebellopontine angle tumors, multiple sclerosis, and brain stem strokes (especially Wallenberg's syndrome).[12] Rarely, a delay in the corneal reflex has been reported ipsilateral to a hemispheric lesion.[13]

A pathologic jaw jerk reflex may indicate dysfunction of afferent sensory or efferent motor V3 fibers. Afferent axons for the jaw jerk reflex are from stretch receptors (muscle spindles) within the masseter, temporalis, and medial pterygoid muscles, which project centrally to the mesencephalic nucleus and induce a rapid, single jaw closure (jerk)

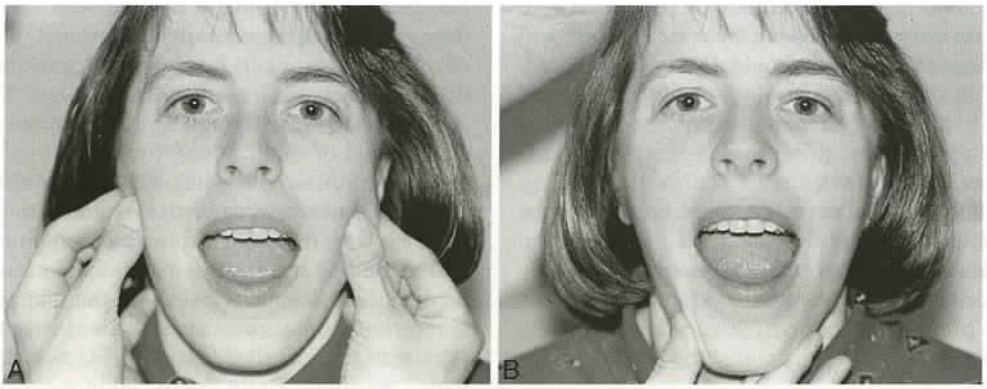


Figure 10-3. Motor examination of the trigeminal nerve. **A,** Palpation of the masseter muscles to assess muscle bulk, which may be diminished in lesions affecting the trigeminal motor nucleus or trigeminal nerve. **B,** Assessing strength of jaw opening is clinically easier than jaw closure.

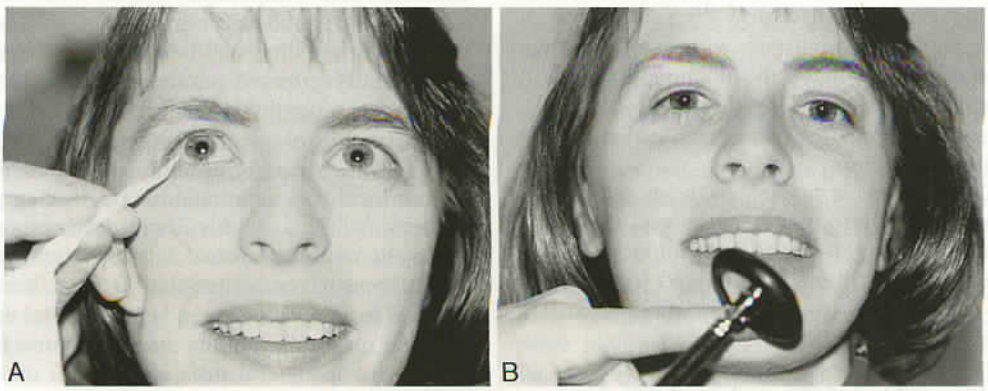


Figure 10-4. Trigeminal reflexes. **A,** The corneal reflex is elicited by lightly touching the cornea with a tissue or cotton swab. **B,** The jaw jerk reflex may be elicited by gently tapping a finger placed on the chin. Both of these reflexes may be brisk in supranuclear processes but diminished in nuclear or peripheral lesions.

mediated via motor trigeminal neurons that project back to these muscles. The jaw jerk is elicited by tapping the chin when the mouth is closed and the jaw relaxed (Fig. 10-4B). Other variations include tapping the thumb placed on the chin or a tongue blade placed on the lower teeth. Peripheral or brain stem nuclear processes that affect V3 neurons attenuate the jaw jerk reflex, whereas lesions involving supranuclear trigeminal motor projections may exaggerate the reflex.

There are several other reflexes that include the participation of trigeminal nerve divisions. The oculocardiac reflex is bradycardia associated with ocular compression and can complicate ophthalmalogic surgery. The corneomandibular reflex is a pathologic reflex seen after a corticobulbar lesion in which corneal stimulation causes contralateral deviation of the mandible due to contraction of the inferior head of the lateral pterygoid.[14] Other reflexes include the snout and trigemino-abducens reflexes.[15]

Associated Neurological Findings

CEREBRAL. The presence of apraxia, hemispacial neglect, aphasia, or Gerstmann's syndrome in association with facial numbness is very helpful in identifying parietal lobe dysfunction in affected patients. Other important manifestations of parietal lobe dysfunction include a homonymous hemianopia (especially within the inferior quadrant); a cortical sensory syndrome in which astereognosis, diminished two-point discrimination, and agraphesthesia are features; and abolition of optokinetic nystagmus toward the side of the lesion.

CRANIAL NERVES. Ophthalmoparesis involving cranial nerves III, IV, or VI with trigeminal symptoms suggests cavernous sinus or superior orbital fissure pathology. Optic neuropathy, in addition to deficits of cranial nerves III, IV, or VI, with V1 sensory loss, localizes to the orbital apex. If cranial nerves VI, VII, and/or VIII are involved (ophthalmoparesis, nystagmus, and hearing changes), a petrous apex process such as Gradenigo's syndrome or lesion such as tumor within the lateral pons or cerebellopontine angle should be suspected (Video 201, Cranial Nerve VII Anatomy). Similarly, detection of Horner's syndrome may indicate lateral brain stem or upper cervical spinal cord pathology (Video 17, Horner's Syndrome).

MOTOR/REFLEXES/CEREBELLAR/GAIT. Hemiparesis can result from lesions within the precentral gyrus and can overlap with sensory loss. Cerebellar abnormalities such as gait ataxia or nystagmus in association with facial numbness may point to a process within the cerebellopontine angle (Video 26, Lower Extremity Dysmetria). Detection of Horner's syndrome alone or in combination with dysphagia and ataxia is consistent with a lesion in the lateral medullary region.

SENSORY. Although the distribution of sensation on the lower face is via V3, the angle of the jaw is innervated by

the C2 and C3 spinal nerves. Numbness or paresthesias in this region may reflect an intramedullary cervical cord process, but a psychogenic etiology should also be considered. "Crossed sensory" syndrome, wherein facial hypesthesia is central to body hypesthesia, indicates a brain stem lesion. Face and body hypesthesia on one side suggest a cortical, subcortical, or midbrain lesion.

NEUROVASCULAR. The detection of a bruit over the orbit is suggestive of a carotid-cavernous sinus fistula, especially in the setting of recent head trauma, and may be helpful in discerning trigeminal dysfunction from a cavernous sinus process. Other signs suggestive of carotid or systemic vascular disease increase the suspicion of stroke syndromes.

EVALUATION GUIDELINES

In virtually every patient who presents with overt or subtle manifestations of trigeminal nerve dysfunction, some form of additional laboratory evaluation is indicated (Table 10-3). Careful and directed neurological examination dictates the most important tests to obtain.

NEUROIMAGING. Once a lesion has been reasonably localized to the cortex, white matter pathways, thalamus, or brain stem, neuroimaging is essential to support a definitive clinical diagnosis.[16] Although computed tomography (CT) scanning can provide useful information regarding bony change or intracranial hemorrhage, magnetic resonance imaging (MRI) renders high-resolution models of regions not readily visible by CT, such as the brain stem. In addition, subtle abnormalities, such as early multiple sclerosis plaques, small tumors, or infarcts, can often be visualized with gadolinium-enhanced MR images. MRI with gadolinium is a very useful way to visualize Meckel's cave[17] and to detect enhancement within the trigeminal nerve roots or gasserian ganglion. MRI or CT with fine sections through the orbits is useful in assessing an orbital mass lesion and pain referable to V1. MR or CT angiography may be utilized to identify compression of the trigeminal nerve by the superior cerebellar artery.[18] CT is the method of choice to evaluate the petrous apex bone, especially in disorders such as Gradenigo's syndrome.

ELECTROPHYSIOLOGY. If symptoms described are paroxysmal or intermittent, focal seizures must be considered in the differential diagnosis, and electroencephalography (EEG) can be diagnostic. In addition, EEG may reveal focal slowing or epileptiform abnormalities such as sharp waves or spikes in patients with significant cortical or hemispheric lesions. Because tumors, infarctions, and hemorrhages may also cause seizures in addition to sensorimotor trigeminal dysfunction, EEG may be very useful in these settings. Brain stem auditory evoked potentials (BAEPs) may be useful in assessing the possibility of an intrinsic brain stem process as well as lesions within the adjacent cerebellopontine angle. For example, BAEPs may assist in identifying people with occult multiple sclerosis or small vessel brain stem strokes that may have subclinically affected pontine or medullary regions adjacent to the trigeminal nuclei.

Electrophysiological assessment of the corneal (blink) reflex latency can be reliably measured in an attempt to further localize a supranuclear, nuclear, or peripheral nerve process.[11,19] This electrically elicited response allows measurement of the response latency after stimulating either the afferent trigeminal or the efferent facial nerve components. The facial nerve can be stimulated directly at its exit near the mastoids, and the direct response latency (contraction of the ipsilateral orbicularis oculi muscles) in normal adults is typically measured to be between 3.0 and 5.0 msec. In contrast, the afferent and efferent limbs of the trigeminofacial blink reflex can be tested by stimulating the supraorbital nerve or tapping the glabellar regions and measuring response time to bilateral orbicularis contraction. Separate components of the electrophysiologic muscle response correspond to peripheral nerve conduction or to brain stem interneural synaptic processing.[20] Therefore, prolongation of the blink latency may identify extra-axial

TABLE 10-3

Useful studies in the Evaluation of the Trigeminal Nerve

SYNDROME	NEUROIMAGING	ELECTROPHYSIOLOGY	FLUID AND TISSUE ANALYSIS	NEUROPSYCHOLOGICAL TESTS
Supranuclear	MRI with gadolinium for stroke, tumor, MS	EEG focal slowing or sharp waves	Increased protein, mild pleocytosis	Acalculia, neglect
Nuclear lesions	MRI with gadolinium for stroke, tumor, MS	Abnormal BAEP, slowed blink reflex (V1)	Increased or normal protein, pleocytosis	NA
Preganglionic C-P angle	MRI with gadolinium for stroke, tumor, MS, meningitis, brain stem compression	Slowed blink reflex (V1)	Increased protein, pleocytosis, decreased glucose, abnormal cytology, positive CSF culture	NA
Gasserian ganglion	MRI with gadolinium for infection, tumor	Slowed blink reflex (V1)	Increased or normal protein, abnormal cytology, positive CSF culture	NA
Cavernous sinus	MRI with gadolinium for infection, thrombosis, aneurysm	Slowed blink reflex (V1)	CSF pleocytosis, low CSF glucose	NA
Peripheral CN V branches	Neuropathies	Slowed blink reflex (V1)	Increased or normal protein	NA
Trigeminal neuralgia	CN V root compression on MRI	No change	No change	NA

BAEP, brain stem auditory evoked potentials; C-P, cerebellopontine; MRI, magnetic resonance imaging; NA, not applicable.

processes such as Guillain-Barré syndrome, hereditary motor and sensory neuropathy type I, and diabetes, as well as intrinsic brain stem lesions (Fig. 10-5). In contrast, the clinical utility of trigeminal somatosensory evoked potentials is limited by technical problems of reliability and reproducibility.[20]

BODY FLUID AND TISSUE ANALYSIS. Laboratory studies may reveal evidence of vasculopathies such as systemic lupus erythematosus or Sjögren's syndrome. White blood count elevations may suggest infections, and eosinophilia may indicate fungal disease. Altered glucose tolerance is seen with diabetes mellitus. Vitamin levels may indicate deficiencies of thiamine, folate, vitamin B_{12}, pyridoxine, or vitamin A.

CEREBROSPINAL FLUID EVALUATION. If infectious, neoplastic (especially meningeal carcinomatosis), or inflammatory (sarcoidosis) etiologies are suspected, cerebrospinal fluid (CSF) evaluation is warranted. CSF glucose level, protein level, differential white and red blood cell counts, and cytology tests are compulsory, whereas other studies to isolate mycobacterial, fungal, rickettsial, parasitic, and viral pathogens should be addressed on an individual basis. In the immunocompromised person (e.g., one with cancer, acquired immunodeficiency syndrome, or organ transplant), opportunistic pathogens causing infections such as cryptococcosis, candidiasis, mucormycosis, toxoplasmosis, and cytomegalovirus need to be seriously considered in the setting of any acute or subacute neurological presentation.

CLINICAL SYNDROMES

The trigeminal nerve may be involved in various neurological conditions, and in most instances, the patient complains of sensory loss, paresthesias, pain, or difficulty eating (Table 10-4).[15] Particular details in the history and physical examination will aid in the proper localization of the pathologic process.

Supranuclear Syndromes

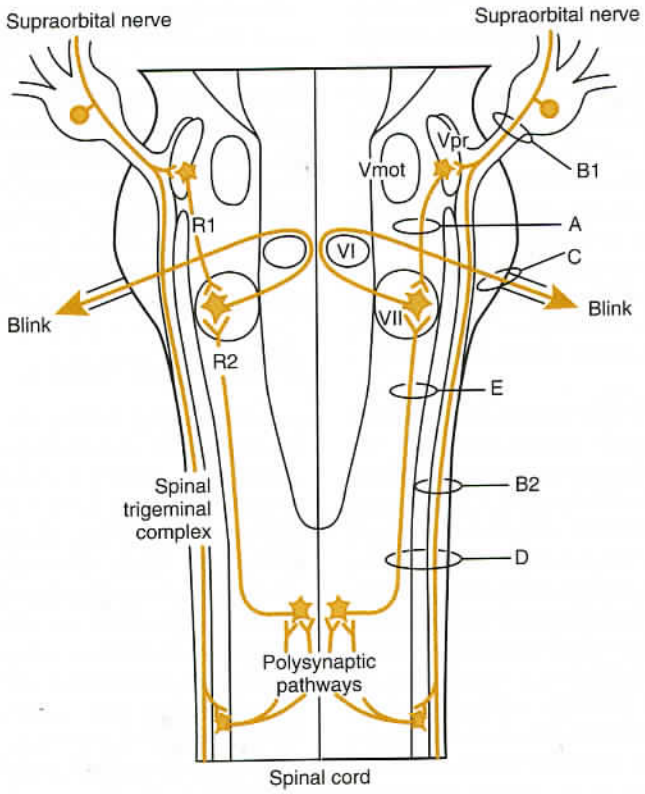
Facial sensory loss may occur in the setting of lesions involving the trigeminothalamic pathways, corona radiata or internal capsule white matter projections from the VPM nucleus of the thalamus to primary sensory cortex, or within sensory cortex. Specific pathological processes affecting these pathways include ischemia, hemorrhage, neoplasm, and demyelinating diseases. All result in contralateral hemifacial and hemibody numbness. In the cheiro-oral syndrome, ipsilateral numbness in the hand and at the corner of the mouth reflects an insult, typically vascular, at adjoining portions of the ventroposterolateral and ventroposteromedial nuclei of the thalamus, where the anatomical distributions of these regions are directly adjacent to one another (Fig. 10-6). In seizures, facial tingling may also occur in association with hand numbness, suggesting a focus in the postcentral gyrus, given the proximity of the cortical regions representing these areas. Patients with thalamic lesions affecting the VPM nucleus, including tumors, infarctions, and multiple sclerosis, may have persistent deep, aching, poorly localized facial pain. This syndrome, named after Dejerine and Roussy, is often associated with small vessel infarctions of the thalamogeniculate artery.[21] The syndrome begins with transient facial hemisensory loss but then evolves into painful facial dysesthesias. Migraine headache can include facial pain, but the duration of pain often allows straightforward distinction from disorders such as trigeminal neuralgia. Another supranuclear trigeminal disorder is Whipple's disease, an infection with *Tropheryma whippelii*, which has pathognomonic contractions of the masticatory muscles concurrent with pendular nystagmus.[22]

Nuclear (Brain Stem) Syndromes

Ischemic injury within the brain stem commonly affects the trigeminal system. Brain stem syndromes may be characterized by sensory paresthesias, numbness, or pain in the distribution of V1 to V3, along with combinations of cranial nerve palsies and distinct motor, sensory, and cerebellar system signs. Reflecting the lateral circumferential arterial supply to the lateral pons, ischemic lesions of the pontine tegmentum are often associated with dissociation of sensory modalities such that pain and temperature perception are dramatically diminished, whereas midline fiber tracts carrying light touch and deep pressure are spared. Pain similar to that of trigeminal neuralgia is rare.

The lateral medullary or Wallenberg's syndrome[23] typically results from interruption of either the vertebral or posterior inferior cerebellar arteries, which provide vascular supply to the lateral medulla. The syndrome may include an ipsilateral Horner's syndrome, skew deviation, ataxia, and difficulty swallowing, but the hallmark of Wallenberg's syndrome is crossed hemifacial and hemibody sensory loss. Lesions affecting the spinothalamic and spinal trigeminal tracts in the lateral medulla are responsible for this crossed loss of pain and temperature sensation. The pattern of facial analgesia in patients with lateral medullary syndrome typically adheres to the cutaneous distribution of V1 to V3, although an onion skin or radicular pattern of sensory loss may occur (see Fig. 10-1). The initial sensory deficit is usually in the ipsilateral face (with descending trigeminal tract involvement) but may be in the contralateral face (with ascending secondary trigeminal tract involvement) or the bilateral face (with involvement of both tracts). Persistent ipsilateral "burning" or "cold" paresthesias are a form of nonthalamic central poststroke pain and are an important sequlae in up to 50% of patients with a lateral medullary syndrome.[23,24] The pain is typically in a V1 or V2 distribution, can occur after a delayed onset, and may persist for months to years. On the other hand, lesions involving more medial medullary regions, which tend to cause contralateral body weakness and tongue deviation, may cause strictly contralateral face and body sensory deficits. The sensory deficits in a medial medullary syndrome are presumably due to lesions of the spinothalamic and the crossed ventral trigeminothalamic tracts.

Other pathological processes within the brain stem can produce trigeminal dysfunction. Tumors, hemorrhage (hypertensive, ruptured arteriovenous malformation), infarctions, demyelinating disease such as multiple sclerosis (Fig. 10-7), infections such as brain stem abscesses and brain stem encephalitis, and inflammatory conditions



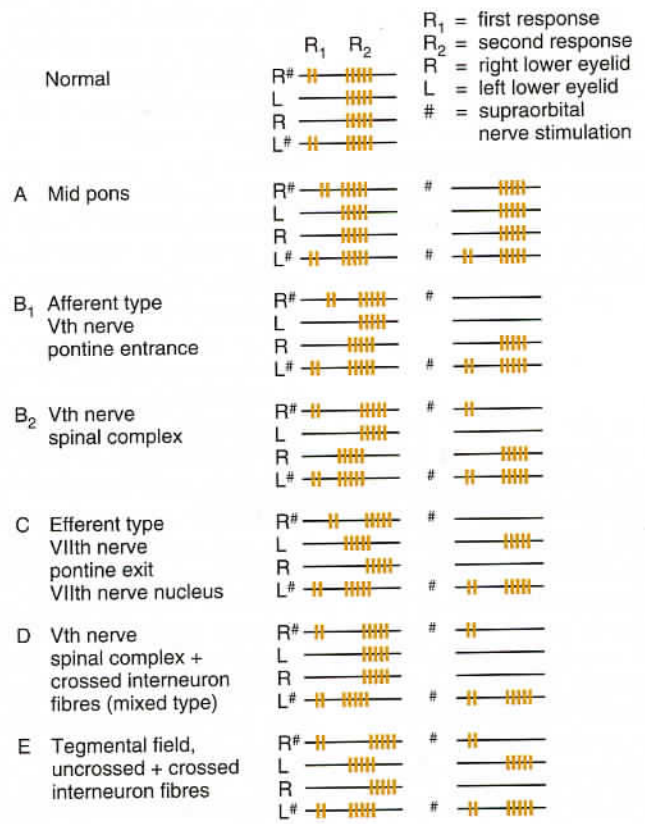


Figure 10-5. *Top*, schematic representation of various brain stem lesions affecting the blink reflex response. *Bottom*, consequent blink reflex response abnormalities after stimulation (#) of the supraorbital nerves, in the right (R) and left (L) orbicularis oculi muscles. If the lesion is incomplete, blink reflex responses are delayed (*left column*); if the lesion is complete, they are absent (*right column*). Characteristically perturbed patterns of the first (R1) or second (R2) electrophysiologic response localize the pathologic process. VII, facial nucleus; VI, abducens nucleus; Vpr, principal trigeminal nucleus; Vmot, trigeminal motor nucleus. (Modified from Aramideh M, Ongerboer de Visser BW: Brain stem reflexes: Electrodiagnostic techniques, physiology, normative data, and clinical applications. Muscle Nerve 2002;26:14–30. Copyright 2002 Wiley Periodicals, Inc. Used by permission of the publisher.)

TABLE 10-4

Selected Etiologies Associated with Trigeminal Nerve Disorders

ETIOLOGICAL CATEGORY	SELECTED SPECIFIC ETIOLOGIES	CHAPTER
Structural Disorders		
Developmental	Brain stem vascular loop, syringobulbia	28
Degenerative and compressive	Paget's disease	29
Hereditary and Degenerative Disorders		
Chromosomal abnormalities and neurocutaneous disorders	Hereditary sensorimotor neuropathy 1 Neurofibromatosis (schwannoma)	32
Degenerative motor, sensory, and autonomic disorders	Amyotrophic lateral sclerosis	36
Acquired Metabolic and Nutritional Disorders		
Endogenous metabolic disorders	Diabetes	38
Exogenous disorders: Toxins and illicit drugs	Trichloroethylene, trichloroacetic acid	39
Nutritional deficiencies and syndromes associated with alcoholism	Thiamine, folate, B_{12}, pyridoxine, pantothenic acid, vitamin A deficiency	40
Infectious Disorders		
Viral infections	Herpes zoster, unknown	41
Nonviral infections	Bacterial, tuberculous meningitis, brain abscess, Gradenigo's syndrome, leprosy, cavernous sinus thrombosis	43
HIV and AIDS	*Opportunistic infections, abscesses, herpes zoster*	44
Neurovascular Disorders	Stroke, hemorrhage, aneurysm	45
Neoplastic Disorders		
Primary neurological tumors	Glial tumors, meningioma, schwannoma	46
Metastatic neoplasms and paraneoplastic syndromes	Lung, breast, lymphoma, carcinomatous meningitis	47
Demyelinating Disorders		
Demyelinating disorders of the central nervous system	Multiple sclerosis, acute demyelinating encephalomyelitis	48
Demyelinating disorders of the peripheral nervous system	Guillain-Barré syndrome, chronic inflammatory demyelinating polyneuropathy	49
Autoimmune and Inflammatory Disorders	Tolosa-Hunt syndrome, sarcoidosis, lupus, orbital pseudotumor	50
Traumatic Disorders	Carotid–cavernous fistula, cavernous sinus thrombosis, maxillary/mandibular injury	51
Epilepsy	Focal seizures	52
Headache and Facial Pain	Raeder's neuralgia, cluster headache	53
Drug-Induced and Iatrogenic Neurological Disorders	Orbital, facial, dental surgery	55

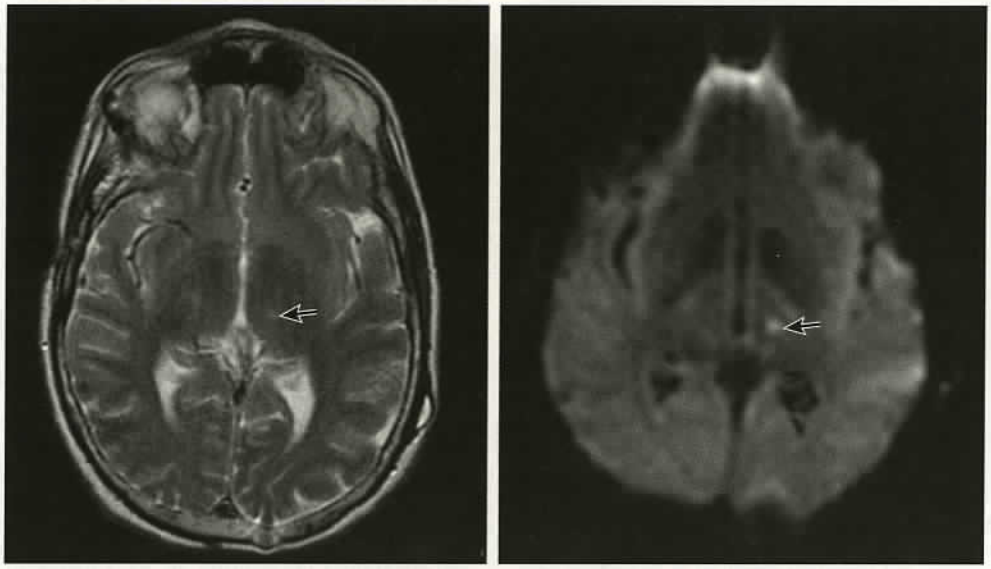


Figure 10-6. The cheiro-oral syndrome. T2-weighted and diffusion-weighted MRI demonstrate an acute thalamic stroke that manifested with contralateral peri-oral and finger numbness.

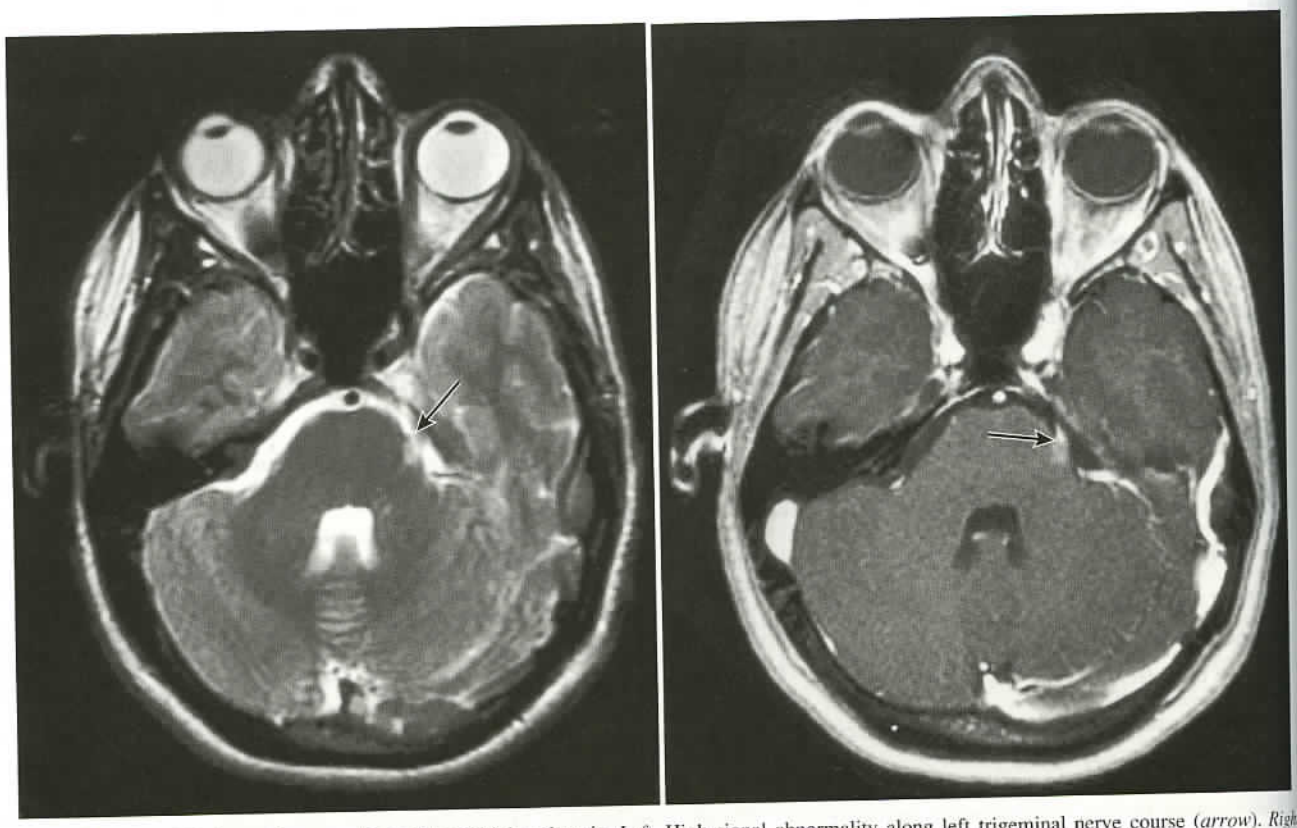


Figure 10-7. Axial MRI image from a patient with multiple sclerosis. *Left*, High signal abnormality along left trigeminal nerve course (*arrow*). *Right*, The nerve enhances after gadolinium injection (*arrow*).

such as tuberculosis or sarcoidosis may affect the lateral pons or midbrain. Facial sensory loss is ipsilateral in pontine involvement and contralateral in midbrain involvement. These disorders may also cause severe paroxysmal hemifacial pain. Facial weakness, muscle atrophy, difficulty chewing, and diminished jaw jerk reflex may be identified in amyotrophic lateral sclerosis as well as other motor neuron disorders damaging the motor trigeminal nuclei. Traumatic or congenital syringobulbia can affect the sensory and motor portions of the trigeminal system within the midbrain, pons, or medulla.

Preganglionic Syndromes

Trigeminal nerve compression can occur in the area between the brain stem nuclei and the gasserian ganglion, specifically within the brain stem or in the cerebellopontine angle. Patients can present with reduced facial sensation in association with poor hearing, nystagmus, limb ataxia, facial weakness, and a diminished corneal reflex. Common lesions in this area include tumors[25] such as acoustic or trigeminal neuromas, meningiomas, metastatic cancers, carcinomatous meningitis, and invasive nasopharyngeal carcinomas; inflammatory disorders such as sarcoidosis; or infectious processes such as mycobacterial (especially tuberculosis), fungal (candidal and histoplasmotic), parasitic, and bacterial organisms. Traumatic injury to this region may also result in sensory loss or motor deficits. Trigeminal neuralgia (discussed later) is commonly due to preganglionic compression of the trigeminal nerve.

Gasserian Ganglion Syndromes

Numerous pathological processes occurring within the middle cranial fossa can result in trigeminal dysfunction by affecting the gasserian ganglion. Gradenigo's syndrome is seen in the setting of osteitis of the petrous apex following suppurative otitis media or mastoiditis, leading to inflammation and infection of the trigeminal ganglion. The syndrome is characterized by headache, trigeminal facial pain or sensory loss, a CN VI palsy, a CN VII facial palsy, and deafness (due to CN VIII involvement). The pain is described as boring or throbbing, worse at night, and aggravated by jaw or ear movement. Gradenigo's syndrome has become increasingly rare with appropriate antibiotic use, but it may still be seen in immunosuppressed patients.[26] Patients with Bell's palsy often have dysesthetic sensations before or during episodes, which are hypothesized to reflect involvement of the trigeminal ganglion or nuclei in the brain stem.[27] A benign, self-limited trigeminal sensory neuropathy has been reported in children 1 to 3 weeks following a nonspecific febrile illness or upper respiratory infection.[28] Like other postinfectious cranial neuropathies, laboratory evaluations are normal or show only a mild CSF pleocytosis. Symptoms resolve usually within 1 or 2 months. It is unknown whether these postinfectious neuropathies result from peripheral nerve, ganglion, or brain stem pathology. Trigeminal sensory neuropathy may occur in association with connective tissue disorders such as mixed connective tissue disease, systemic sclerosis, Sjögren's syndrome, and systemic lupus erythematosus.[29,3] Symptoms may include facial dysesthesias, numbness, an

loss of taste.[31] Such cases will likely have radiographical and electrophysiological evidence of gasserian ganglion involvement. In these autoimmune disorders, there is presumably an antigen-mediated immunological attack on the gasserian ganglion because of incomplete protection by the blood-brain barrier. In disorders of widespread autoimmune-related sensory dysfunction due to involvement of the gasserian and dorsal root ganglia, all deep tendon reflexes may be lost except the jaw jerk because the afferent neuronal cell bodies for jaw proprioception are housed within the central nervous system in the mesencephalic nucleus and protected from circulating antibodies.[20] Various infectious processes within the middle cranial fossa, including syphilis, tuberculosis, and bacterial meningitis, can also affect the gasserian ganglion by inflammation, ischemia, or direct compression. Similarly, neoplasms in this region (meningiomas and schwannomas) can compress the ganglion within Meckel's cave.

Syndromes of Lesions Involving Peripheral Branches of Cranial Nerve V

Several processes are capable of disrupting one or more peripheral branches of the trigeminal nerve. The skull base and exit points of V1 to V3 (i.e., at the superior orbital fissure, foramen rotundum, or foramen ovale) can be diseased and can result in focal sensory or sensorimotor trigeminal dysfunction. For example, acute or resolved bacterial, tuberculous, carcinomatous, or granulomatous (sarcoid) meningitis can result in inflammation, infiltration, or congestion of the basal meninges through which V1 to V3 nerve roots exit the skull (Fig. 10-8). In Paget's disease, narrowing of the skull foramina can also lead to cranial neuropathies, including trigeminal dysfunction.

Various pathological processes, including tumors, aneurysms, infarctions, trauma, and infections, can damage the ophthalmic division of the trigeminal nerve.[32] Superior orbital fissure involvement is characterized by numbness, paresthesias, or pain in the distribution of V1 and within the orbit; Horner's syndrome; and ophthalmoparesis. Involvement of the optic nerve is an important localizing distinction and suggests extension into the orbital apex. If there is evidence of venous congestion on funduscopic examination, cavernous sinus thrombosis, a carotid-cavernous sinus fistula, or a mass lesion should be considered. Cavernous sinus thrombosis is almost always caused by spread of an infection from the face, nose, or mouth. Patients may initially complain of fever, malaise, and frontal headache, but they subsequently develop proptosis, ptosis, ophthalmoparesis, and vasocongestion. Initially, the CSF test result may be normal, but findings characteristic of meningitis may occur if treatment is delayed. Mortality is linked to spread of bacteria to the meninges, which warrants early and intensive antibiotic therapy. Pulsating proptosis, conjunctival erythema, ophthalmoparesis, and a bruit over the globe suggest a carotid-cavernous sinus arteriovenous fistula. These may be congenital in children, but in adults they are more commonly the result of trauma. Carotid-cavernous sinus arteriovenous fistulae also occur in women during pregnancy or at childbirth. Diagnosis by MR or conventional angiography is usual, and treatment with neurosurgical or invasive radiological approaches is warranted.

Cluster headache is considered a trigeminal autonomic cephalgia because it is likely due to disruption of normal autoregulatory trigeminovascular innervation.[33] The strictly unilateral headaches in this syndrome appear as multiple short attacks of severe head or facial pain, and they may be confused with trigeminal neuralgia.[33,34] Cluster headaches, however, have a striking cicannual and circadian periodicity, and they tend to cluster into a period of weeks to months.[34] They typically occur in middle-aged men, are more prominent at night, and may be triggered by alcohol consumption. Unlike trigeminal neuralgia, trigger points are not a characteristic feature. The associated autonomic symptoms, such as lacrimation, conjunctival injection, sweating, ipsilateral nasal blockage, miosis, and ptosis, are quite distinct from symptoms of trigeminal neuralgia. These last only for the duration of the attack, except for a partial Horner's syndrome, which may occasionally persist.[34] High-flow 100% oxygen, or a subcutaneous or intranasal triptan, can be rapidly effective to abort a cluster headache. A steroid taper can be useful for short-term prevention, and calcium channel blocking agents (e.g., verapamil) are used for long-term prevention.[34] Paroxysmal hemicrania is a similar disorder, but the headaches are more frequent, of shorter duration, with

Figure 10-8. Left-sided trigeminal nerve involvement from sarcoid involving the skull base and meninges. Weakness of the pterygoids and masseters manifested as ipsilateral (leftward) jaw deviation and weakness of jaw opening.

faster onset and offset, and have the distinguishing feature of being remarkably sensitive to treatment with indomethacin.[34]

Crescendo orbital pain or frontal headache can herald impending internal carotid artery occlusion presumably from irritation or ischemia to peripheral trigeminal branches. Similarly, a cluster of symptoms including facial, orbital, or neck pain or facial paresthesias in association with an ipsilateral Horner's syndrome may reflect dissection of the cervical portion of the internal carotid artery.[35] These symptoms may also be prodromal. Excruciating supraorbital headache in association with a pupil-involving CN III palsy is almost pathognomonic for an intracranial (especially posterior communicating artery) aneurysm. Ipsilateral orbital or ocular pain has also been reported in association with posterior cerebral artery occlusion, which may reflect ischemic damage to regions of the tentorium adjacent to the occipital lobes that are innervated by V1.

Circumscribed facial paresthesias in V1 to V3 distributions have been identified in patients with diabetes mellitus, Guillain-Barré syndrome, hereditary sensory motor neuropathy I,[36] chronic inflammatory demyelinating polyneuropathy, nutritional deficiencies, and other peripheral neuropathological disorders. Vascular infarction of the nerve branches, such as in vasculitis, can also result in sensory loss. Compressive or infiltrative processes affecting any of the peripheral trigeminal branches result in focal, well-circumscribed sensory loss or paresthesias (see numb chin syndrome, later in the chapter). Dental trauma and exposure to various toxic substances, such as trichloroethylene and trichloroacetic acid, can also result in circumscribed facial sensory loss or paresthesias in the trigeminal distribution.

The temporomandibular joint (TMJ) syndrome refers to recurrent pain in the region of the jaw, ear, occiput, and supraorbital regions, which is believed to result from degeneration or malocclusion of the TMJ. Erosion of the bony surfaces within the glenoid fossa may cause irritation of several adjacent nerves, including the auriculotemporal and chorda tympani trigeminal nerves. Patients may report an increase in pain in the evening and pain referred to the oropharynx. Rarely, a sensation of hearing dullness or auricular congestion may be noted. The TMJ syndrome may result from local trauma, neoplastic invasion, ankylosis, or inflammation, although some cases reflect nonorganic or ill-defined joint pain syndromes. On examination, the TMJ may appear lax and may be painful to passive motion or palpation. Correction of an underlying malocclusion may be curative, but other measures include analgesics, jaw exercises, soft diet, and tricyclic antidepressants.[37]

The numb chin syndrome (mental neuropathy) often reflects a bony lesion affecting the mental foramen through which V3 passes to innervate the chin and mandible.[38,39] Patients often report numbness or pain on one or both sides of the chin, which may extend to the lip or submandibular region. Frequent causes include granulomatous diseases such as histiocytosis X; primary bony malignancies such as osteosarcoma, fibrosarcoma, and plasmacytoma; and metastatic lesions from lung, breast, and prostate carcinoma[40] as well as lymphoma (especially Burkitt's lymphoma). Development of a numb chin in a patient with cancer in remission may indicate relapse. Nonmalignant etiologies include collagen vascular disorders, trauma, periodontal disease, benign bony cyst, focal idiopathic osteolysis (Gorham's disease),[41] and sickle cell disease. A variant of the numb chin syndrome is the numb cheek syndrome, which results from a bony lesion affecting the infraorbital foramen or the maxillary sinus and trigeminal branch V2.[42] Rarely, focal motor weakness affecting the masticatory muscles results from damage to motor branches of V3.

Evaluation of sensory loss over the chin or malar region begins with determining whether there is a distal or proximal trigeminal lesion. Specifically, mental neuropathy causes focal sensory loss over the lower lip and chin, whereas proximal V3 dysfunction results in more widespread sensory disturbance and may be associated with dysfunction of other cranial nerves. Motor involvement is characterized by ipsilateral jaw deviation, flaccidity of the floor of the mouth, and wasting of the ipsilateral temporalis muscle. Weakness of the tensor tympani results in difficulty detecting low-pitched sounds. Careful examination should detect erythema and edema over a focal bony lesion. Plain radiographs of the mandible may be very useful, and if abnormal, bone scan and biopsy of the lesion may be indicated. A search for occult malignancy may be necessary. If radiographs are normal, evaluation of the brain and cranial nerves by MRI (with contrast) and lumbar puncture for cytology is indicated because a brain stem lesion or carcinomatous meningitis may cause focal trigeminal dysfunction.

Corneal hypesthesia and orbital pain may result from local corneal dystrophies or reflect damage to branches of V1, which innervate these structures. Clinically, a diminished corneal reflex may be detected. Viral (herpetic) infections, diabetes, leprosy, and vitamin A deficiency can result in unilateral or bilateral corneal hypesthesia. In addition, the pain associated with anterior uveitis, acute angle-closure glaucoma, and optic neuritis is mediated through V1 orbital sensory fibers. In the orbit, inflammatory conditions such as cellulitis, pseudotumor, or neoplasms (lymphoma and metastatic tumors) may present as orbital pain in association with ophthalmoparesis. Trigeminal involvement in orbital pseudotumor is uncommon. Infections within the orbit, including those from bacterial and fungal pathogens such as *Streptococcus* and *Mucor*, respectively, can also result in a painful ophthalmoplegia. The Tolosa-Hunt syndrome (painful ophthalmoplegia) is characterized by steady, unremitting retro- and supraorbital pain (in the cutaneous V1 distribution) in association with paresis of cranial nerves III, IV, and VI and a diminished corneal reflex.[43] Sensory loss and pain in V2 distribution may also occur. Less frequently, the optic nerve and oculosympathetic fibers may be affected as well. Symptoms may persist for weeks to months. Pathologically, a low-grade, noninfectious, granulomatous process adjacent to the cavernous sinus or within the superior orbital fissure has been identified consisting of lymphocytes and plasma cells. The Tolosa-Hunt syndrome typically responds dramatically to systemic corticosteroids, although symptoms may recur over months to years. Spontaneous remissions have also been reported.

Other causes of decreased sensation within the globe and conjunctiva are orbital surgery or orbital trauma, which affect nasociliary and frontal branches of V1. In herpe

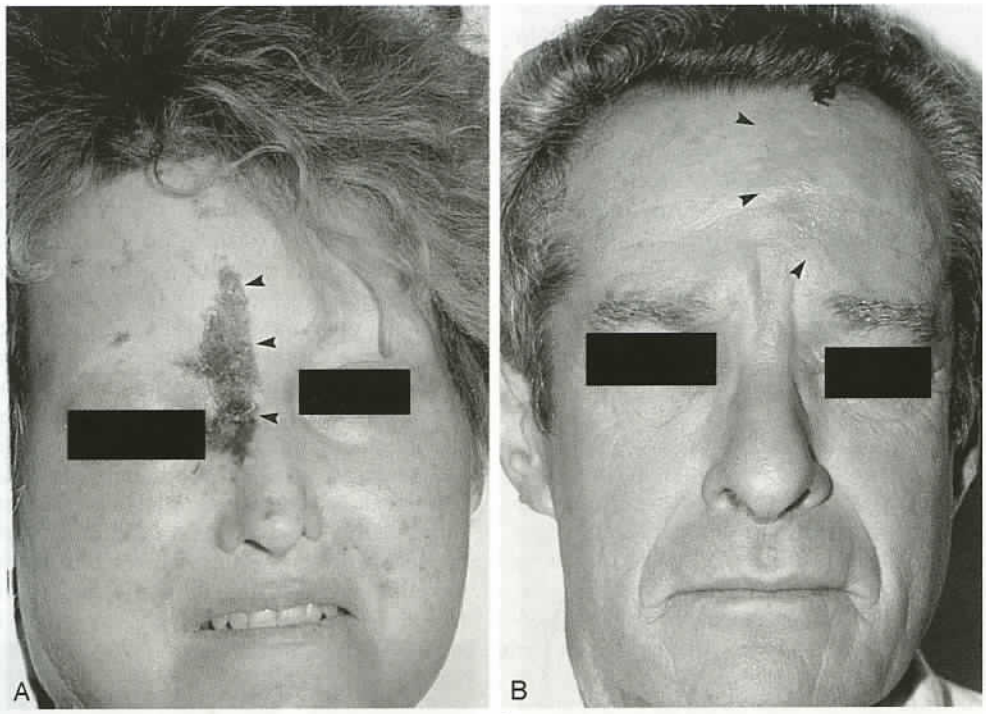


Figure 10-9. Acute (**A**) and resolving (**B**) herpes zoster (*arrows*). In A, there is selective involvement of the nasociliary branch of the trigeminal nerve.

zoster ophthalmicus (Fig. 10-9), inflammation and vesicular eruption involving all branches of V1 as well as small arterioles within the gasserian ganglion may result in excruciating, lancinating pain in the periorbital region (Video 107, Herpes Ophthalmacus).[44] Symptoms of herpes zoster ophthalmicus typically begin 2 or 3 days before the appearance of vesicles and may diminish after 2 or 3 weeks. Hypalgesia and paresthesias may be noted during the outbreak of the syndrome and after lesions heal. Pain may persist after the rash is gone only to evolve into post-herpetic neuralgia. This syndrome consists of burning, lancinating, aching pain in the V1 territory often in association with paresthesias and hyperpathia. As in trigeminal neuralgia, trigger points can evoke pain in response to cutaneous stimuli.[45,46] A randomized, double-blind, placebo-controlled trial suggests that a zoster vaccine effectively reduces the incidence of postherpetic neuralgia.[47]

Atypical facial pain can also reflect trigeminal branch disorders.[44,48] Some patients experience persistent facial pain that is not confined to the distribution of V1 to V3 and that differs in character from classic trigeminal neuralgia. Many of these atypical facial pain syndromes, including Charlin's nasociliary neuralgia, Sluder's pterygopalatine ganglion syndrome, and Vail's vidian neuralgia, involve portions of the trigeminal nerve. They are also characterized by numerous autonomic symptoms, such as lacrimation, conjunctival injection, altered sweating, salivation, facial flushing, and nasal congestion, which are believed to result from involvement of the autonomic ganglia (ciliary and pterygopalatine) in the face. These atypical facial neuralgias are additionally characterized by nondermatomal localization of pain; bilateral symptoms; continual instead of paroxysmal pain; lack of clear trigger zones; and deep, poorly localized pain.[48] Appropriate therapy for these debilitating and often refractory disorders is often unsatisfactory and has consisted of surgical ablation of peripheral pain fibers, peripheral or sympathetic nerve blockade, transcutaneous electrical stimulation, tricyclic antidepressants, and narcotic and non-narcotic analgesics.

Trigeminal Neuralgia (Tic Douloureux)

Trigeminal neuralgia, or tic douloureux, is a paroxysmal disorder that presents with excruciating, lancinating painful spasms affecting one or more divisions of CN V (Video 106, Trigeminal Neuralgia).[49] Trigeminal neuralgia is unilateral and usually affects the second or third division of CN V. In less than 5% of cases, V1 is affected, whereas V3 is affected in more than 70% of cases.[50] Rarely, pain may occur bilaterally, although simultaneous bilateral spasms are quite atypical. The pain occurs spontaneously as brief lightning-like spasms lasting seconds to minutes, or pain may be precipitated by cutaneous or auditory stimuli. It is reported as lancinating, stabbing, searing, burning, or electrical, and the intensity is such that the patient often winces or grimaces in a ticlike fashion. In many instances, there is a demonstrable trigger point that can reproduce pain, and some patients may be unable to chew, eat, drink, shave, or brush their teeth for fear of triggering a spasm.[51] Paroxysms recur throughout the day and night. Between attacks, there are no symptoms, but the patient is usually anxious about having another attack. Objective sensory or motor deficits are not a feature, although a subjective report of hypesthesias over the face may be reported. Often, there is a temporal summation of stimuli necessary to invoke a response. Trigeminal neuralgia affects approximately 4 people per 100,000 population, has a slight female predominance (3:2), and has a peak incidence in middle age.[52] The age of onset is important because the appearance of trigeminal neuralgia in a young

patient should raise the suspicion of demyelinating disease such as multiple sclerosis[53,54] or another structural brain stem disorder.[55–57]

Trigeminal neuralgia is caused by demyelination of trigeminal sensory fibers within the proximal nerve root (within the central nervous system) or, less commonly, within the brain stem. In most cases (80–90%) the demyelination is due to compression by an overlying blood vessel, most commonly the superior cerebellar artery or the anterior inferior cerebellar artery (Fig. 10-10).[18,58–60] Because of the anatomic distribution of fibers within the nerve root, cranial compression tends to cause V1 symptoms, medial compression tends to cause V2 symptoms, and lateral or caudal compression may cause V3 symptoms (Fig. 10-11).

Pathologic examination of trigeminal biopsy specimens taken during vascular decompression shows focal demyelination only in the immediate vicinity of the point of vascular indentation, with close apposition of demyelinated axons and fewer intervening glial processes (Fig. 10-12).[61] These cytoarchitectural changes lead to increased ectopic generation of spontaneous nerve impulses and abnormal nonsynaptic ephatic conduction to adjacent fibers. It is in the region of the trigeminal nerve root that the fibers subserving light touch and those involved in generating pain are closest in proximity, creating the physiological substrate for the paroxysmal pain characteristically provoked by cutaneous stimuli.[58]

Trigeminal neuralgia is also a well-recognized complication, and can even be a presenting symptom, of primary demyelinating diseases such as multiple sclerosis. This occurs when a demyelinating lesion extends along the proximal part of the nerve root, in some cases to the junction of the peripheral nervous system (Fig. 10-13).[58] Even in cases of multiple sclerosis, however, vascular compression can be the cause of trigeminal neuralgia, and some patients could potentially benefit from surgical intervention.[58,62] In some cases of MS, gadolinium enhancement of the trigeminal nerve and root entry zone can be seen by MRI, even in the absence of trigeminal symptoms.[63] The exact mechanisms of central versus peripheral demyelination (i.e., oligodendrocyte vs Schwann cell pathology) remain unclear in cases of trigeminal neuralgia associated with multiple sclerosis.

On physical examination, objective neurological deficits are not present in the typical patient with trigeminal neuralgia. The patient, however, may appear emaciated if, for example, a trigger point is initiated during chewing, or males may appear disheveled if shaving induces a spasm. Laboratory study results are normal. Careful inspection and palpation of the teeth, gums, nares, nasal sinuses, palate, and pharynx should be performed because disease processes such as infections or inflammatory disorders in these regions can cause significant facial pain. MRI of patients with trigeminal neuralgia may be helpful in identifying other etiologies or associated disorders.

The diagnosis of tic douloureux can usually be made by history alone, but the disorder must be distinguished from other causes of facial pain syndromes such as glossopharyngeal neuralgia, which can be confused with tic douloureux that involves the third division of cranial nerve V. Herpes zoster or post-herpetic neuralgia may also cause some diagnostic confusion. Tumors or vascular lesions of the cerebellopontine angle[25] or within the trigeminal ganglion may induce pain similar to that of trigeminal neuralgia, although the pain in these cases is often continuous and unremitting rather than episodic.[58] Furthermore, these disorders can be distinguished by findings of trigeminal sensory loss, atrophy of facial masticatory muscles, diminished corneal reflexes, and involvement of other adjacent brain stem structures that are not characteristic of trigeminal neuralgia.

Prompt relief of the severe pain associated with this disorder must not be neglected. Both medical and surgical approaches should be considered when appropriate. Over the short term, nonsteroidal anti-inflammatory agents and narcotics may provide symptomatic relief. In patients with refractory neuropathic pain, carbamazepine or gabapentin are considered the first-line treatments.[64] Tricyclic compounds such as amitriptyline and nortriptyline may also

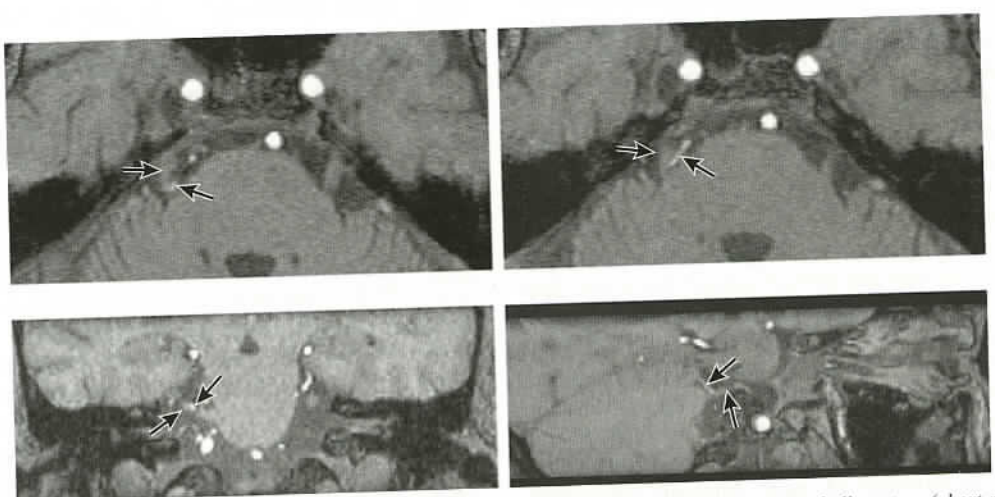


Figure 10-10. Compression of the medial aspect of the trigeminal root entry zone (*long arrow*) by the superior cerebellar artery (*short arrow*), identified magnetic resonance angiography (MRA); axial, coronal, and sagittal views. (From Yoshino N, Akimoto H, Yamada I, et al: Trigeminal neuralgia: Evaluation of neuralgic manifestation and site of neurovascular compression with 3D CISS MR imaging and MR angiography. Radiology 2003;228(2):539–

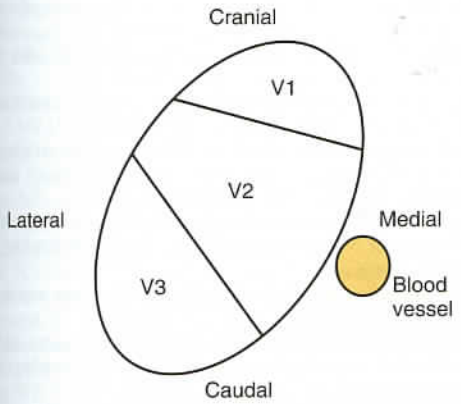


Figure 10-11. Anatomic distribution of fibers to V1, V2, and V3 in the trigeminal root entry zone, and typical medial compression by an offending blood vessel. (From Yoshino N, Akimoto H, Yamada I, et al: Trigeminal neuralgia: Evaluation of neuralgic manifestation and site of neurovascular compression with 3D CISS MR imaging and MR angiography. Radiology 2003;228(2):539–545. Copyright 2003 RSNA. Used by permission of the publisher.)

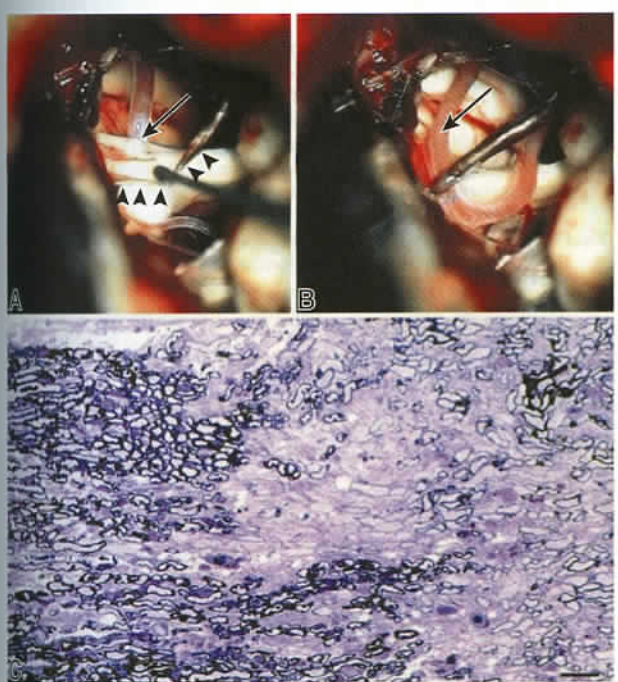


Figure 10-12. Trigeminal neuralgia due to vascular compression of nerve root. **A,** Posterolateral surgical approach, and retraction of a vein (*arrowheads*), reveals an area of indentation (*arrow*) on the trigeminal nerve by an anteriorly placed artery. **B,** The offending artery has been mobilized and repositioned behind the nerve root. **C,** Pathologic specimen of toluidine blue-stained semithin sections from the region of nerve root compression demonstrates demyelination within the proximal nerve root. (From Love S, Coakham HB: Trigeminal neuralgia: Pathology and pathogenesis. Brain 2001;124:2347–2360. Copyright 2001 Oxford University Press. Used by permission of the publisher.)

be used alone or in combination with an anticonvulsant. Alternate options are muscle relaxants, such as baclofen or tizanidine, or an antiarrhythmic such as tocainide.[64] Pregabalin is a new compound that has been proven effective in other painful neuropathies, and it may be useful in treating trigeminal neuralgia as well.[65] In patients with

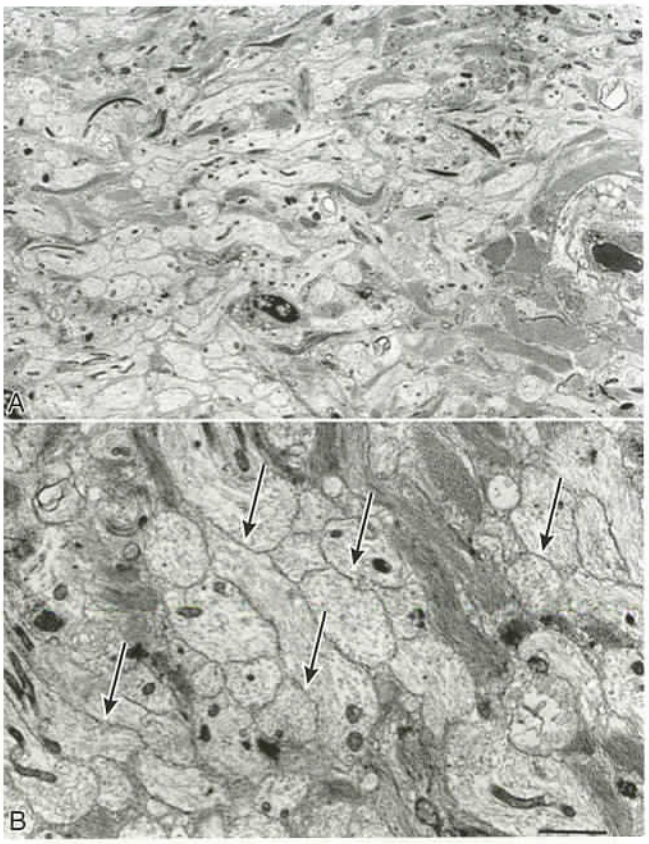


Figure 10-13. Trigeminal neuralgia due to multiple sclerosis. **A,** Electron micrograph illustrating a focus of chronic nerve root demyelination in a patient with multiple sclerosis (scale bar = 10 μm). **B,** Higer magnification shows areas of apposition (some indicated by *arrows*) between several nerve axons (scale bar = 2 μm). (From Love S, Coakham HB: Trigeminal neuralgia: Pathology and pathogenesis. Brain 2001;124:2347–2360. Copyright 2001 Oxford University Press. Used by permission of the publisher.)

medically intractable facial pain, more invasive therapeutic approaches have been attempted. These strategies include radiofrequency thermocoagulation, peripheral glycerol injections,[66] stereotactic gamma knife radiosurgery,[67] percutaneous balloon compression of the trigeminal ganglion,[68] and even repetitive transcranial magnetic stimulation.[69] There are no randomized controlled trials comparing these various interventions, but a review of observational studies suggests that radiofrequency thermocoagulation may offer greater pain relief, at the expense of more frequent permanent facial sensory loss, than glycerol rhizolysis or stereotactic radiosurgery.[70]

GENERAL MANAGEMENT GOALS

In approaching any patient with symptoms referable to the trigeminal system, it is necessary to localize the pathological process; identify associated symptoms; determine prognosis; and provide relief from pain, discomfort, and functional disability. Regardless of etiology, a detailed and directed neurological examination most often yields the correct anatomical localization.

Once it is determined that the likely etiology is, for example, within the brain, brain stem, or cranial vault, a rational

first step is MRI of the brain with and without gadolinium contrast. Fine cuts may be obtained through the orbits, using fat saturation sequences to diminish intraorbital fat artifact. Similarly, dedicated coronal images may be taken to focus on the cavernous sinus. Once appropriate neuroimaging has been performed, other diagnostic studies such as lumbar puncture may be indicated, especially if infectious or carcinomatous processes are suspected. Electrophysiological studies such as somatosensory evoked potentials may be somewhat helpful in peripheral trigeminal neuropathies. For either central or peripheral causes, neurosurgical consultation may be warranted, especially when there is compression of the trigeminal nerve roots or branches.

Pain management may be straightforward in patients with trigeminal pain, but occasionally a sequential approach, including surgical options, is required. In addition to analgesics, antiepileptics play an important role in disease management and pain control. Newer pharmacological and nonpharmacological options provide the clinician with an enhanced array of therapeutic options for the patient with intractable trigeminal pain.

REVIEWS AND SELECTED UPDATES

Atlas S: Magnetic Resonance Imaging of the Brain and Spine, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, 2003.

Brodal P: The trigeminal nerve. In The Central Nervous System, 2nd ed. New York, Oxford University Press, 2003.

Love S, Coakham HB: Trigeminal neuralgia: Pathology and pathogenesis. Brain 2001;124:2347–2360.

Miller N: Facial pain and neuralgia. In Miller NR, Newman NJ, Biousse V, Kerrison JB (eds): Walsh and Hoyt's Clinical Neuro-Ophthalmology, 6th ed. Philadelphia, Lippincott Williams & Wilkins, 2004.

Rowland LP: Injury to cranial and peripheral nerves. In Rowland LP (ed): Merritt's Textbook of Neurology, 7th ed. Philadelphia, Lea & Febiger, 1995.

Valls-Sole J: Neurophysiological assessment of trigeminal nerve reflexes in disorders of central and peripheral nervous system. Clin Neurophysiol 2005;116(10):2255–2265.

Zakrzewska JM, Lopez BC: Trigeminal neuralgiacas. Clin Evid 2006; Jun(15):1827–1835.

REFERENCES

1. Blom S: Trigeminal neuralgia: Its treatment with a new anticonvulsant drug (G-32883). Lancet 1962;Apr: 21(1):839–840.
2. Carpenter MB: Core Text of Neuroanatomy, 4th ed. Philadelphia, Williams & Wilkins, 1991, pp 176–182.
3. Burr HS, Robinson GB: An anatomical study of the gasserian ganglion, with particular reference to the nature and extent of Meckel's cave. Anat Rec 1925;29:269–282.
4. Gudmundsson K, Rhoton AL, Rushton JG: Detailed anatomy of the intracranial portion of the trigeminal nerve. J Neurosurg 1971;35:592–600.
5. Feindel W, Penfield W, McNaughton F: The tentorial nerves and localization of intracranial pain in man. Neurology 1960;10:555–563.
6. Torvick A: Afferent connections to the trigeminal sensory nuclei, the nucleus of the solitary tract, and adjacent structures: An experimental study in the rat. J Comp Neurol 1956;106:51–141.
7. Jones EG: The Thalamus. New York, Plenum, 1988.
8. Williams MN, Zahm DS, Jacquin MF: Differential foci and synaptic organization of the principle and spinal trigeminal projections to the thalamus in the rat. Eur J Neurosci 1994;6:429–453.
9. Patten JP: Neurological Differential Diagnosis: An Illustrated Approach, 2nd ed. Berlin, Springer-Verlag, p 139.
10. Radolsky I: Dorsal pontines tumor syndrome. Z Gesamte Neurol Psychiatr 1935;152:530–537.
11. Tensor RB, Corbett JJ: Myokymia and facial contraction in brain stem glioma. Arch Neurol 1974;30:425–427.
12. Kimura J, Rodnitzky RL, Van Allen MW: Electrodiagnostic study of the trigeminal nerve: Orbicularis oculi reflex and masseter reflex in trigeminal neuralgia, paratrigeminal syndrome and other lesions of the trigeminal nerve. Neurology 1970;20:574–577.
13. Kimura J: Effects of hemispheral lesions on the contralateral blink reflex: A clinical study. Neurology 1974;24:168–174.
14. Aramideh M, Ongerboer de Visser BW: Brainstem reflexes: Electrodiagnostic techniques, physiology, normative data, and clinical applications. Muscle Nerve 2002;26(1):14–30.
15. Miller N: Facial pain and neuralgia. In Miller N (ed): Walsh and Hoyt's Clinical Neuro-Ophthalmology, 4th ed. Baltimore, Williams & Wilkins, 1998.
16. Atlas S: Magnetic Resonance Imaging of the Brain and Spine. New York, Raven Press, 1991.
17. Rubenstein D, Stears RLG, Stears JC: Trigeminal nerve and ganglion in the Meckel cave: Appearance at CT and MR imaging. Radiology 1994;193:155–159.
18. Yoshino N, Akimoto H, Yamada I, et al: Trigeminal neuralgia: Evaluation of neuralgic manifestation and site of neurovascular compression with 3D CISS MR imaging and MR angiography. Radiology 2003;228(2):539–545.
19. Kimura J: Electrodiagnosis in Diseases of Nerve and Muscle: Principles and Practice, 2nd ed. Philadelphia, Davis, 1989.
20. Valls-Sole J: Neurophysiological assessment of trigeminal nerve reflexes in disorders of central and peripheral nervous system. Clin Neurophysiol 2005;116(10):2255–2265.
21. Dejerine J, Roussy G: Le syndrome thalamique. Rev Neurol 1906;14:521–532.
22. Schwartz MA, Selhorst JB, Ochs AL, et al: Oculomasticatory myorhythmia: A unique movement disorder occurring in Whipple's disease. Ann Neurol 1986;20(6):677–683.
23. Currier RD, Giles CL, DeJong RN: Some comments on Wallenberg's lateral medullary syndrome. Neurology 1961;11:778–791.
24. Kim JS, Choi-Kwon S: Sensory sequelae of medullary infarction: Differences between lateral and medial medullary syndrome. Stroke 1999;30(12):2697–2703.
25. Posner JB: Cancer involving cranial and peripheral nerves. In Posner JB (ed): Neurologic Complications of Cancer. Philadelphia, Davis, 1995, pp 181–182.
26. Motamed M, Kalan A: Gradenigo's syndrome. Postgrad Med J 2000;76(899):559–560.
27. Hanner P: Trigeminal dysfunction in patients with Bell's palsy. Acta Otolaryngol 1986;101:224–226.
28. Blau JN, Harris M, Kennett S: Trigeminal sensory neuropathy. N Engl J Med 1969;281:873–877.
29. Lecky BRF, Hughes RAC, Murray NMF: Trigeminal sensory neuropathy. Brain 1987;110:1463–1485.
30. Olney RK: AAEM minimonograph #38: Neuropathies in connective tissue disease. Muscle Nerve 1992;15:531–542.
31. Forster C, Brandt T, Hund E, et al: Trigeminal sensory neuropathy in connective tissue disease: Evidence for the site of the lesion. Neurology 1996;46:270–271.
32. Glaser J: Textbook of Clinical Neuro-Ophthalmology. Philadelphia, Lippincott, 1990.
33. Goadsby PJ, Edvinnson L: Human in vivo evidence for trigeminovascular activation in cluster headache. Brain 1994;117:427–434.
34. Matharu MS, Goadsby PJ: Trigeminal autonomic cephalgias. J Neurol Neurosurg Psychiatr 2002;72(Suppl 2):ii19–ii26.
35. Fisher CM: The headache and pain of spontaneous carotid dissection. Headache 1981;22:60–65.
36. Coffey RJ, Fromm GH: Familial trigeminal neuralgia and Charcot-Marie-Tooth neuropathy. Surg Neurol 1991;35:49–53.
37. Reik L, Hale M: The temporomandibular joint pain-dysfunction syndrome: A frequent cause of headache. Headache 1981;21:151–156.
38. Massey EW, Moore J, Schold SC: Mental neuropathy. Neurology 1981;31:1277–1281.
39. Brazis PW, Vogler LB, Shaw KE: The numb cheek-lip lower lid syndrome. Neurology 1991;41:327–328.
40. Lossos A, Siegal T: Numb chin syndrome in cancer patients: Etiology, response to treatment, and prognostic significance. Neurology 1992;42:1181–1184.
41. Malter IM: Massive osteolysis of the mandible: Report of a case. J Am Dental Assoc 1972;85:148–150.
42. Campbell WW: The numb cheek syndrome: A sign of infraorbital neuropathy. Neurology 1986;36:421–423.

43. Kline LB: The Tolosa-Hunt syndrome. Surv Ophthalmol 1982;27: 79–86.
44. Schott GD: Neurogenic facial pain. Trans Ophthalmol Soc 1980;100: 253–256.
45. Weller THE: Varicella and herpes zoster. N Engl J Med 1983;309: 1434–1440.
46. Olson ER, Ivy HB: Stellate block for trigeminal zoster. J Clin Neuro-Ophthal 1981;1:53–55.
47. Oxman MN, Levin MJ, Johnson GR, et al: A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. N Engl J Med 2005;352(22):2271–2284.
48. White JC, Sweet WH: Pain and the Neurosurgeon. A Forty Year Experience. Springfield, IL, Charles C Thomas, 1969, pp 129–147.
49. Illingworth R: Trigeminal neuralgia: Surgical aspects. In Rose FC (ed): Handbook of Clinical Neurology Amsterdam, Elsevier, 1986, pp 449–458.
50. Dandy WE: Concerning the cause of trigeminal neuralgia. Am J Surg 1934;24:447–455.
51. Roberts AM, Person P: Etiology and treatment of idiopathic trigeminal and atypical facial neuralgias. Oral Surg 1979;48:298–308.
52. Katusic S, Beard CM, Bergstralh E, Kurland LT: Incidence and clinical features of trigeminal neuralgia, Rochester, Minnesota, 1945-1984. Ann Neurol 1990;27(1):89–95.
53. Rushton JG, Olafson RA: Trigeminal neuralgia associated with multiple sclerosis. Arch Neurol 1965;13:383–386.
54. Olafson RA, Rushton JG, Sayre GP: Trigeminal neuralgia in a patient with multiple sclerosis: An autopsy report. J Neurosurg 1966;24:755–759.
55. Leibrock LG, Moore GF, Yetter M: Malpositioned endolymphatic shunt causing trigeminal neuralgia: Case report. Acta Neurochir 1994;126:192–194.
56. Janetta PJ: Arterial compression of the trigeminal nerve at the pons in patients with trigeminal neuralgia. J Neurosurg 1967;26:159–167.
57. Janetta PJ: Observations on the etiology of trigeminal neuralgia, hemifacial spasm, acoustic nerve dysfunction, and glossopharyngeal dysfunction: Definitive microsurgical treatment and results in 117 patients. Neurochirgica 1977;20:145–154.
58. Love S, Coakham HB: Trigeminal neuralgia: Pathology and pathogenesis. Brain 2001;124:2347–2360.
59. Hamlyn PJ, King TT: Neurovascular compression in trigeminal neuralgia: A clinical and anatomic study. J Neurosurg 1992;76:948–954.
60. Bakshi R, Lerner A, Fritz JV, Sambuchi GD: Vascular compression in trigeminal neuralgia shown by magnetic resonance imaging and magnetic resonance angiography image registration. Arch Neurol 2001;58:1290–1291.
61. Hilton DA, Love S, Gradidge T, et al: Pathological findings associated with trigeminal neuralgia caused by vascular compression. Neurosurgery 1994;35(2):299–303.
62. Broggi G, Ferroli P, Franzini A, et al: Operative findings and outcomes of microvascular decompression for trigeminal neuralgia in 35 patients affected by multiple sclerosis. Neurosurgery 2004;55 (4):830–839.
63. da Silva CJ, da Rocha AJ, Mendes MF, et al: Trigeminal involvement in multiple sclerosis: Magnetic resonance imaging findings with clinical correlation in a series of patients. Multiple Sclerosis 2005;11 (3):282–285.
64. Backonja MM, Serra J: Pharmacologic management part 1: Better-studied neuropathic pain diseases. Pain Med 2004;5(Suppl 1): S28–S47.
65. Lyrica product information (2005) Pfizer [online]. Available at www.pfizer.com/pfizer/download/uspi_lyrica.pdf. Accessed December 3, 2005.
66. Erdem E, Alkan A: Peripheral glycerol injections in the treatment of idiopathic trigeminal neuralgia: Retrospective analysis of 157 cases. J Oral Maxillofac Surg 2001;59:1176–1180.
67. Friedman DP, Morales RE, Goldman HW: Role of enhanced MRI in the follow-up of patients with medically refractory trigeminal neuralgia undergoing stereotactic radiosurgery using the gamma knife: Initial experience. J Comput Assist Tomogr 2001;25:727–732.
68. Skirving DJ, Dan NG: A 20-year review of percutaneous balloon compression of the trigeminal ganglion. J Neurosurg 2001;94: 913–917.
69. Lefaucheur JP, Drouot X, Nguyen JP: Interventional neurophysiology for pain control: Duration of pain relief following repetitive transcranial magnetic stimulation of the motor cortex. Neurophysiol Clin 2001;31:247–252.
70. Lopez BC, Hamlyn PJ, Zakrzewska JM: Systematic review of ablative neurosurgical techniques for the treatment of trigeminal neuralgia. Neurosurgery 2004;54(4):973–982.

Interactive study questions and referenced videos for this chapter are available on the DVD-ROM.