CHAPTER 25

The Trigeminal Nerve and Its Central Connections

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Because the three divisions of the trigeminal nerve run in close proximity to cranial nerves II, III, IV, and VI, sensory dysfunction in the face may be a symptom in neuro-ophthalmic patients with vision loss and eye movement disorders. In addition, the trigeminal nuclei are located at all levels of the brainstem, and subsequent central pathways connect these nuclei with the thalami and sensory cortices. Thus, sensory abnormalities of the face often accompany neurologic syndromes due to lesions throughout the central nervous system.

An understanding of the relevant anatomy, along with accurate sensory and motor testing, enables the clinician to localize the lesion more accurately. This chapter covers trigeminal system anatomy and physiology, the examination of the trigeminal nerve system, and topical diagnosis of disturbances of the trigeminal nerve and its central connections.

ANATOMY AND PHYSIOLOGY OF THE TRIGEMINAL NERVE AND ITS CENTRAL CONNECTIONS

This section discusses the anatomy and physiology of the trigeminal nerve and its central connections centripetally. The branches of the trigeminal nerve are considered first, then the gasserian ganglion and trigeminal roots are reviewed. The central connections are discussed last.

MAJOR DIVISIONS OF THE TRIGEMINAL NERVE

Somatic sensory impulses converge upon the gasserian ganglion from the eye, the deep and superficial structures of the face, and the cranium via three major nerves: the ophthalmic, the maxillary, and the mandibular divisions of the trigeminal nerve (Fig. 25.1). Although these nerve trunks represent an afferent system, we describe their anatomy and that of their branches in a centrifugal sequence, from the gasserian ganglion to their connections in the periphery. The mandibular nerve is the only one of the three divisions that contains axons of the motor division of the trigeminal system. Some peripheral branches of the trigeminal nerve contain pre- or postganglionic parasympathetic fibers or post-

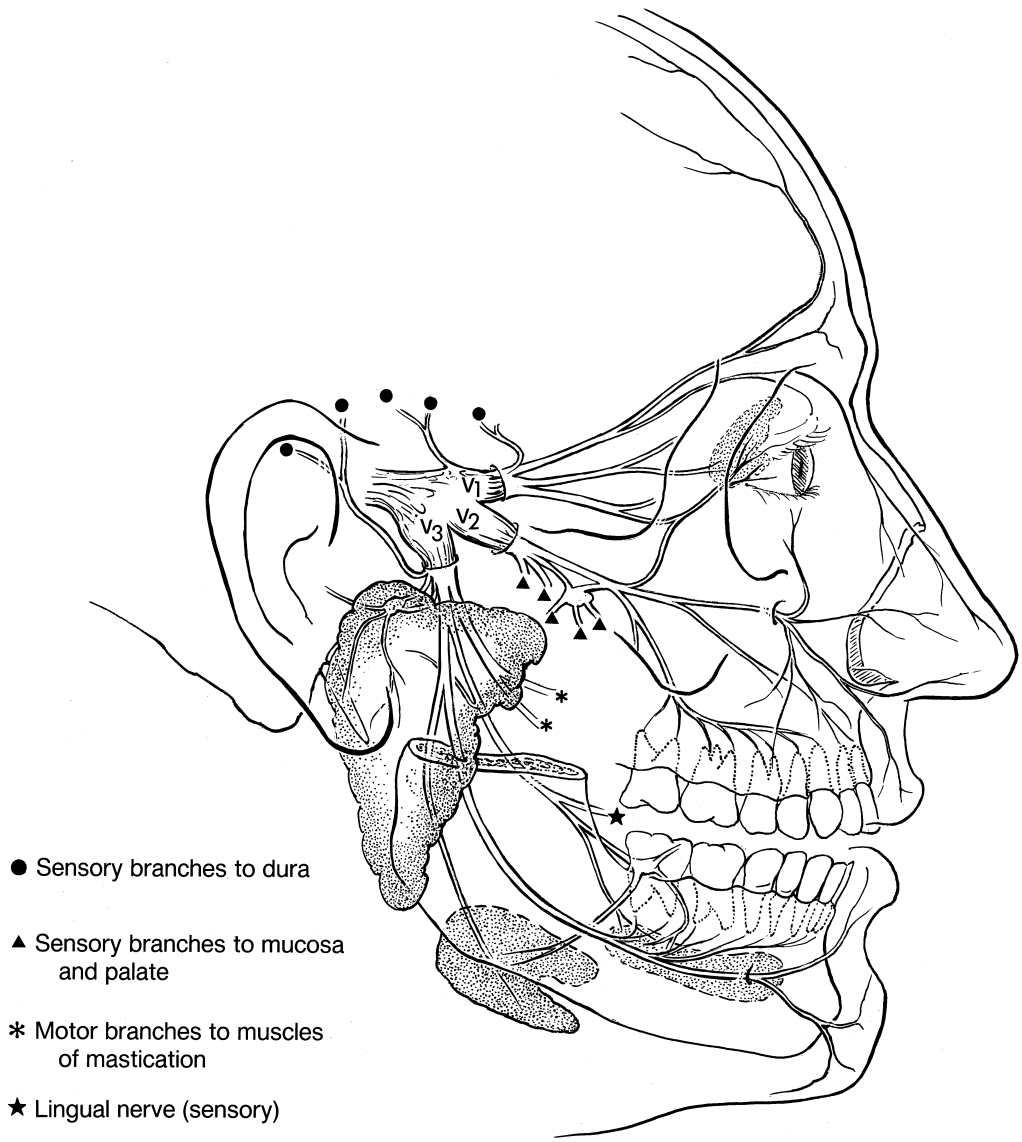


Figure 25.1. Peripheral motor and sensory distribution of the trigeminal nerve. V_1, ophthalmic branch; V_2, maxillary branch; V_3, mandibular branch. Details of branches highlighted in Figure 25.5 (V_1), Figure 25.7 (V_2), and Figure 25.8 (V_3).

ganglionic sympathetic fibers to supply salivary, sweat, or other glands of face, eyes, and mouth (1).

Ophthalmic Nerve (V1)

The ophthalmic or first division is purely sensory and is smaller than the other two divisions. It supplies sensation to the entire eyeball, forehead, lacrimal gland, caruncle, and lacrimal sac. It also supplies the upper eyelids, the frontal sinuses, and the side of the nose. Its cutaneous representation is overlapped by that of the maxillary division (Figs. 25.1 and 25.2).

The ophthalmic nerve arises from the anteromedial aspect of the gasserian ganglion (2). It immediately enters the cavernous sinus inferiorly, where it lies embedded in the lateral wall below the trochlear nerve (Fig. 25.3). Umansky and Nathan (3) studied the cavernous sinus in 70 specimens and found that the lateral wall of the sinus is composed of two layers, a superficial dural layer and a deep layer. The deep layer is formed by the sheaths of the oculomotor (III) and trochlear (IV) nerves, by the sheaths of the ophthalmic and maxillary nerves (V1,2), and by a reticular membrane that extends between the sheaths.

Within the cavernous sinus, the ophthalmic nerve gives off fine twigs to the oculomotor, trochlear, and abducens nerves, thereby supplying sensation to the muscles innervated by these structures. At this level it also gives off recurrent branches that cross, are adherent to the trochlear nerve, and are distributed to the tentorium cerebelli and dura over the posterior pole of the brain (discussion following).

Sympathetic filaments join the ophthalmic nerve from the

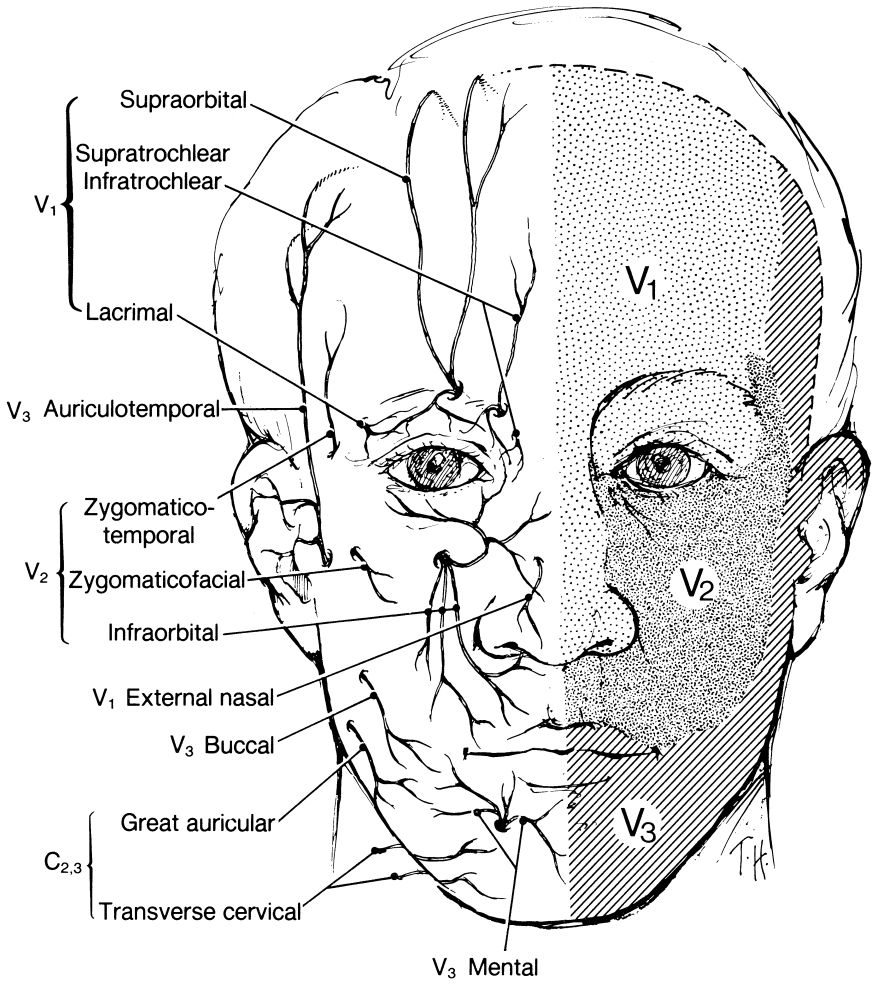


Figure 25.2. Sensory nerves of the face and scalp. Note the distribution of the three divisions of the trigeminal nerve and their areas of overlap.

cavernous plexus situated around the internal carotid artery. According to Parkinson and coworkers (4–6), the sympathetic nerve is a single trunk that runs with the carotid artery. In the cavernous sinus, the trunk joins the abducens nerve briefly before separating and joining the ophthalmic nerve (Fig. 25.4).

Toward the front of the cavernous sinus, and before leaving it, the ophthalmic nerve slopes slightly upward and divides into its three main branches—the lacrimal, frontal, and nasociliary nerves—all of which enter the orbit through the superior orbital fissure (7) (Fig. 25.5).

Trigeminal Innervation of Intracranial Structures

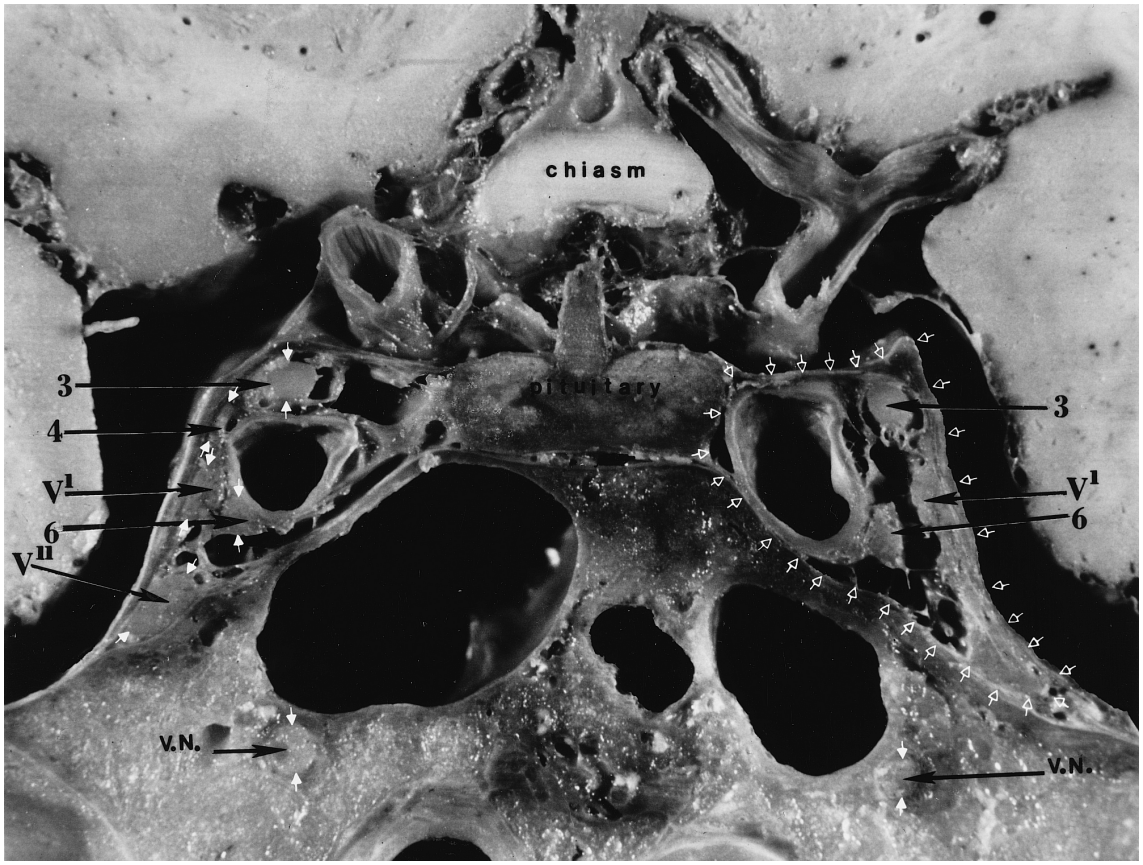
The brain is not innervated by nociceptors. The innervation of the dura of the middle fossa and the middle meningeal vessels is through the maxillary and mandibular (second and third) divisions of the trigeminal nerve, whereas fibers from the ophthalmic (first) division innervate the dura of the anterior fossa (excluding the lateral convexity), the tentorium, and both the falx and the superior sagittal sinus anteriorly and posteriorly.

In monkeys, it has been confirmed that the ophthalmic division of the trigeminal nerve, with a minor contribution from the maxillary division, innervates the vessels in the circle of Willis (8,9). Within the gasserian ganglion of rats, cells that innervate the forehead tend to be clustered around those that send afferents to the ipsilateral middle cerebral artery (10). Their proximity may provide, in part, the anatomic substrate for referred headache pain. The central connections of these neurons are discussed later in this chapter.

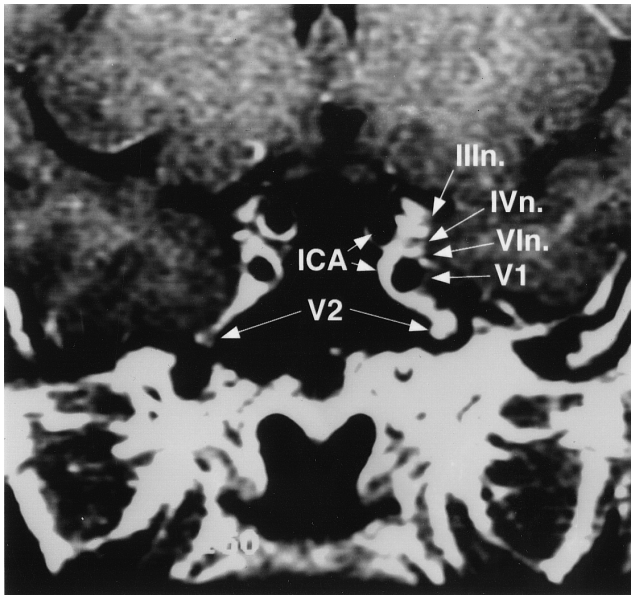
The trigeminal innervation of cerebral blood vessels and dura has important theoretic implications regarding the pathophysiology and treatment of migraine (11–13) (see Chapter 26).

Lacrimal Nerve

This nerve passes through the lateral side of the superior orbital fissure above the lateral rectus muscle to enter the lacrimal gland. It divides into two divisions, either just before entering the gland or within the gland itself. The superior division, which supplies the gland, ends in the conjunctiva and the skin of the upper eyelid, whereas the lower division descends along the orbital wall to anastomose with a branch from the maxillary division.



A



B

Figure 25.3. *A,* Location of the trigeminal trunks in the cavernous sinus. 3, oculomotor nerve; 4, trochlear nerve; V^1, ophthalmic branch of the trigeminal nerve; V^2, maxillary branch of the trigeminal nerve; 6, abducens nerve; V.N., vidian nerve. On the left side, the location of each nerve is identified by *solid white arrows.* On the right side, the boundaries of the cavernous sinus are identified by *open white arrows. B,* Contrast-enhanced T1-weighted magnetic resonance image, coronal view through the cavernous sinus similar to that in *A*. ICA, internal carotid artery; IIIn., oculomotor nerve; IVn., trochlear nerve; VIn., abducens nerve; V1, ophthalmic branch of the trigeminal nerve; V2, maxillary branch of the trigeminal nerve.

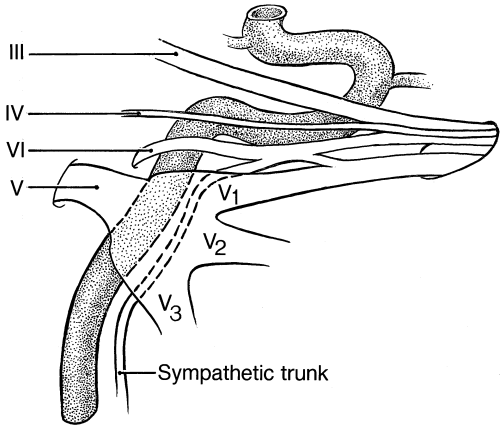


Figure 25.4. Drawing of relationship between the sympathetic fibers, the abducens nerve, and the ophthalmic division of the trigeminal nerve. The sympathetic trunk ascends with the internal carotid artery. It joins briefly with the abducens nerve (VI) then leaves the nerve to join with the ophthalmic branch (V_1) of the trigeminal nerve (V_1).

Frontal Nerve

The frontal nerve enters the orbit above the superior rectus muscle and the levator palpebrae superioris. It hugs the roof of the orbit, and, at about the middle of the orbit, it gives off the supratrochlear nerve, after which point it becomes the supraorbital nerve. The supraorbital nerve supplies the skin of the forehead near the midline, the skin and conjunctiva of the upper eyelid, and the skin on the side of the nose. The supraorbital nerve leaves the orbit by passing through the supraorbital notch in company with the supraorbital artery and proceeds superiorly giving off twigs to the eyelids and frontal sinus. Whitnall (14) noted that neuralgia in the forehead may persist after resection of the supratrochlear nerve and that in such an instance, resection of the frontal nerve may be necessary.

Nasociliary Nerve

The nasociliary nerve is of particular ophthalmic interest because it is the nerve of sensory supply to the eye. Because of its long course through the orbit and cranial cavity and its supply to the nose, it is in contact with many structures. Consequently, neurologic involvement is not uncommon. According to Whitnall (14), this nerve enters the orbit through the annulus of Zinn between the two divisions of the oculomotor nerve and courses obliquely beneath the superior rectus muscle. It then crosses over the optic nerve along with the ophthalmic artery toward the medial orbital wall, where it lies between the superior oblique and medial rectus muscles, still adjacent to the artery. The nasociliary nerve leaves the orbit by traversing the anterior ethmoidal foramen and reenters the cranial vault, where it crosses the anterior portion of the cribriform plate beneath the dura of the anterior cranial fossa, adjacent to the olfactory lobe. It then crosses through a slit, the nasal fissure or anterior nasal canal, at the side of the crista galli and enters the nasal cavity, breaking up into three terminal branches. Two of these branches, the medial and lateral internal nasal branches, are distributed to the anterior nasal cavity, whereas the third continues anteriorly to the end of the nose as the external nasal nerve.

The branches of the nasociliary nerve are as follows: (*a*) the long or sensory root leaves the nerve either just before it enters the orbit or immediately thereafter and passes to the ciliary ganglion into the short ciliary nerves; (*b*) the long ciliary nerves, usually two but occasionally three, surround the optic nerve and pass forward to the iris, ciliary body, and cornea—these nerves also carry dilator fibers from the cavernous sympathetic plexus to the dilator pupillae; (*c*) the infratrochlear nerve is distributed to the medial canthus, to the skin and conjunctiva of the upper eyelid, and to the root of the nose, lacrimal sac, and caruncle; (*d*) nasal branches, usually three, supply the mucous membrane of the anterior part of the nasal septum, the anterior portion of the lateral nasal wall, and the middle and inferior turbinate bones as well as the skin over the cartilaginous tip of the nose (Figs. 25.1, 25.2, and 25.5).

Maxillary Nerve (V2)

The maxillary division is a purely sensory division of the trigeminal nerve. It supplies the skin of the cheek, part of the temporal region, the lower eyelid, upper lip, side of the nose, part of the mucous membrane of the nose, the teeth of the upper jaw, nasopharynx, maxillary sinus, soft palate, tonsil, and roof of the mouth (Fig. 25.2).

The maxillary nerve arises from the frontal central portion of the gasserian ganglion and is usually described as entering the cavernous sinus to lie beneath the ophthalmic division, where it may be separated from the sphenoid sinus by only a thin layer of bone (Fig. 25.3). Here the maxillary nerve may produce a bulge into the lateral wall of the sphenoid sinus (15,16). Henderson (17) investigated the causes of certain unexpected, and sometimes unsatisfactory, results after gasserian ganglion injections for trigeminal neuralgia and studied the relationship of the human maxillary nerve to the cavernous sinus. He concluded that the greater part of the nerve is embedded in the dura of the middle fossa just lateral to the cavernous sinus, rather than within the wall of the sinus. He also found that the origin of the nerve crosses a separate dural sinus that connects the cavernous sinus and the pterygoid venous plexus. Henderson (17) postulated that injection of this ''trigeminal'' sinus, rather than the gasserian ganglion, was considered to be responsible for some clinical failures in treatment of trigeminal neuralgia. Umansky and Nathan (3) agreed that there is considerable variation in location of the maxillary nerve within the cavernous sinus. In their specimens, only in some cases were either the maxillary nerve or the gasserian ganglion located partially within the lateral wall of the sinus, although when these structures were present, they were located in the deep layer of the wall.

The most important of the intracranial branches from the maxillary nerve is the middle meningeal nerve that supplies the dura mater of the middle cranial fossa. The maxillary

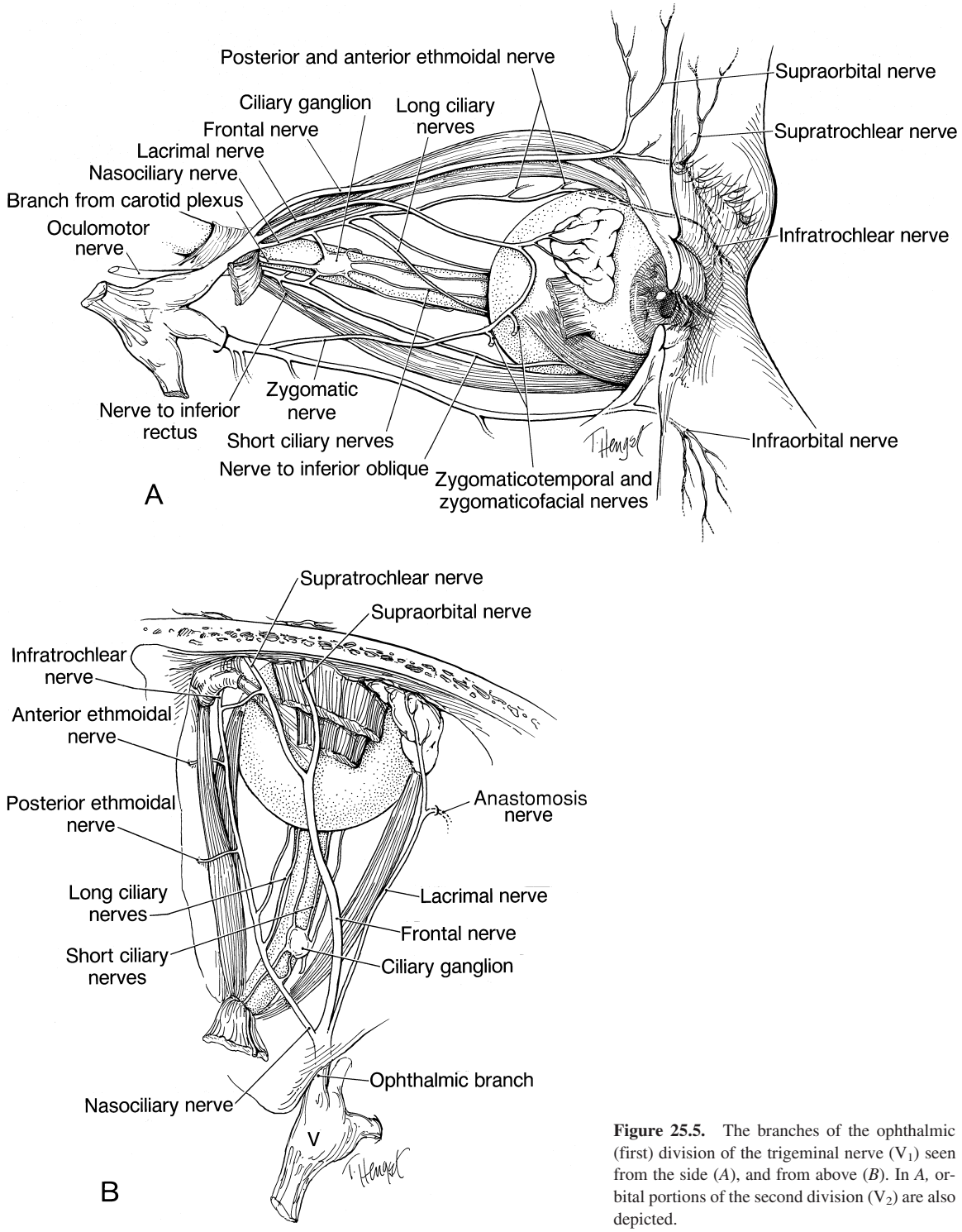


Figure 25.5. The branches of the ophthalmic (first) division of the trigeminal nerve (V_1) seen from the side (*A*), and from above (*B*). In *A*, orbital portions of the second division (V_2) are also depicted.

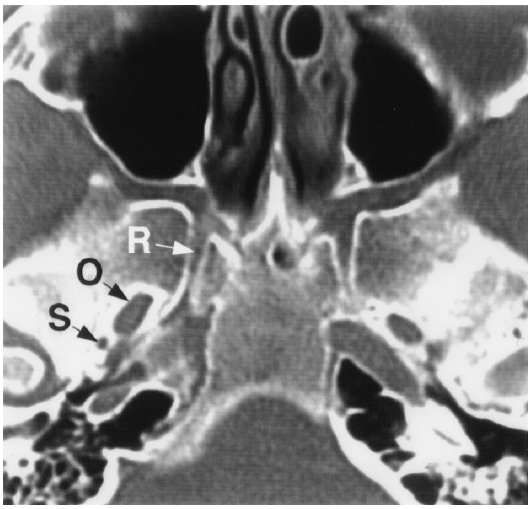


Figure 25.6. Computerized tomography (CT), axial view and bone windows through the skull base demonstrating the foramen rotundum (R), through which the maxillary division (V_2) exits the skull; the foramen ovale (O), through which the mandibular division (V_3) exits the skull; and the foramen spinosum (S), through which the middle meningeal artery enters the skull.

nerve then passes through the foramen rotundum (Fig. 25.6), which lies in the medial aspect of the greater wing of the sphenoid bone (18) to the pterygopalatine fossa (19), where the nerve gives off: (*a*) two large pterygopalatine nerves, which enter the pterygopalatine ganglion, and then divide into branches that supply portions of the nasopharynx, hard and soft palate, and nasal cavity; (*b*) several posterior superior alveolar nerves that pass through the pterygomaxillary fissure to provide sensation for the upper gums and molar teeth; and (*c*) the zygomatic nerve, which enters the orbit through the inferior orbital fissure. This nerve in turn divides into two branches: (*a*) the zygomaticofacial branch, which appears on the face after passing through the zygomatic foramen to supply the skin over the zygomatic bone; and (*b*) the zygomaticotemporal branch, which innervates the skin over the temporal side of the zygomatic bone. Within the orbit the zygomatic nerve communicates with the lacrimal nerve (Figs. 25.2, 25.5, and 25.7). This communication is particularly important because the parasympathetic fibers in the facial nerve gain access to the lacrimal gland via this route (see Chapter 24).

Distal to the pterygopalatine fossa, the maxillary nerve travels through the inferior orbital fissure into the orbit, where it becomes the infraorbital nerve (Fig. 25.7). This nerve is the terminal branch of the maxillary nerve. It passes through the orbital floor in either a canal, the infraorbital canal, or simply a shallow depression only partially covered with bone, the infraorbital groove. While in the canal, it supplies branches to the teeth. The infraorbital nerve exits the orbit through the infraorbital foramen to supply the skin and subcutaneous tissue of the face below and nasal to the orbit (Figs. 25.2, 25.5, and 25.7).

Although it is unclear whether or not the maxillary nerve supplies any sensory fibers that innervate the eye in humans, there is some suggestive evidence of this in animals. In cats and monkeys, Morgan et al. (20) and Marfurt et al. (21) found that the maxillary nerve may carry a small percentage of corneal afferents. Ruskell (22) performed careful dissections of 13 rhesus monkeys and 12 cynomolgous monkeys and showed the presence of an orbitociliary branch of the maxillary nerve. Degeneration experiments combined with

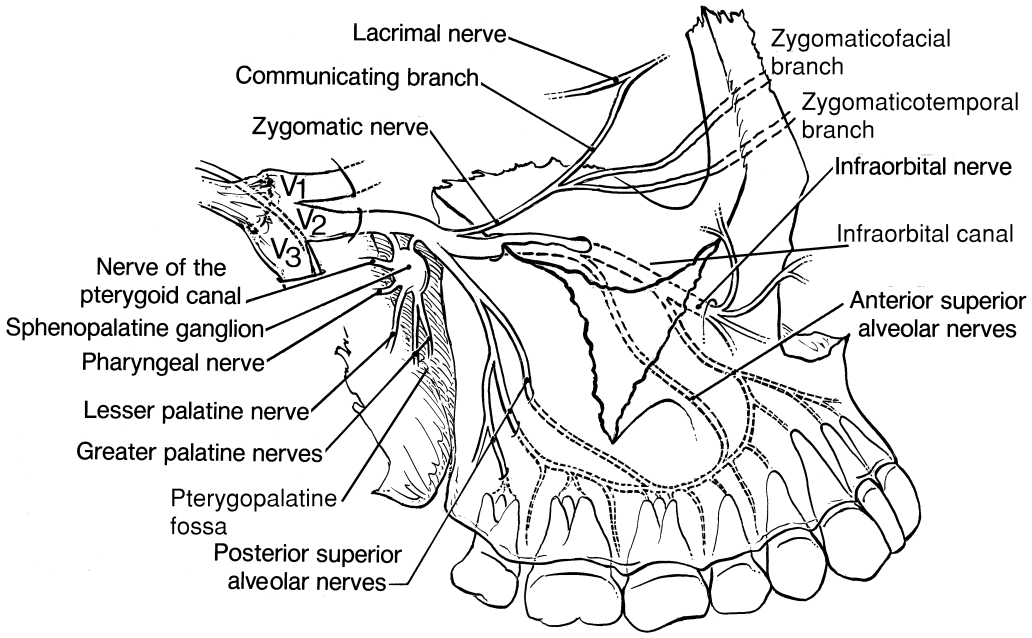


Figure 25.7. The branches of the maxillary (second) division of the trigeminal nerve (V_2).

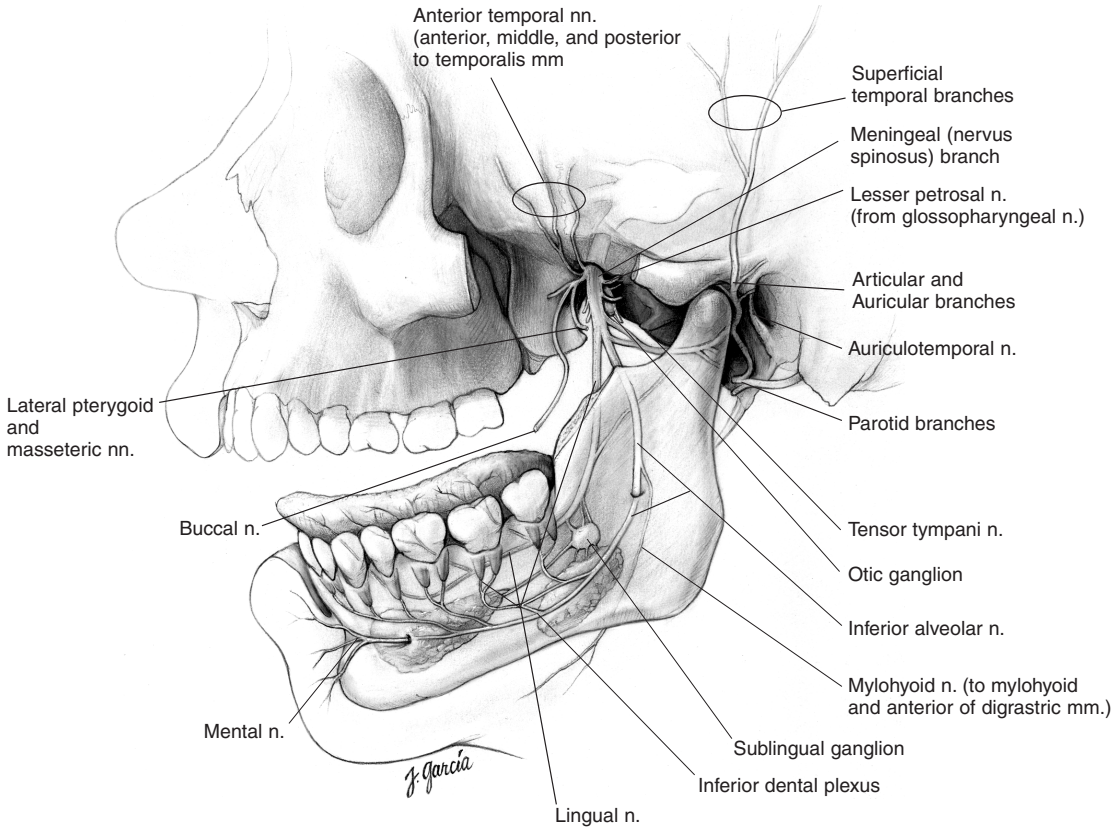


Figure 25.8. The branches of the mandibular (third) division of the trigeminal nerve (V_3).

electron microscopy were used to confirm the pathway and to demonstrate the passage of maxillary fibers through the ciliary ganglion into short ciliary nerves. Whether these nerves serve a sensory function different from that of the nerves that originate from the ophthalmic nerve is not apparent from Ruskell's study. In addition, even though Beauvieux and Dupas (23) observed a ciliary ganglion root of maxillary nerve origin in some of their human preparations, the existence of sensory nerves originating from the maxillary nerve and innervating the eye has not been shown convincingly in humans.

Mandibular Nerve (V3)

The mandibular division, which does not enter the cavernous sinus, contains motor and sensory fibers (Fig. 25.8). The motor portion supplies muscles that derive from the first pharyngeal (branchial) arch of the embryo (1).

The mandibular nerve is formed by a large sensory root from the gasserian ganglion that passes inferiorly together with the motor root of the trigeminal nerve. These two roots lie close together in the middle cranial fossa and pass through the foramen ovale to the infratemporal fossa, where they form a single trunk (Fig. 25.9).The foramen ovale sits in the posteromedial aspect of the greater wing of the sphenoid bone (18) (Fig. 25.6). The undivided trunk lies 3.75 cm medial to the tubercle at the root of the zygoma. This portion

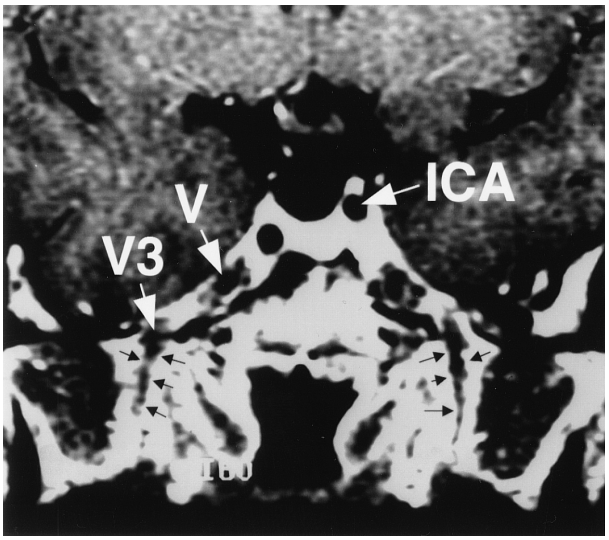


Figure 25.9. Contrast-enhanced T1-weighted magnetic resonance image (MRI), coronal view posterior to that of Figure 25.3*B* (behind the cavernous sinus), demonstrating the gasserian ganglion (V) and the mandibular division (V3) heading caudally through the foramen ovale into the infratemporal fossa, at which point the nerve is highlighted by *white arrows.* ICA, internal carotid artery.

of the nerve gives off: (*a*) a recurrent neural plexus that accompanies the middle meningeal artery through the foramen spinosum (Fig. 25.6) to supply the dura mater on the temporal side of the cranium (24); (*b*) the nerve to the medial pterygoid, which passes through or around the otic ganglion to the tensor tympani and tensor veli palatini muscles (1). The trunk then divides into anterior, principally motor, and posterior, principally sensory, divisions.

The anterior division, containing most of the motor part of the trigeminal nerve, supplies the muscles of mastication. It passes downward and forward, medial to the lateral pterygoid muscle, and separates into the following motor branches: (*a*) a branch to the lateral pterygoid muscle; (*b*) a branch to the masseter muscle that passes over the superior border of the lateral pterygoid muscle and through the mandibular notch of the mandible and gives a filament to the temporomandibular joint; (*c*) two deep temporal branches, anterior and posterior, to the temporal muscle, that also ascend above the lateral pterygoid muscle; and (*d*) the buccinator nerve, which passes obliquely forward between the two heads of the lateral pterygoid muscle to reach the masseter (buccinator) muscle.

Injury to the motor part of the trigeminal nerve results in ipsilateral deviation of the jaw upon protrusion because of paralysis of the ipsilateral lateral pterygoid; upon retraction, the jaw deviates contralaterally as a result of paralysis of the temporalis (discussion following) (1). The sensory portion of the anterior division, the buccal nerve, supplies the skin and mucous membranes of the cheek as well as part of the gums.

The posterior division of the nerve has three major subdivisions, each with mixed functions (1):

1. The auriculotemporal nerve and its branches supply the upper part of the lateral surface of the ear, the upper part of the meatus, the tympanic membrane, the parotid gland, and the skin of the side of the head. Autonomic fibers within the auriculotemporal nerve include secretomotor postganglionic parasympathetic fibers from the otic ganglion destined for the parotid gland and also postganglionic sympathetic fibers from the plexus on the middle meningeal artery. The auriculotemporal nerve lies in close proximity to the temporomandibular joint capsular region, lateral pterygoid muscle, and middle meningeal artery (25,26).
2. The lingual nerve supplies sensation to the the gums and anterior portion of the tongue. The lingual nerve is joined by the chordi tympani of the facial nerve, which contains taste fibers for the anterior two-thirds of the tongue and preganglionic parasympathetic fibers destined for the submandibular ganglion. Postganglionic parasympathetic fibers leave the ganglion and return to the lingual nerve before reaching the salivary glands.
3. The inferior alveolar nerve itself has three branches: the mylohyoid nerve, the motor branch, innervates the mylohyoid muscle and the anterior belly of the digastric muscle; the inferior dental plexus supplies the gums and the teeth of the mandible; and the mental nerve supplies the skin of the chin and the skin and mucous membrane of the lower lip and gums (Figs. 25.1 and 25.2).

Jaw proprioception is mediated by stretch receptors in jaw muscles and mechanoreceptors in the periodontal membrane (27). Afferent axons from these receptors travel primarily within the mandibular nerve, and their cell bodies are located in the mesencephalic nucleus of the trigeminal nerve (discussion following). Collateral branches from the mesencephalic nucleus connect directly to the trigeminal motor nucleus, thereby providing a monosynaptic pathway for the jaw-jerk (masseter) reflex. Interested readers are referred to the electrophysiologic investigations of the trigeminal motor system in humans by Cruccu and colleagues (28,29) and by Türk et al. (30).

GASSERIAN (TRIGEMINAL, SEMILUNAR) GANGLION

The crescent-shaped gasserian ganglion lies on the anterior superior surface of the petrous bone in the middle fossa of the skull (Fig. 25.9). It is an expansion of the proximal sensory root from the brainstem and lies within Meckel's cave, surrounded by arachnoid and dura (31). Meckel's cave is bounded by dura laterally, the ascending precavernous portion of the internal carotid artery medially, and the cavernous sinus anteriorly. Meckel's cave often can be identified on computed tomographic (CT) scanning or magnetic resonance (MR) imaging (32–37).

The fine structure of the gasserian ganglion is essentially similar to that of the spinal root ganglia, although it is significantly larger (38–40). It contains the cells that give rise to the three divisions of the trigeminal nerve. The site of formation of the ophthalmic nerve is widely separated from that of the maxillary and mandibular nerves, which run more closely together.

The gasserian ganglion contains the cells of origin of all the trigeminal sensory axons. These are unipolar cells, whose axons bifurcate into an anterior branch, which proceeds distally in one of the three nerve divisions, and the posterior branch, which extends into the pons. The motor root does not enter the ganglion.

The gasserian ganglion and the proximal portions of the ophthalmic and maxillary divisions receive most of their blood supply from branches of the inferolateral trunk, which itself derives from the intracavernous carotid artery (41,42). Within the cavernous sinus, the distal ophthalmic nerve is supplied by the artery to the superior orbital fissure, whereas the distal maxillary nerve is supplied by the artery to the foramen rotundum. Both of these arteries are distal branches of the inferolateral trunk. The medial third of the gasserian ganglion can also receive blood from the tentorial artery of the meningohypophyseal trunk (also from the intracavernous carotid), while the lateral third can also be fed by the middle meningeal artery.

TRIGEMINAL ROOT

The sensory and motor divisions of the trigeminal nerve exist as separate ''roots'' from the pons. The exit of the motor root lies immediately cephalad to the point of entrance of the sensory root.

Microvascular relationships of the trigeminal roots have

been described by numerous investigators (2,43–45). Hardy and Rhoton (2) and Hardy et al. (44) reported that approximately half of cadaveric trigeminal roots had some contact with an artery, usually the superior cerebellar artery. Haines et al. (43) found contact between the trigeminal root and the superior cerebellar artery in 35% of 40 autopsy specimens. Klun and Prestor (45) discovered contact with the trigeminal root in 32% of specimens, but actual compression in only another 8% either by the superior cerebellar artery (most commonly), the anterior inferior cerebellar artery, a pontine branch of the basilar artery, or in one instance, a vein. Compression of the trigeminal nerve root by surrounding arterial and venous structures is one cause of trigeminal neuralgia (46–51) (see Chapter 26).

The trigeminal roots are supplied by a group of vessels called the trigeminal arteries, which orginate from the superior cerebellar artery, the posterolateral, superolateral, and inferolateral pontine arteries, the anterior inferior cerebellar artery, the basilar artery trunk, and the trigeminocerebellar artery (52). The superolateral pontine artery, which is a small branch of the basilar artery, and the anterior inferior cerebellar arteries are the most common parent vessels.

Sensory Root

The fibers of the sensory root run parallel and become arranged in separate bundles by the enveloping supporting tissues (31).

In their study of 50 human trigeminal nerves, Gudmundsson et al. (53) found that the length of the sensory root from the pons to the gasserian ganglion varied from 18–26 mm, with the average being 22 mm. In half of the nerves studied, small bundles of sensory fibers arose from the pons outside the main sensory fiber bundle. These aberrant or accessory sensory fibers usually arose around the rostral two-thirds of the pons, and most entered the root within 12 mm of the pons. Of the total of 66 aberrant rootlets observed by Gudmundsson et al. (53), 49 passed into the ophthalmic nerve, 10 into the maxillary nerve, and 7 into the mandibular nerve.

Kerr (39) studied the somatotopic organization of the nonhuman primate sensory root. Ophthalmic division fibers were ventrally placed within the sensory root; mandibular division fibers were dorsally placed; and maxillary fibers occupied the intermediate zone. Mira et al. (54) found a similar disposition of fibers in human sensory roots, whereas Gudmundsson et al. (53) and Stechison et al. (55) found that fibers from the ophthalmic division are usually **rostromedial** and the mandibular fibers are usually **caudolateral**. Pelletier et al. (56) confirmed a somatotopic arrangement of the three divisions within the sensory root. However, these investigators found that sensory modalities were diffusely represented within each division, and they offered this as an explanation why large sections (even 50% or more) of sensory root divisions may be performed without appreciable sensory loss.

The vast majority of corneal afferents travel within the ophthalmic division of the trigeminal sensory root. A small minority course within the maxillary division (20).

Stibbe (57,58) and Mira et al. (54) found nerve cells in the human sensory root of both humans and dogs. The nerve cells appear to be localized to the proximal portion of the sensory root in humans. The presence of these nerve cells far from the gasserian ganglion may indicate an accessory relay station for trigeminal sensory fibers. In fact, it has been suggested that some light touch sensation is carried by this group of fibers (59,60). Supporting this concept is the work of Hussein et al. (61), who treated 25 trigeminal neuralgia patients with fractional section of the trigeminal nerve via a posterior fossa approach. The procedure was effective in relieving pain, while preserving corneal sensation and motor root function. Of the patients who were treated, 19 showed slight loss of light touch sensation. In 15 of these patients, there was dissociation of sensory loss between pinprick (pain) and light touch. The pattern of dissociated sensory loss produced in these patients suggests that fibers carrying light touch sensation tend to collect in the medial part of the main sensory root as it enters the pons.

Motor Root

The motor root emerges from the pons as separate bundles at two major levels, the fibers from the dorsal level originating from the mesencephalic nucleus. Gudmundsson et al. (53) found the human motor root to be composed of as many as 14 separately originating rootlets that usually join about 1 cm from the pons. In addition, Gudmundsson et al. (53) demonstrated anastomoses between the motor and sensory roots in the majority of nerves that they examined. These anastomoses may explain the discovery by Mira et al. (54) of nerve cells in the human motor nerve root similar to cells observed in the sensory root (57,58). The function of these cells is unknown, but they may serve some type of sensory function.

The motor root accompanies the sensory root from the lateral pons through the subarachnoid space, through the dura, and into Meckel's cave, where it is concealed by the overlying gasserian ganglion. As it passes the median surface of the ganglion, it is joined by the peripheral sensory fibers that arise from sensory cells in the maxillary region of the ganglion.

AFFERENT TRIGEMINAL FIBERS IN THE BRAINSTEM

The afferent sensory trigeminal fibers arising from their cell bodies in the gasserian ganglion enter the lateral pons and course in a dorsomedial direction. Some of them dichotomize into a short ascending and a long descending branch. Most fibers run caudally without bifurcating. The mass of descending fibers constitutes the **trigeminal spinal tract**, a distinct fiber bundle that is situated just underneath the lateral surface of the medulla oblongata, and slightly deeper in the lower part of the pons, where it is covered by fibers of the middle cerebellar peduncle. The fibers of this tract continue into the two most rostral segments of the spinal cord in the zona terminalis (Figs. 25.10 and 25.11). The fibers that are found in the spinal tract, as well as numerous collaterals, end in a longitudinal cell column medial to the tract, the **nucleus of the trigeminal spinal tract**. Early in-

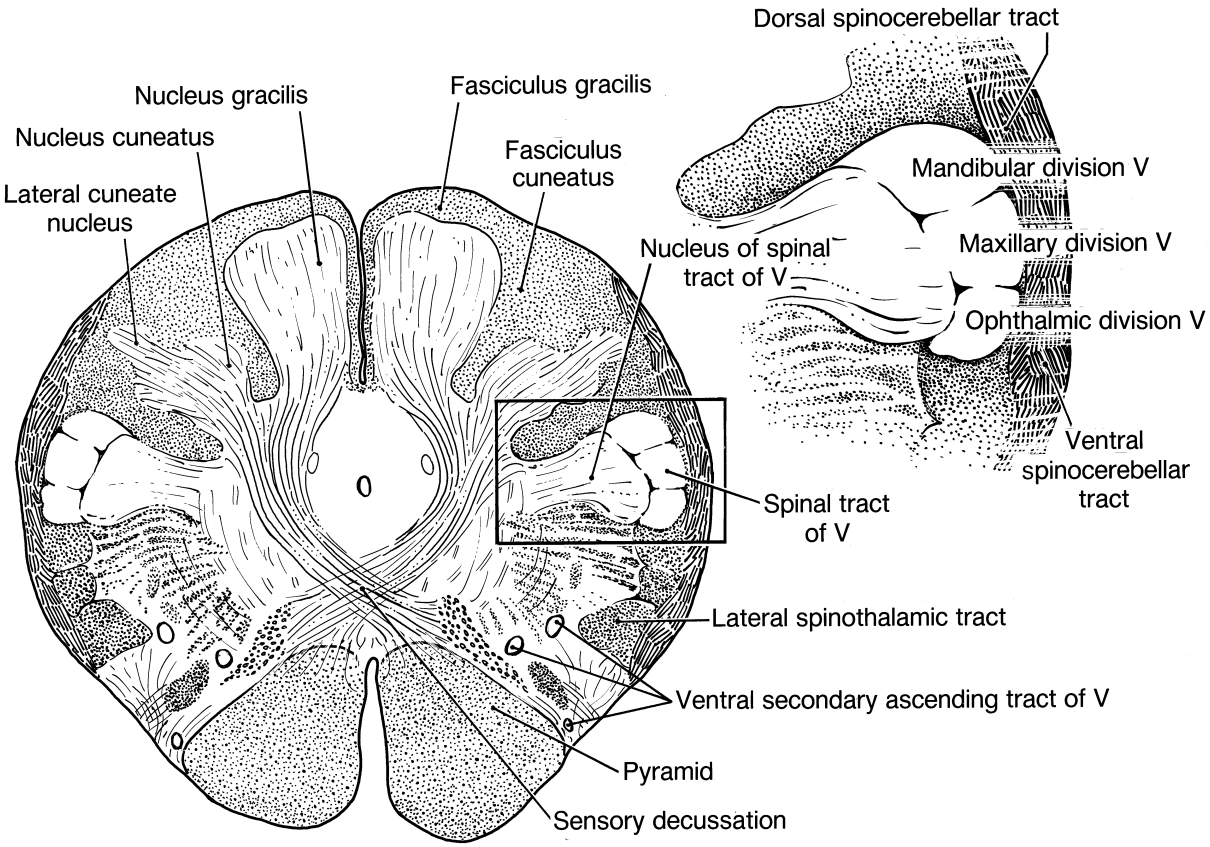


Figure 25.10. Cross section of medulla 6 mm below the obex. The *box* surrounds fibers traveling in the descending tract of the trigeminal nerve. The *inset* shows the relative positions of the fibers from the ophthalmic, maxillary, and mandibular divisions within the descending tract of the trigeminal nerve. The ophthalmic fibers carry impulses for pain (including the cornea) and temperature sensations to the spinal nucleus of the trigeminal nerve. (Redrawn from Taren JA, Kahn EA. Anatomic pathways related to pain in the face and neck. J Neurosurg 1962;19:116–121.)

vestigations on the trigeminal spinal tract and its nucleus indicated that a divisional lamination exists. The ophthalmic component is situated most ventrally in the tract. Kerr (39) studied this lamination and by the Nauta technique was able to show a very discrete segregation of the ventral ophthalmic portion from the more dorsal maxillary and mandibular portions. He showed that the afferent fibers of all divisions proceed in diminishing numbers caudally to C_2. Similar laminations of the ophthalmic and other divisions of the trigeminal nerve are present in the spinal nucleus and in the main sensory nucleus.

The fibers of the trigeminal spinal tract distribute to the nucleus of the spinal tract in an orderly manner (62). The medullary tractotomy of Sjöqvist (63) for the treatment of trigeminal neuralgia is based on this pattern of distribution of fibers. The procedure consists of transecting the trigeminal spinal tract by a superficial incision in the lowest part of the medulla, thus preventing the impulses in the descending fibers of the tract from reaching the nucleus. The procedure abolishes pain sensibility in the ipsilateral half of the face but has little effect on the sense of touch. Further experience (64) has shown that the incision may be made more caudally. Thus, only the most caudal part of the spinal nucleus may be involved in the transmission of pain perception (discussion following). The corneal reflex may be completely spared after the Sjöqvist operation.

Although the majority of primary trigeminal afferent fibers project to the trigeminal nuclear complex through the trigeminal spinal tract, those fibers that enter the pons within the motor root, composed of axons with terminals in the oral cavity and the muscles of mastication, bypass the motor nucleus of the trigeminal nerve to collect into a bundle that continues forward along the ventrolateral, and then the lateral, border of the periventricular gray matter to the rostral end of the midbrain. The cells of origin of this group of fibers, the nucleus of the mesencephalic root, are scattered throughout the rostral pontine and mesencephalic tegmentum.

NUCLEI OF THE TRIGEMINAL NERVE

The nuclei of the trigeminal nerve may be considered as three separate units: (*a*) the motor nucleus (special visceral efferent); (*b*) the sensory mesencephalic nucleus (general somatic afferent); and (*c*) the sensory nuclear complex, actu-

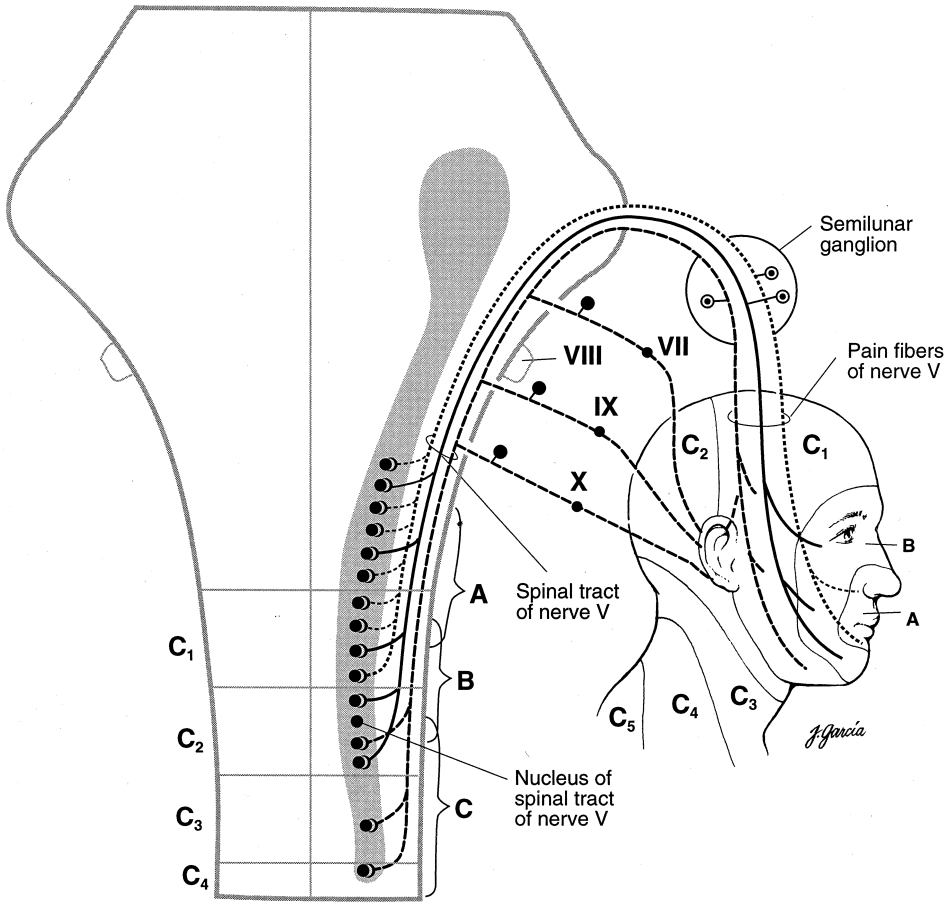


Figure 25.11. Distribution of pain fibers carried via cranial nerves to the nucleus of the trigeminal spinal tract. Also note the ''onionskin'' distribution of pain fibers on the face (A, B, and C) associated with their rostral to caudal representation in the nucleus of the spinal tract of nerve V. (From Crosby EC, Humphrey T, Lauer EW. Correlative Anatomy of the Nervous System. New York: Macmillan, 1962.)

ally composed of two distinct nuclei—the main sensory nucleus and the nucleus of the spinal tract (general somatic afferent) (65) (Figs. 25.12 and 25.13).

Motor Nucleus

The motor nucleus is situated slightly farther from the ventricular floor than are the nuclei of the oculomotor, trochlear, and abducens nerves. It lies medial to the main sensory nucleus. Fibers from the mesencephalic root are closely associated with fibers from the motor nucleus, and both motor and mesencephalic fibers pass forward in the mandibular section of the nerve (Fig. 25.12*A*).

Mesencephalic Nucleus

Most, if not all, neurons in the trigeminal mesencephalic complex are unipolar, primary afferent cells comparable to sensory ganglion cells (66). Unlike sensory ganglion cells, however, the cell bodies of these neurons have remained within the central nervous system. These are the only primary sensory neuron cell bodies in the central nervous system that derive from the neural crest (27). They form a column at the edge of the central gray matter that extends from the posterior commissure rostrally to the level of the trigeminal motor nucleus caudally (Fig. 25.12). Most of these neurons are **proprioceptive** in function (67,68), with receptor terminals responding to stretch in the muscles of mastication. Other mesencephalic neurons innervate the dental supporting tissues (67–69).

Trigeminal Sensory Nuclear Complex

Main Sensory Nucleus

The main sensory nucleus forms the most rostral portion of the trigeminal nuclear complex (excluding the separate mesencephalic nucleus) and is situated lateral to the motor nucleus (70) (Figs. 25.12 and 25.13). Because the sense of touch is mediated by fibers that are somewhat thicker than those mediating pain, and the fibers that end in the main sensory nucleus are, in general, thicker than those to the spinal nucleus, it has generally been proposed that the main sensory nucleus provides the brainstem relay for **tactile** sen-

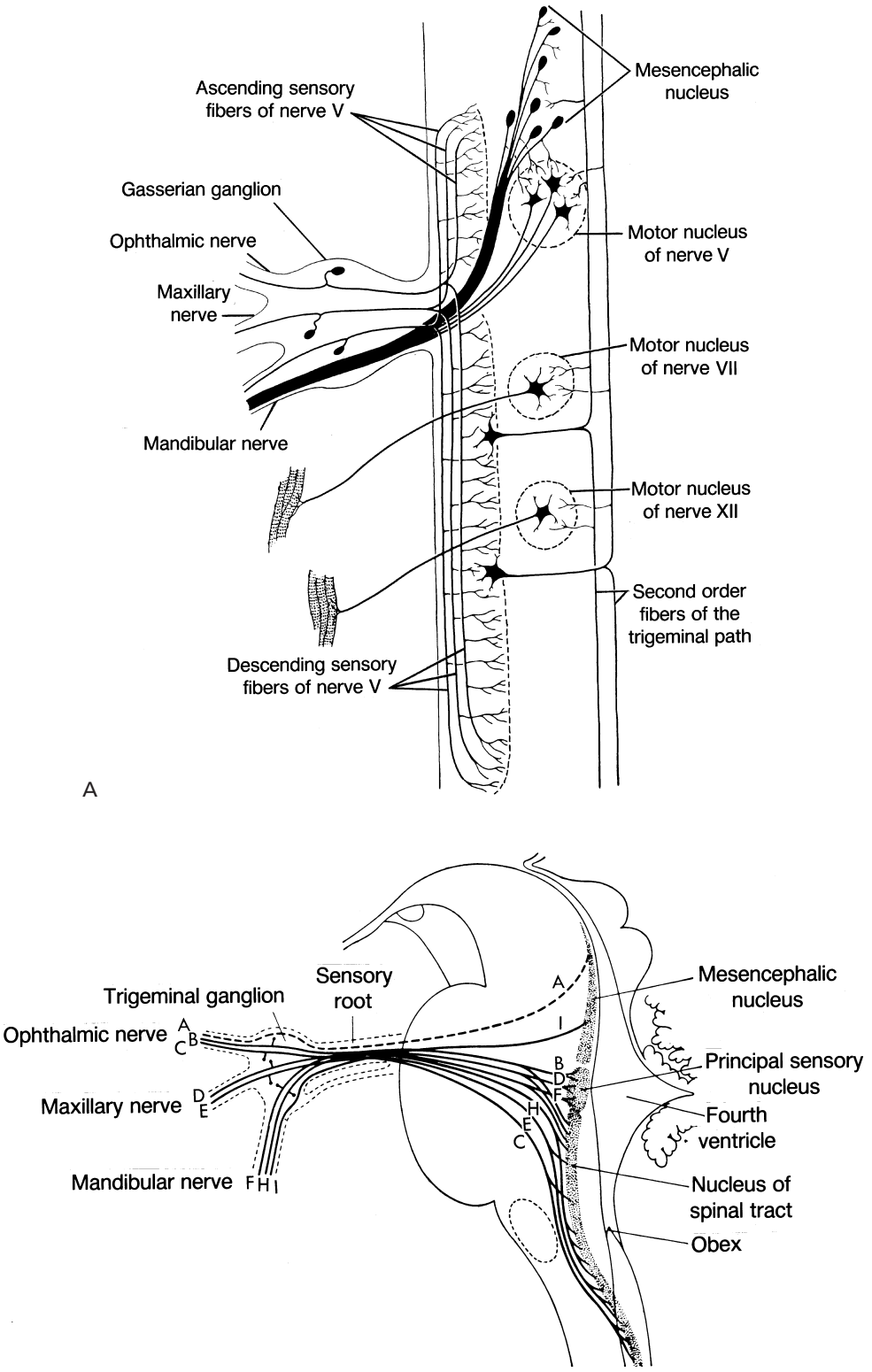


Figure 25.12. *A,* Diagram of nuclei and central connections of the trigeminal nerve. *B,* Nuclei receiving the primary afferent fibers of the trigeminal nerve. A, proprioceptive fibers from the extraocular muscles; B, tactile and pressure fibers from the ophthalmic area; C, pain and temperature fibers from the ophthalmic area; D, tactile and pressure fibers from the maxillary area; E, pain and temperature fibers from the maxillary area; F, tactile and pressure fibers from the mandibular area; H, pain and temperature fibers from the mandibular area; I, proprioceptive fibers from the muscles of mastication. (From Williams PL, Warwick R. Gray's Anatomy. Ed 35. Philadelphia: WB Saunders, 1975.)

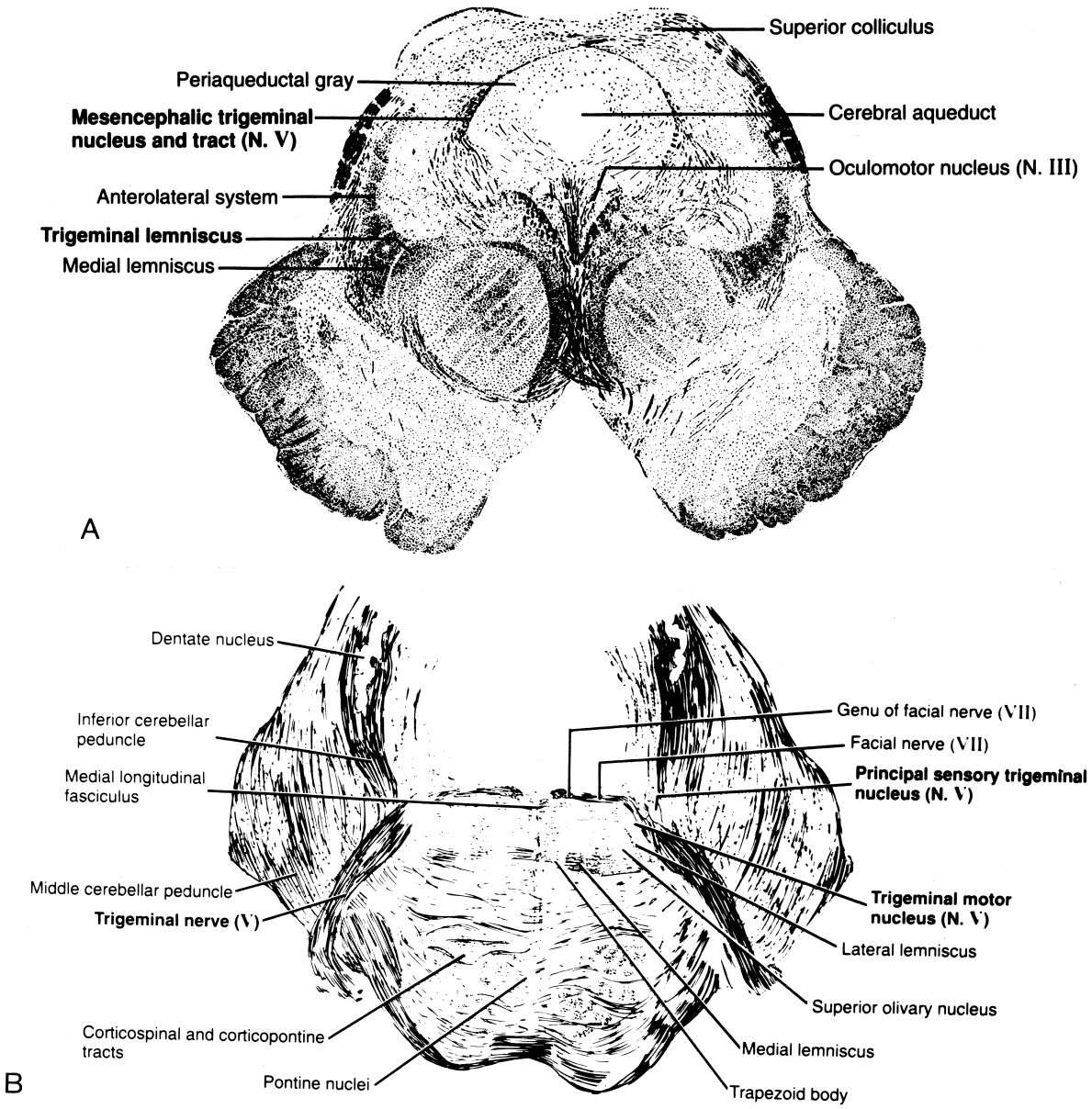


Figure 25.13. Cross sections of the mesencephalon (*A*) and pons (*B*), highlighting the locations of trigeminal structures. Section through the medulla is illustrated in Figure 25.10.

sations from the head, although this is probably an oversimplification.

Most neurons within this nucleus project to the contralateral **nucleus ventralis posteromedialis** (VPM) of the thalamus. These fibers emerge from the ventromedial margin of the main sensory nucleus and pass to the contralateral brainstem to ascend in the trigeminal lemniscus (71) (Fig. 25.14). A smaller population of neurons in the dorsomedial portion of the nucleus, with an input from oral structures, project to the ipsilateral VPM (discussion following). Functionally and anatomically, the main sensory nucleus and its contralateral ascending projections are analogous to the cuneate and gracile nuclei in the medulla and their thalamic connections. The cuneate and gracile nuclei receive tactile information from dorsal horn sensory neurons and then send fibers that decussate and ascend within the medial lemniscus to reach the thalamus (27).

Nucleus of the Spinal Tract

The nucleus of the spinal tract is a long nucleus that extends down the spinal cord as far as the second cervical root and merges with the substantia gelatinosa (70) (Figs. 25.11 and 25.12). In mammals, this nucleus is divisible into three distinct portions: (*a*) the nucleus oralis; (*b*) the nucleus inter-

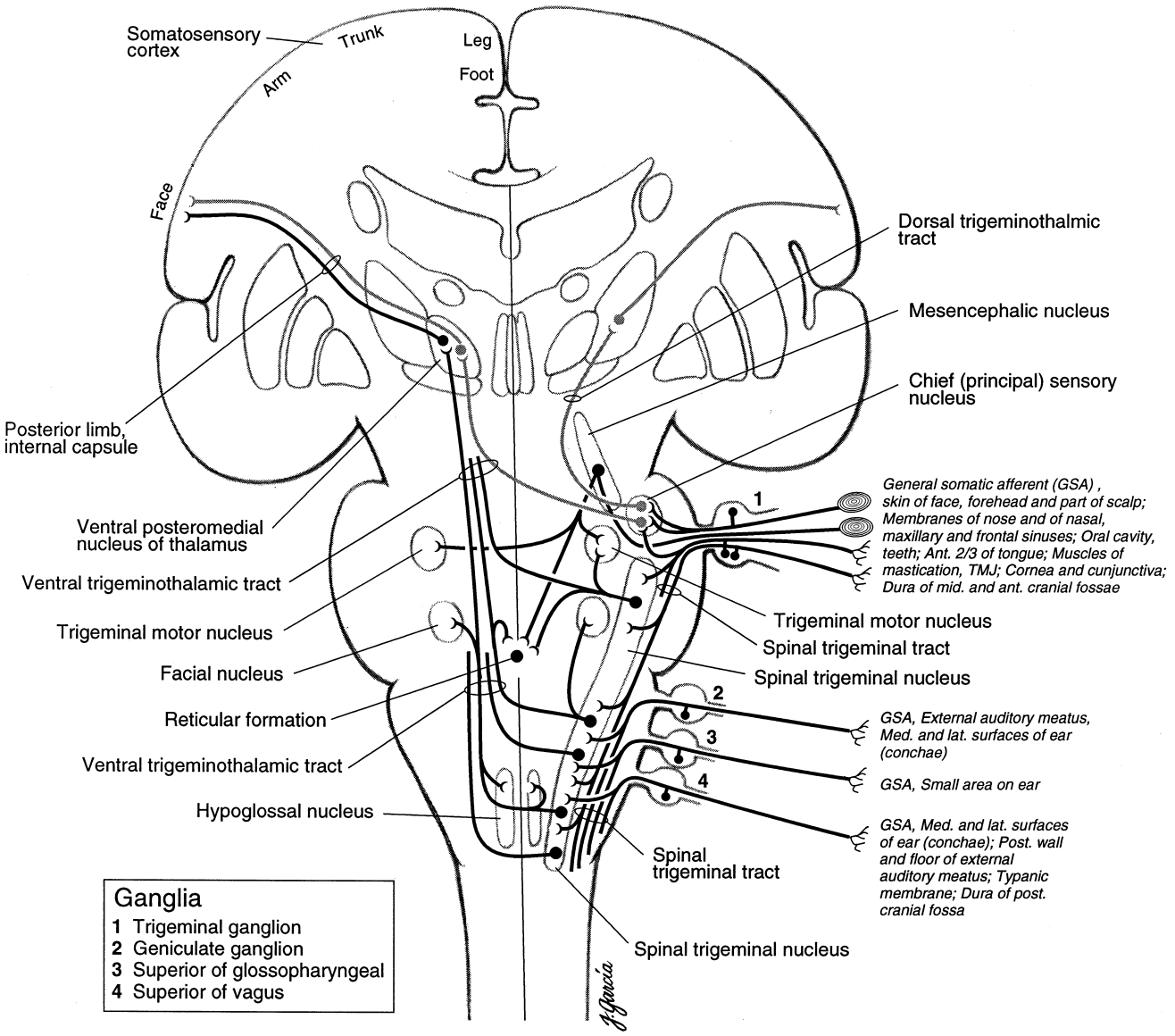


Figure 25.14. Summary of the central connections and ascending projections of the trigeminal system. (From Haines DE. Neuroanatomy. An Atlas of Structures, Sections, and Systems. Ed 4. Baltimore, Williams & Wilkins, 1995:170–171.)

coolers; and (*c*) the nucleus caudalis (65). Each of these nuclei receives input from all the trigeminal roots via the descending spinal trigeminal tract. The fibers from each of the three divisions of the nerve are somatotopically arranged in this tract, with those from the ophthalmic division located most ventrally and those from the mandibular located most dorsally. In humans the ophthalmic division extends farthest caudally. The nucleus of the spinal trigeminal tract is related primarily to the transmission of impulses that are perceived consciously as **pain** and **temperature**. Although the nucleus caudalis is still considered the main termination of trigeminal nociceptive fibers, there is accumulating evidence that the more rostral subnuclei also receive nociceptive information from orofacial structures (72). Readers interested in more details regarding the processing of nociceptive information in the trigeminal nuclei are referred to the in-depth reviews by Shults (73). Nucleus oralis and interpolaris have important roles in oral and dental sensation (74).

Nucleus (pars) Oralis

This nucleus extends from the rostral pole of the facial nucleus to the rostral third of the inferior olive in the mammal. The axons of most neurons in this nucleus join the contralateral medial lemniscus and project to the VPM (75).

Nucleus (pars) Interpolaris

This nucleus, which is continuous with the nucleus oralis, extends from the rostral third of the inferior olive to the

obex. The thalamic projection is entirely to the contralateral VPM (76). Interpolaris neurons can be classified functionally according to their responsiveness to cutaneous stimuli as low-threshold mechanoreceptive or cutaneous nociceptive (77).

Nucleus (pars) Caudalis

This nucleus extends from the obex to the first cervical root and is considered an upward extension of the spinal dorsal horn. The nucleus is organized into three main subnuclei (65) or four laminae (78): (*a*) subnucleus marginalis (or zonalis) (lamina I of Rexed); (*b*) subnucleus gelatinosus (laminae II and III of Rexed); and (*c*) subnuclei magnocellularis (lamina IV of Rexed). The laminar organization is similar to that found in the posterior horn of the spinal cord.

The primary afferent projection to nucleus caudalis includes both myelinated fibers (79) and unmyelinated fibers. Both groups of fibers penetrate the nucleus from the spinal tract in a spatially ordered radial pattern. The larger fibers terminate mainly within the deep zone of subnucleus gelatinosus (lamina III) (80,81) and within subnucleus magnocellularis. A few smaller fibers may be traced to subnucleus marginalis and into the subjacent reticular formation. It is believed that unmyelinated fibers terminate in the superficial zone of subnucleus gelatinosus (lamina II). More extensive description of these regions is found in reviews by Darian-Smith (66) and Bereiter et al. (82).

Afferent fibers from the perioral region synapse rostrally in nucleus caudalis, whereas those from peripheral areas of the face connect to more caudal parts of the nucleus. This creates a concentric, onionskin organization of the face for pain (Fig. 25.11).

Interconnections among the Trigeminal Spinal Nuclei and Subnuclei

Many neurons of the spinal trigeminal tract send their axons into an extensive longitudinal axon plexus consisting of interconnected small bundles of myelinated and unmyelinated axons (the deep bundles). These bundles run through the entire nucleus of the spinal tract and contain both ascending and descending axons. The axons of the bundles give off widely spaced, simple collaterals that effectively link different levels of the nucleus (83). The reader is referred to the detailed review by Ikeda et al. (84) of the various intra- and internuclear connections of the trigeminal brainstem structures.

Location of Corneal Afferents in the Trigeminal Nuclei

The somatotopic localization of the afferent fibers and neurons subserving the corneal reflex are of practical interest in neuro-ophthalmology. Marfurt and Del Toro (85) and Marfurt and Echtenkamp (86) demonstrated that corneal afferents project to multiple levels of the spinal nucleus. In monkeys, connections were mainly to caudal pars interpolaris and rostral pars caudalis, along with less dense projections to pars oralis, caudal pars caudalis, and the trigeminal main sensory nucleus. Sparse projections to C_1 and C_2 were also found. In the rat, fibers relaying nociceptive information from the cornea synapse in the ventrolateral caudal interpolaris and rostral caudalis (87).

Location of Dural and Blood Vessel Afferents in Trigeminal Nuclei

Stimulation experiments in cats demonstrate nociceptive afferents from the middle meningeal artery and sagittal sinus synapse primarily in the nucleus caudalis, with other connections to nucleus oralis and nucleus interpolaris (88,89). Nociceptive afferents from the dura overlying these areas project to the rostral two-thirds of the nucleus caudalis and caudal nucleus interpolaris (90,91). These neurons in turn project to cells in the VPM nucleus of the thalamus (92) (discussion following). These structures are thought to comprise the central anatomic substrate that subserves migraine headache pain (11,93).

SUPRANUCLEAR TRIGEMINAL CONNECTIONS AND PROJECTIONS

Pathways between the Trigeminal Nuclei and Other Brainstem Areas

These pathways, composed of short neurons in the tegmentum, connect the various trigeminal sensory nuclei with motor nuclei of the brainstem, including the ocular motor nuclei, the motor nuclei of the trigeminal nerve, the facial, glossopharyngeal, vagal, and hypoglossal nuclei, and the vestibular nuclei. Ascending components of this diffuse system conduct impulses slowly cephalad by multisynaptic pathways through the dorsal part of the hypothalamus to the ventromedial nuclei of the thalamus, from which they are diffusely distributed to many areas of the cerebral cortex. Cells within the trigeminal nuclei send collateral axons to the superior colliculus, cerebellar cortex, and deep nuclei (94,95).

Pathways from the Trigeminal Nuclei to the Thalamus

The ascending pathways from the main sensory nucleus and the nucleus of the spinal tract of the trigeminal nerve form an important secondary ascending system—the **ventral secondary ascending tract of the trigeminal nerve** (also termed the trigeminothalamic tract, or ventral trigeminal tract) (Fig. 25.14). The fascicles of this tract, transmitting impulses of pain and temperature and arising from all levels of the trigeminal nuclei, turn obliquely forward to cross the midline at a considerable distance in front of the cell bodies of the neurons from which they arise. After crossing, these bundles gradually accumulate in the lateral part of the brainstem so that by the time they reach the pons, they overlie and are intermingled dorsally with the other components of the medial lemniscus. Where the medial lemniscus shifts dorsally at the level of the midbrain, the ventral secondary ascending tract of the trigeminal nerve lies medial to it. The system terminates in the VPM nucleus of the thalamus.

An entirely separate projection system to higher centers passes from the main sensory nucleus of the trigeminal nerve. This is the **dorsal secondary ascending tract of the**

trigeminal nerve (trigeminal lemniscus, or dorsal trigeminal tract) that, after its origin from the main sensory nucleus, swings into the mid-dorsal tegmental region of the pons. Most fibers decussate, but dorsomedial axons remain ipsilateral (Fig. 25.14). In its course, the dorsal secondary ascending tract of the trigeminal nerve lies dorsal to the red nucleus and medial to the medial lemniscus at upper midbrain levels. The partial decussation makes it impossible to lose finer tactile sensibility on one side of the face unless there is damage to the trigeminal peripheral roots or the trigeminal nucleus (in the pons) is damaged. Section of one tract does not eliminate tactile sensibility from either side of the face, whereas bilateral section of the tract produces loss of discriminatory tactile sensibility on both sides of the face. In addition, lesions in the region of the Sylvian aqueduct may also produce bilateral loss of facial tactile sensibility, but only when both tracts are damaged. The dorsal secondary ascending tract of the trigeminal nerve also projects to the VPM nucleus of the thalamus.

Incoming pain stimuli from the face are relayed to the thalamus via the ventral secondary ascending tract of the trigeminal nerve (Fig. 25.14). The caudal portion of this tract and its nucleus extend at least to the level of the second cervical segment. Pain impulses from the neck enter the cord at C1 and C2. Second-order neurons that are in the same area as the spinal nucleus of the trigeminal nerve relay the pain impulses to the thalamus via the lateral spinothalamic tract. Clinically, the sensation of pain in the face may be associated with pain in the neck. Cervical disease may produce face pain, and stimulation of the trigeminal nerve in the face may produce occipital pain. Taren and Kahn (96) concluded from studies of patients with medullary tractotomies that pain stimuli to the face (or cervical region) have two possible anatomic pathways to the thalamus: the lateral spinothalamic tract and the ventral secondary ascending tract of the trigeminal nerve, each ending in definite portions of the posterior ventral thalamus. They also proposed that pain stimuli from either the face or cervical region could ''cross-synapse'' into either ascending cervicothalamic pathway. Kerr (97) in a discussion of the paper by Taren and Kahn (96) noted that these investigators had been able to follow the overlapping zones of the descending trigeminal pathways and the root fibers of C_1, C_2, and C_3 to cervical levels as low as C_6. He found that in identical levels of the dorsal horn in the first and second cervical segments, afferent descending fibers seemed to terminate on the same nuclear groups. To clarify this problem, he carried out a microelectrode study of the area and found that some neurons receive convergent fibers from the trigeminal and cervical systems. Thus, the same neuron could be triggered by stimuli delivered to the peripheral branches of the trigeminal and cervical roots. Kerr (97) estimated that 25–30% of the neurons in this area responded to stimuli from either peripheral sensory region and stated: ''Stimulation of the dorsal root of the first dorsal cervical segment produces referred pain to the back of the eye, the forehead, and, occasionally, to the vertex; rarely is pain evoked in the back of the head.''

Corticofugal Fibers to the Trigeminal Nuclei

Corticofugal fibers project downward to the main sensory nucleus of the trigeminal nerve and to the subdivisions of the nucleus of the spinal tract of the trigeminal nerve. These fibers arise from widespread areas of the cerebral cortex, including frontal, temporal, parietal, and occipital regions. The fibers are both ipsilateral and contralateral, with the crossed bundles predominating. They are likely functionally related to the inhibition of the sensory impulses projected on the primary nuclei.

The motor nucleus of the trigeminal nerve receives fibers from the corticobulbar tracts of each side, although the majority of the fibers reaching the nucleus are crossed.

Thalamus and Thalamocortical Projections

The sensory system of the face and eye projects from the brainstem to the thalamus (Fig. 25.14). The thalamocortical sensory system mediates somesthetic sensation from the periphery through the thalamus to the primary sensory area of the cerebral cortex.

Thalamus

Lying deep between the brainstem and the cortex is the large sensory nucleus, the thalamus. Through this midline cellular mass pass all sensory tracts except that for olfaction, and within it are the relays for all sensory information from the external environment—the head and body relays that modify incoming information and pass it on to the cerebral hemispheres for processing.

The thalamus is a large, ovoid ganglionic mass situated obliquely between the midbrain and hypothalamus below and the corpus striatum above. It is roofed completely by the cerebral hemispheres. It lies along the lateral wall of the third ventricle, which forms its main medial relation. Its anterior extremity bulges into the floor of the lateral ventricle. Its lateral surface is related to the internal capsule that separates it from the lentiform nucleus. Anteriorly, the two thalami are close together. The posterior extremity of each is enlarged and prominent, forming the pulvinar that overhangs the medial and lateral geniculate bodies, also part of the thalamic complex.

The internal structure of the thalamus is composed of an intricate conglomeration of nuclei that act as discrete and separable cellular masses associated with the various thalamic projecting systems. The subdivisions of the various parts of the thalamus have been the object of many investigations. The important work of Walker (98) is the basis for most classifications of this structure; however, certain modifications of this classification have been made since Walker's original description (99,100).

The **nucleus ventralis posterior** (posterior ventral thalamic nucleus) is the largest cell mass in the ventral nuclear group. It occupies the caudal half of the diencephalon. It lies ventral and ventrolateral to the dorsomedial nucleus and the internal medullary lamina, ventral and ventromedial to the lateral nuclear group, dorsal to the zona incerta, and internal to the external medullary lamina and the scattered cells of

the reticular nucleus. Lateral to the reticular nucleus lies the posterior limb of the internal capsule. The nucleus ventralis posterior is usually subdivided into a larger lateral and a smaller medial group.

The posterior ventral thalamic nucleus is the site of termination of many of the major ascending sensory systems, including those discussed in this chapter. The lateral part of the posterior ventral nucleus receives the terminal fibers of the gracile and cuneate components of the medial lemniscus. These components of the medial lemniscus carry impulses produced by tactile and proprioceptive stimuli from the body.

From uppermost cord and lower brainstem levels, impulses evoked by painful, thermal, and tactile stimulation of the face are projected contralaterally via the ventral secondary ascending tract of the trigeminal nerve to the nucleus ventralis posteromedialis (posteromedial ventral thalamic nucleus; arcuate nucleus; VPM) (Fig. 25.14). Refined tactile, and perhaps proprioceptive, impulses from the face are probably relayed bilaterally to this nucleus.

The **nucleus ventralis posterolateralis** (posterolateral ventral thalamic nucleus; VPL) is the region of termination not only of the ventral spinothalamic tract but also of the lateral spinothalamic tract. In addition to mediating impulses that are interpreted as pain, some fibers in the lateral spinothalamic tract carry impulses interpreted as itching.

The posterior ventral thalamic nucleus has a well-defined somatotopic organization. The ascending systems from the lower extremity terminate in the most dorsolateral part of the complex; those from the upper extremity end in an intermediate position; and those from the face, ear, and mouth (including taste) distribute most ventromedially in the nucleus.

Cells within the VPM nucleus are likely organized somatotopically into rods (101,102). In turn, the rods project in an organized fashion to columns in the sensory cortex. Sensory information from the rest of the body is probably processed in a similar manner.

Thalamocortical Connections

The outgoing impulses from the posterior ventral nucleus discharge particularly to the cerebral cortex, although this nucleus has other connections, such as those with the basal ganglia. The projection to the cerebral cortex leads to the paracentral and postcentral gyri. Their fibers fan out in broad sweeps into the posterior limb of the internal capsule. From the dorsolateral portion of the nucleus comes the dorsocaudal part of the thalamocortical (or sensory) radiations. Those from the intermediate parts of the nucleus are intermediate in the bundle. Fibers from the most medial part of the nucleus are in the ventrorostral segment of the sensory radiations, as the latter intersects with the internal capsule. As the upper limits of the internal capsule are reached, the bundle fans out with the most ventrorostral fascicles being distributed to the lower part of the postcentral gyrus and the other bundles systematically distributed above them. The face and forehead are represented among the intermediate bundles of the thalamocortical projection.

Corticothalamic Projections

In addition to the connections already discussed, there are also corticofugal connections from the postcentral gyrus to the posterior ventral nucleus of the thalamus. Apparently these also end in accordance with a somatotopic pattern, with those projecting to the medial part of the nucleus having originated from the ''face'' area of the postcentral cortex.

Primary Somatic Sensory Cortex

A broad band in the anterior part of the parietal cortex forms the area of the primary sensory cortex that represents the cortical end station of the main somatic afferent system. Anteriorly, it reaches into the depths of the central sulcus and extends posteriorly to occupy the entire postcentral gyrus to the postcentral sulcus. On the medial surface, it continues into the paracentral lobule.

Stimulation of primary somatic sensory cortex in animals and humans, as well as data from intraoperative somatory sensory-evoked potential studies (103), reveal that the surface of the opposite side of the body is topographically represented in an orderly sequence. As elsewhere in the sensory system, the arrangement is in the order of spinal innervation, representing the metametric order of the dermatomes (''sensory homunculus''). The face, the occiput, and the upper arm are represented in an intermediate superior segment of the posterior central gyrus. The mouth, tongue, and pharynx are represented most inferiorly in the gyrus near the Sylvian fissure. The degree and extent of the cortical representation of a particular region depend on the richness of the peripheral neural innervation. Thus, the representation of the forefinger and thumb are huge compared with that of the trunk. With regard to structures in the trigeminal sensory system, the lips and other oral structures have the largest representation in primary somatic sensory cortex.

In the monkey, the region of the somatic sensory cortex subserving the eye is located between the areas for the forelimb or the forehead and nose (104). By testing the reactions of human subjects during surgery, Penfield and Rasmussen (105) found that ocular sensation in humans is usually elicited by stimulation of the corresponding area in the precentral gyrus. Just as the motor eye field is displaced anterior to the main motor strip, so is the sensory representation of the eyes. Penfield and Rasmussen (105) found that ocular sensation could be elicited by stimulation of the postcentral gyrus in only one of their eight patients. Stimulation of the sensory field of the eye produced curious sensations described as a ''twisting feeling'' or ''tingling'' usually felt in the contralateral eye but sometimes in both eyes.

EXTRAOCULAR MUSCLE AFFERENTS

The trigeminal pathways of the extraocular muscle afferents are becoming more clearly delineated and it is evident that proprioceptive information is important at least in eye movement control and perhaps also in other visual functions. The central nervous system has three possible ways of checking eye movement accuracy: visual feedback, corollary dis-

charge (an internal efference copy of the motor command [106]), and eye muscle proprioception (107,108). The reader is referred to Steinbach's review (107), in which he summarizes the possible role of eye muscle proprioception in (*a*) maintence of stability in conjugacy and fixation; (*b*) specification of visual direction; (*c*) development of some aspects of normal visual function; and (*d*) depth perception, vergence, and other binocular functions. In the final analysis, it is most likely that the muscle afferents in human extraocular muscles provide no conscious perception of eye position but are certainly involved in subconscious control and monitoring of muscular contractions (109,110).

PRINCIPLES AND TECHNIQUES OF THE EXAMINATION OF THE TRIGEMINAL NERVE SYSTEM

Because the trigeminal nerve is mainly a sensory afferent, sensory testing remains the mainstay of the clinical examination. However, a thorough understanding of the efferent motor pathways and trigeminal reflexes allows the examiner to evaluate the various functions of the trigeminal system more effectively, leading to more accurate neuroanatomic localization. In addition, trigeminal nerve function should be examined within the context of its three divisions.

TESTS OF CUTANEOUS SENSATION

The sense of touch may be easily tested with a small wisp of cotton or the edge of a tissue. One may also use a light brush of the fingertips against the skin of the face. If reliability is in doubt, the patient should be asked to close the eyes and then indicate each touch. Although the most sensitive test is to compare the sense of light touch on one side with the other, this method frequently leads to spurious information. The nasal mucosa is highly sensitive to the lightest touch, and the comparison of the ''nasal tickle'' response may also be useful. Because the gingiva is also innervated by the trigeminal nerve, testing inside the mouth may produce useful information. In particular, patients with nonorganic sensory loss often do not note sensory changes inside the mouth. One may use the sharp end of a broken tongue blade to check gingival sensation, again comparing one side with the other. It is imperative to check all three branches of the trigeminal nerve bilaterally, as they may be differentially affected, depending on the location of the lesion.

Pain sensation is estimated by response to pinpricks. If an area of decreased response or subjectively blunted sensation is found, it can be outlined by proceeding from the region of blunted sensation outward, noting the borders of normal sensation. As is observed in plotting relative defects in the visual field, there is often a graduated cutaneous sensory loss with margins that vary with the degree of stimulation. Consequently, heavier pinpricks are likely to show a smaller field of sensory loss than are light pinpricks. When an area of suspected decreased sensation is found, it should be compared directly with the equivalent area of skin on the other side of the body. The use of the Wartenberg wheel, a pinwheel that applies a constant stimulus by rolling over the skin, can no longer be recommended because of universal precautions that need to be followed to avoid the transmission of blood-borne illness, such as hepatitis C or the acquired immune deficiency syndrome (AIDS). Many clinicians employ a single-use straight pin or safety pin to test pain sensation, but there are disposable plastic-tipped sharp devices designed specifically for this task.

Sensations of heat and cold may be tested with glass tubes containing comfortably hot and cold water. With the patient's eyes closed, the skin is lightly touched by tubes alternately while the patient indicates if the sensation is hot or cold. Another convenient method is to use the coolness of a metal examination tool, such as a tuning fork or ophthalmoscope handle, to compare the sense of cold between the right and left sides.

Vibratory testing is frequently used to detect nonorganic sensory findings. Because vibration sense is carried by bone, there should be very little difference between a stimulus applied to the left of midline and the same stimulus applied to the right of midline, especially over the frontal area. When patients report inability to feel vibration on one side of the forehead, it usually implies a nonorganic component to the exam.

TESTS OF CORNEAL SENSATION

Assessment of response to corneal pain stimulation is made by both subjective report and objective observation. The patient's report of differences in sensation after equal stimulation of the two corneas may indicate unilateral reduction in ophthalmic division sensory function; however, only the alert, relatively intelligent, and comfortable patient can contribute this information reliably. More often, the examiner must rely upon objective signs, such as involuntary blink reflex and head withdrawal. These are of particular value in examination of the obtunded or semicomatose individual. Both depth of coma and difference in corneal sensitivity can be assessed by the patient's involuntary response to corneal stimulation. It should be noted that long-time contact wearers may have a substantial reduction in response to corneal stimulation, but this should be symmetric.

Corneal sensitivity varies widely among normal persons. Clinically, a mild depression in corneal sensitivity must be judged by comparison of sensitivity between the two corneas. Before attributing such a difference to a trigeminal nerve lesion, one must be satisfied that neither unilateral ocular disease (e.g., herpetic keratitis) nor weakness of one orbicularis oculi muscle (e.g., Bell's palsy) is responsible for a difference in response between the two eyes. When testing corneal sensitivity in the presence of unknown or suspected unilateral eyelid weakness, the comparison should be made between blink responses of the normally innervated eyelids when one cornea, then the other, is alternately stimulated.

A small piece of clean cotton or the end of a cotton-tipped applicator drawn to a fine point can serve as a useful corneal

stimulator, as can the rolled corner of a piece of facial tissue. After being reassured that the test is not harmful, the patient is directed to stare upward and away from the laterally approaching stimulus. It is preferable first to stimulate the relatively insensitive bulbar conjunctiva in order to evaluate the patient's general tendency to blink. Then the cornea is touched with the cotton tip or tissue without touching the eyelashes or eyelid margins, and the patient's response is observed. When testing the corneas, the same relative quadrants should be stimulated since there are substantial regional differences in corneal sensitivity in normal persons, with sensitivity being greater centrally than peripherally and greater in the horizontal than in the vertical meridian.

When corneal sensitivity needs to be quantified, for study purposes for instance, anesthesiometers can be used. For example, the instrument designed by Cochet and Bonnet (111) has a nylon filament that is 0.12 mm in diameter and can be varied in length so that the pressure applied to the cornea varies from 11–200 mg per 0.0113 mm^2 (scale reading, 6.0–0.5 cm). The end point occurs when the nylon filament becomes bent about 5° from the perpendicular.

TESTS OF MOTOR FUNCTION

Clinical Tests

Strength of the masseter and temporalis muscles is tested by noting their volume and firmness during forceful closure of the jaws. If the patient has dentures or many missing teeth, it is helpful to place a moist towel or another soft cloth between the jaws. Although bilateral lesions of the motor division produce weakness of muscles of jaw closure and chewing, the more common unilateral lesions produce only an asymmetry of muscular contraction on the two sides.

Strength of the pterygoid muscles is estimated by feeling the forcefulness of mouth opening against pressure and the strength of forceful deviation of the opened jaw to either side, recalling that contraction of each muscle causes deviation of the jaw to the opposite side. Therefore, weakness of the right internal and external pterygoid muscles is manifested by a spontaneous deviation of the opened mandible to the right and by weakness of forceful movement toward the left. Deviation is best seen by noting the relationship between the upper and lower incisors when the jaw is opened and closed; not by the position of the lips (112).

Less frequently performed tests of the motor division of the trigeminal nerve include observations of the force of contraction of the muscles in the floor of the mouth upon swallowing (mylohyoid muscle and anterior belly of the digastric), slight tilt of the uvula to the affected side (tensor veli palatini), and subjective or objective dysacousis, especially for high tones (tensor tympani muscle).

Neurophysiologic Tests

Needle electromyographic (EMG) evaluation of the trigeminal nerve is relatively straightforward because only the mandibular division has any motor output. Only two muscles are routinely examined—the masseter and the temporalis—because both muscles are superficial and easily studied with minimal discomfort. The pterygoid is a much deeper structure and more difficult to assess, and thus it is not routinely evaluated by most electromyographers. Abnormal spontaneous activity, such as fibrillations and positive sharp waves, indicate peripheral denervation. Voluntary units may be examined, but their configuration is quite different from most skeletal muscle, leading to some confusion for the less experienced examiner. It is also hard for many patients to fully relax these muscles, creating further difficulty in the examination. EMG is most useful in peripheral nerve trauma, such as may result from facial fractures. Myokymia may also be detected on EMG.

TRIGEMINAL REFLEXES: PHYSIOLOGY AND NEUROLOGIC SIGNIFICANCE

Afferent trigeminal impulses evoke a number of other motor reflexes that depend on polysynaptic pathways in the brainstem tegmentum (113). Some of these reflexes are proprioceptive or myotactic (with short latency), whereas others are nociceptive (with long latency). Still others are part of complex synkineses.

Trigeminal Blink Reflexes

Stimulation of the ophthalmic division of the trigeminal nerve, by a gentle tap on the forehead, touching the cornea, cutaneous stimulation, or supraorbital nerve stimulation, leads to bilateral reflex contraction of the orbicularis oculi with a latency following stimulation that varies extensively (25–40 msec) (Fig. 25.15). Ongerboer de Visser et al. (114) found latencies ranging from 36–64 msec in normal adults, with a definite increase in latency with increasing age. There appears to be a minimal latency difference between the ipsilateral and contralateral sides, with the ipsilateral response occurring less than 6 msec before the contralateral response. When the blink reflex is elicited by a glabellar tap, blinks cease or markedly diminish in amplitude in normal children and adults after two to five taps delivered at the rate of one per second. Zametkin et al. (115) examined 164 children between the ages of 2 days and 18 years, as well as 18 adults aged 18–50 years. They found that the blink reflex was extinguished promptly in infants and children up to 1 year of age, after which the number of responses elicited before extinction occurred rose steadily during early childhood, remained stable until approximately 6 years of age, and then declined rapidly, reaching the adult level at 12 years of age.

The afferent fibers of the blink reflex are within the ophthalmic branch of the trigeminal nerve and are probably the small myelinated (A delta fibers) that run in the long ciliary branches of the nerve (116). There is at least one synapse in the descending nucleus and possibly one in the main sensory nucleus. From there, secondary and tertiary fibers connect with both facial nuclei to activate the orbicularis oculi on both sides (efferent arm). Other synapses undoubtedly exist between the sensory and motor nuclei, because the central delay for this reflex is about 40 msec. Stimulation of the sclera or eyelashes gives a much more latent reaction than that obtained by direct corneal stimulation, but these sites have the lowest thresholds for activation of the blink reflex.

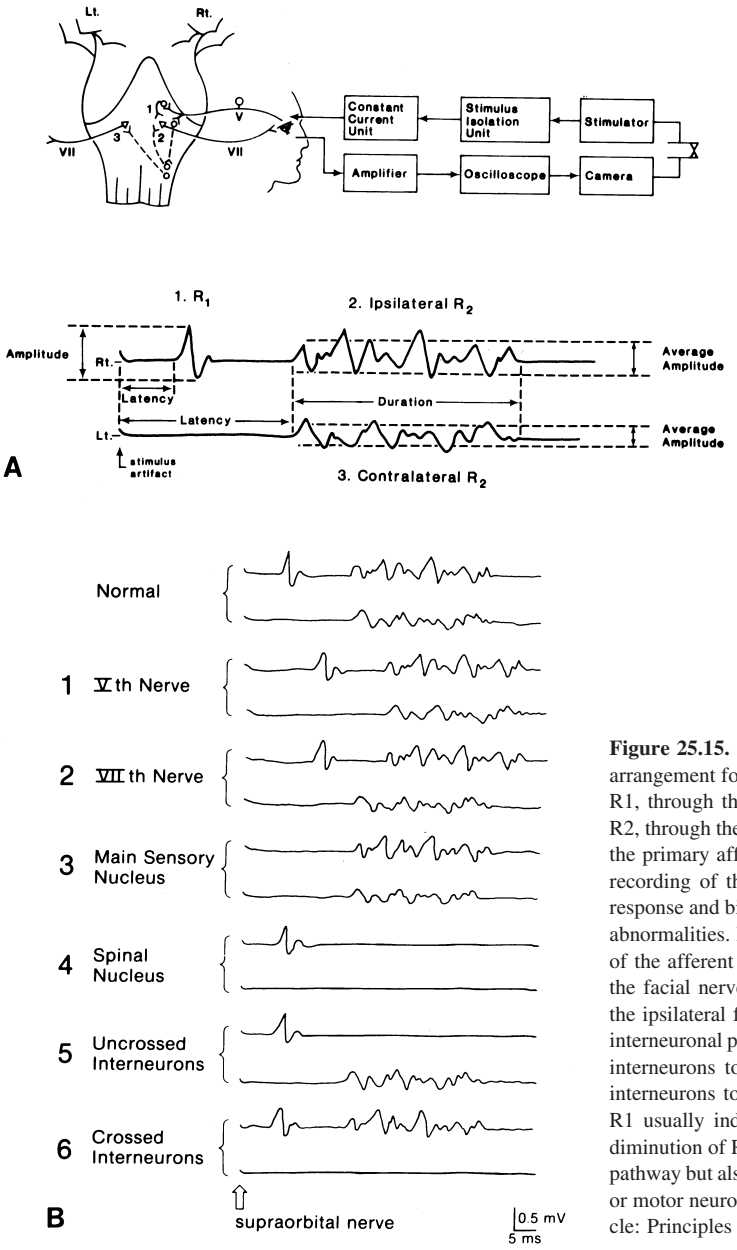


Figure 25.15. Testing the corneal blink reflex. *A*, *top,* Stimulation and recording arrangement for the blink reflex, with the presumed pathway of the first component, R1, through the pons (1), and the ipsilateral and contralateral second component, R2, through the pons and lateral medulla (2 and 3). The schematic illustration shows the primary afferents of R1 and R2 as one fiber. *A, bottom,* A typical oscilloscope recording of the blink reflex after right-sided stimulation. Note an ipsilateral R1 response and bilateral simultaneous R2 responses. *B*, Five basic types of blink reflex abnormalities. From *top to bottom*, the finding suggests the conduction abnormality of the afferent pathway along the trigeminal nerve (1); the efferent pathway along the facial nerve (2); the main sensory nucleus or pontine interneurons relaying to the ipsilateral facial nucleus (3) (1 in *A*); the spinal tract and nucleus or medullary interneuronal pathways to the facial nuclei on both sides (4); the uncrossed medullary interneurons to the ipsilateral facial nucleus (5) (2 in *A*); and crossed medullary interneurons to the contralateral facial nucleus (6) (3 in *A*). Increased latencies of R1 usually indicate the involvement of the reflex arc itself, whereas the loss or diminution of R1 or R2 may result not only from lesions directly affecting the reflex pathway but also from those indirectly influencing the excitability of the interneurons or motor neurons. (From Kimura J. Electrodiagnosis in Diseases of Nerve and Muscle: Principles and Practice. Ed 2. Philadelphia: FA Davis, 1989:309.)

Kugelberg (117) first described two components in blink reflexes as recorded by EMG from the ipsilateral orbicularis oculi muscle after tapping the glabella or percutaneously stimulating the supraorbital nerve. He concluded that the initial, early component of the blink reflex (R1) had a constant latency (about 12 msec), was relatively constant in size and shape, and was always ipsilateral to the mechanical or electric stimulation. This component was thought to be proprioceptive in nature. The second, late component (R2) had variable latency (20–40 msec), was bilateral, and showed habituation. It was thought to be of polysynaptic origin—a nociceptive reflex evoked by cutaneous stimulation. Subsequent investigations leave little doubt that the second component is a polysynaptic reflex, but the nature of the first component remains somewhat controversial. Kugelberg (117) believed that it was a typical monosynaptic stretch reflex. In contrast, Shahani (118,119) and Shahani and Young (120,121) did not agree with the hypothesis that the first component of the blink reflex is proprioceptive. They postulated that the reflex is instead elicited by stimulating cutaneous afferent nerve fibers.

Alterations in the blink reflex occur in adults with various posterior fossa disorders, including acoustic neuroma, multiple sclerosis, Parkinson disease, trigeminal nerve lesions, and brainstem strokes, tumors, or syrinxes, for instance. Increased latency of the first component of the reflex seems to be a relatively specific sign of a lesion within the pons (122–128). Increased latency of the second component has

been reported with lesions of the lateral medulla (129–132). The second component of the blink reflex is likely mediated via medullary pathways that run both ipsilateral and contralateral to the stimulated side before making connections with the ipsilateral and contralateral facial nuclei (133).

Changes in the latency, duration, and amplitude of the second component of the corneal blink reflex also occur in patients with cerebral hemisphere lesions (123,124,131,134, 135). Fisher et al. (136) studied blink reflexes obtained in 34 patients with cerebrovascular lesions, 31 of whom were supratentorial. In 13 patients, the latency of the first component of the reflex on the clinically affected side was significantly delayed acutely but usually resolved within the first week after the event, correlating clinically with the severity of the event. The second component of the reflex was absent in 17 of 34 patients during the early period after the cerebrovascular accident and was associated with decreased corneal sensitivity. Fisher et al. (136) believed that these changes reflect decreased excitability of brainstem structures rather than a lesion within the brainstem in patients with hemisphere dysfunction. Ongerboer de Visser (131) studied corneal reflex latencies in 53 patients with cerebral lesions and identified five distinct types of abnormality in 30 of the individuals. He was in agreement with Fisher et al. (136) that the lower postcentral region has an excitatory influence upon interneurons of the lateral reticular formation of the lower brainstem mediating trigeminofacial connections of the corneal reflex. A decrease in this excitatory influence occurs with postcentral hemisphere lesions and produces an abnormality in corneal reflex latency.

The blink reflex normally habituates (137). Results from functional neuroimaging suggest cerebellar regions may play a role in the modulation of this reflex over time (138).

Loeffler et al. (139) performed an EMG study of the orbicularis muscles in Parkinson disease and noted marked alteration in the latency of the blink reflex in some of their cases. In some patients with advanced disease, the latent period was prolonged to 80–100 msec. Pearce et al. (140) reported that 19 of 20 patients with parkinsonism failed to habituate the blink response to glabellar tap (Myerson's sign) and also reported persistence of the reflex (i.e., decreased habituation) in 13 of 56 patients with parenchymal disease of the brain. Stevens (141) found an increased blink rate or an absent glabellar reflex in nearly one-third of a population of medication-free patients with schizophrenia. Taiminen et al. (142) found reduced habituation of the blink reflex in individuals with schizophrenia and psychotic depression. These findings suggest a possible relationship between the corneal blink rate and central dopamine activity.

Abnormalities of the blink reflex in patients with migraine have lended support to the notion of altered excitability of brainstem trigeminal structures in this condition (143–147).

Trigeminovascular Reflexes

Oculocardiac Reflex

The oculocardiac reflex, also known as Aschner's ocular phenomenon, results in bradycardia in response to mechanical manipulation of the orbit. The afferent pathway of the reflex is the ophthalmic branch of the trigeminal nerve to the brainstem. The sensory impulses pass through polysynaptic pathways in the reticular formation to the visceral motor nuclei of the vagus nerve. There appear to be two distinct types of oculocardiac reflexes: a direct tension dependent pull on extraocular muscles with relatively rapid extinction that may be mediated through stretch receptors, and a prolonged reflex related to diffuse orbital pressure.

Abnormalities of the oculocardiac reflex, particularly of its potentiation or facilitation, are of great importance in ocular surgery. Although the reflex is most frequently encountered during strabismus surgery, cases have been reported in association with laser in situ keratomileusis (LASIK) (148). Vagal reflex activity is increased by many factors. These include drugs such as the phenothiazines, high pCO_2, hypoxia, hyperkalemia, and possibly the direct effect of certain anesthetic agents (149). Preexisting cardiac disease may render the patient abnormally susceptible to the ordinary effects of the oculocardiac reflex, and cardiac arrest may occur.

Diving Reflex

The diving reflex is similar to the oculocardiac reflex, but it is elicited by facial immersion in water. The reflex may be defined as a characteristic pattern of cardiac, respiratory, and vascular responses triggered by immersion of the face. It is a polysynaptic pathway involving trigeminal afferents, brainstem interneurons, and vagal efferents (150). The reflex leads to bradycardia, inhibition of respiration, and peripheral vasoconstriction with increased blood flow to the brain and vital organs.

Corneomandibular Reflex

This reflex is an automatic, involuntary movement of the mandible elicited by corneal stimulation (133). The jaw moves quickly to the opposite side, and at times the mandible moves slightly forward. The mandible moves simultaneously with closure of the eye because of contraction of the ipsilateral external pterygoid. Rarely, both pterygoids contract. The reflex is inconstant and easily fatigued. Any muscular tension interferes with its demonstration. The patient should be relaxed with the mouth opened slightly, allowing the jaw to hang loosely. Mere blinking is not enough to cause the phenomenon, nor is pressure on the globe when the lids are closed. The pathologic corneomandibular reflex indicates bilateral lesions of the corticobulbar tracts to the motor nucleus of the trigeminal nerve, as in amyotrophic lateral sclerosis (151) and strokes (152), for instance. It can be elicited even in comatose patients, in whom the evoked movement of the mandible may be evident even when reflex blinking from corneal stimulation does not occur.

Palpebromandibular Reflex

Pullicino et al. (153) described 14 patients with a reflex characterized by spontaneous anterior or anterolateral movements of the jaw associated with eye blinks. This palpebromandibular reflex is similar to the corneomandibular reflex.

These patients all had either brainstem lesions above the midpons or bilateral cortical disease.

Masseter Reflex (Jaw Jerk)

The jaw jerk is a monosynaptic muscle stretch reflex that is elicited by a brisk tap with the reflex hammer on the front of the chin while the mouth is slightly opened and the jaw is relaxed. The examiner's thumb may be placed on the chin and tapped. The reflex can be reinforced by having the patient bite down lightly on a tongue blade or with Jendrassik's maneuver. The expected response is a contraction of the masseter and temporalis muscles, which causes a sudden closing of the mouth. A unilateral response can occasionally be elicited by tapping the angle of the jaw or tapping a tongue blade placed over the molars of one side. The typical response is usually quite small, and many normal people have no easily elicitable jaw jerk. The masseter reflex can also be exaggerated by anxiety, usually in association with diffuse hyperreflexia.

The reflex is mediated by masseter muscle spindles, whose afferents pass through the trigeminal sensory root and synapse in the mesencephalic trigeminal tract and nucleus (154). A unilateral lesion that destroys the corticobulbar fibers destined to the trigeminal motor nucleus does not alter the functioning of the muscles of mastication, because the motor nucleus of each side receives both crossed and uncrossed fibers. However, when the corticobulbar fibers are bilaterally interrupted in the motor cortex, subcortical regions, internal capsule, or midbrain, there is masticatory paresis that is part of a pseudobulbar palsy. An increased jaw jerk is characteristic of supranuclear involvement of the motor portion of the trigeminal nerve and may be exaggerated to the point of sustained jaw clonus.

Snout and Sucking Reflexes

The **snout reflex**, in which a tap on the upper lip produces lip protrusion or snouting, is one of a group of perioral reflexes whose afferent pathway follows the trigeminal nerve. When the response is increased, tapping the upper or lower lip or philtrum is followed by contraction of the orbicularis oris, as well as the muscles at the base of the nose, leading to closure of the mouth and pursing of the lips as in whistling. In a similar reflex referred to as the **sucking reflex**, stimulation of the lips or skin at the edge of the mouth results in a head turn to that side; the mouth opens, and the patient may suck, bite, or chew. The appearance of these responses is variable in normal persons, and the interpretation of them as pathologic signs is problematic. However, it is clear that the perioral reflexes are more commonly seen, especially in an exaggerated form, in patients with diseases affecting the cortex bilaterally, such as the dementias, Parkinson disease, amyotrophic lateral sclerosis, and bilateral cortical damage from infarct or trauma.

TOPICAL DIAGNOSIS OF DISTURBANCES OF THE TRIGEMINAL NERVE AND ITS CENTRAL CONNECTIONS

Topical diagnosis in the trigeminal somatic sensory system is based on analysis of the pattern and character of various sensory and motor abnormalities. These abnormalities include objective signs (loss or alteration of sensation, muscle weakness, or hyperactivity, as well as changes in trigeminal reflexes) and subjective symptoms (facial pain, neuralgia, headache, and facial paresthesias). The objective trigeminal signs of sensory loss in the face, weakness of jaw muscles, or both, are dependable indicators of the location of the neurologic lesion. On the other hand, topical diagnosis of isolated subjective symptoms of facial pain, neuralgia, or paresthesia is less precise. In either case, an associated neurologic sign (oculomotor nerve palsy, Horner's syndrome, or a brainstem sign) may provide an important clue to the location and nature of the sensory loss or pain.

ALTERATIONS IN CORNEAL SENSATION

For the reader interested in pursuing this topic further, we recommend the comprehensive review of corneal hypesthesia written by Martin and Safran (155).

Physiologic Influences

Alterations in corneal sensitivity occur normally with variations in physiologic and environmental factors. Corneal sensitivity decreases steadily with age (156). In addition, the corneas of brown-eyed individuals are generally less sensitive than those in blue-eyed individuals (157). However, persons with congenital heterochromia have no significant difference in corneal sensitivity between eyes (158), suggesting that the difference in sensitivity between blue eyes and brown eyes may not be related to differences in corneal innervation but rather to inherent differences in a higher sensory mechanism subserving corneal sensation.

Iatrogenic Corneal Hypesthesia

Topical anesthetic agents, such as proparicaine, are commonly used to produce corneal anesthesia. The nonsteroidal anti-inflammatory agents diclofenac and ketorolac also reduce corneal sensitivity when administered topically (159–161) and are used to reduce pain after photorefractive keratectomy. Topical timolol maleate and betaxolol both reduce corneal sensitivity in at least a small proportion of treated subjects (162–166). Elderly patients appear to be particularly susceptible, and affected patients may be at risk of developing keratitis (163,166). The evidence regarding whether or not topical atropine affects corneal sensitivity is conflicting (155).

Ocular surgery, particularly corneal and cataract operations (167,168) but occasionally retinal detachment surgery (169,170), may denervate parts of the cornea, as may panretinal photocoagulation (171). A permanent reduction of corneal sensitivity occurs in 10% of patients who undergo radial keratotomy for myopia and in almost 50% of patients who also receive transverse incisions for astigmatism (172). Photorefractive keratectomy causes a mild decrease in corneal

sensitivity that usually resolves within 3 months of surgery (173,174), but corneal hypesthesia may persist after deep stromal ablations (175). Corneal sensitivity may be reduced transiently for months following laser in situ keratomileusis (LASIK) (176,177).

Contact lens wearers typically have reduced corneal sensation (178–181). Millodot (182) showed that both hard and soft contact lenses cause a daily progressive diminution in corneal sensitivity.

Corneal Hypesthesia from Acquired Disease

Isolated corneal hypesthesia may be congenital or heredodegenerative (e.g., corneal dystrophies), but it is usually a result of acquired local disease of the cornea or sclera. Most ocular diseases that cause corneal hypesthesia, such as scleritis (183) or acute angle closure glaucoma (184), are easily recognized and therefore do not cause confusion in neurologic diagnosis. In such circumstances, there is often associated corneal opacity either as a consequence of the primary disease or from secondary traumatic erosion. In most instances, a single eye is affected.

Neurotropic viruses, especially herpes simplex, are a common cause of corneal hypesthesia. Herpes simplex keratitis usually produces a dendritic ulcer but may also cause other corneal lesions such as superficial punctate keratitis (185). Draeger (186) found that corneal sensitivity usually does not recover after interstitial herpetic keratitis and may take more than 2 years to recover after superficial herpetic keratitis.

Subtle unilateral corneal hypesthesia without other changes in facial sensation is often the first objective sign of pressure upon the trigeminal root by a tumor or other lesion in the cerebellopontine angle (CPA). Cushing (187) stated that aside from 8th nerve findings, corneal hypesthesia is the next most frequent early sign of an acoustic neurinoma. This was confirmed in a retrospective study of 126 patients with acoustic neurinomas diagnosed by MR imaging (188). The explanation for the early involvement of corneal sensation is not clear. To explain dysfunction of trigeminal axons in the rostral portion of the nerve from a lesion that encroaches on the nerve caudally, Stechison et al. (55) suggested a ''tenting-up phenomenon of distortion.'' An alternative hypothesis is that the fine-caliber pain fibers (the C fibers) supplying the cornea are particularly vulnerable to stretch or compression.

Unilateral corneal hypesthesia may also occur with various orbital diseases (189), with Adie's tonic pupil (190), with a variety of lower brainstem lesions (191), and with iatrogenic lesions of the trigeminal pathway (rhizotomy for trigeminal neuralgia, for example) (192–195). Bilateral corneal hypesthesia is commonly associated with systemic diseases that cause sensory neuropathies, including diabetes mellitus (196–199), leprosy (200–202), amyloidosis (203), and vitamin A deficiency. In diabetes, the degree of loss of corneal sensation usually parallels the severity of diabetic retinopathy. In addition, corneal sensitivity improves markedly in diabetic patients who are treated topically with an aldose reductase inhibitor (204,205). Nazarian and O'Leary (206) measured corneal touch thresholds in 11 patients with myasthenia gravis and for unclear reasons found that six had decreased thresholds in one or both eyes.

Toxins that may cause decreased corneal sensation include carbon disulfide (in the rayon industry) and hydrogen sulfide. The associated neurologic or systemic signs and the chief complaints of patients with this type of corneal insensitivity usually preclude any mistaken diagnosis of local ocular disease.

Congenital and Inherited Corneal Hypesthesia

Congenital corneal hypesthesia occurs in a variety of clinical settings—as an isolated finding, as a component of congenital trigeminal anesthesia, in a number of corneal dystrophies, and in association with other developmental anomalies. In addition, Singh and Gibson (207) reported an unusual case of presumed prenatal herpes zoster ophthalmicus that caused permanent corneal anesthesia together with iris heterochromia and atrophy.

Isolated congenital corneal hypesthesia is rare. It is usually bilateral and becomes apparent during infancy or early childhood when painless erosion and opacity of the cornea occur (208,209). Inherited congenital corneal hypesthesia, either unilateral or bilateral, without other findings was reported as an autosomal-dominant condition in two families (210,211). In addition, patients with congenital corneal hypesthesia may have decreased or absent cutaneous sensation in the distribution of the trigeminal nerve, particularly the first division (212–218). This type of congenital trigeminal anesthesia is typically bilateral but may be unilateral. Patients with congenital trigeminal anesthesia usually have normal CT or MR scans. However, there are examples where imaging showed bilateral hypoplasia of trigeminal nerves and gasserian ganglia (215), mild atrophy of cerebellum and brainstem (212), or clinically undetected atrophy of masticator muscles (217).

Isolated corneal hypesthesia and trigeminal hypesthesia occur in association with various congenital anomalies (155,212), including oculoauriculovertebral dysplasia (Goldenhar's syndrome); Möbius syndrome; epidermal nevus syndrome (219); MURCS association (mullarian duct aplasia, renal aplasia, and cervical somite dysplasia) (220); VACTERL (vertebral, anal, cardiovascular, tracheoesophageal, renal, and limb defects) (221); and others (212,222). Decreased corneal sensitivity may also be associated with nephropathic cystinosis (223), abetalipoproteinemia (224), Refsum's syndrome, and progressive hemifacial atrophy (Parry-Romberg syndrome) (225). Because of the potential risk to the cornea in affected persons, many have been treated with either intermittent pressure patching, tarsorrhaphy, or soft contact lenses. In affected infants and young children, recurrent ulcerations of the corneas and erosions of the nasal septum may be caused by self-inflicted injury. Arm splinting may be needed in such persons to allow healing and prevent recurrence (213).

INVOLVEMENT OF THE OPHTHALMIC DIVISION OF THE TRIGEMINAL NERVE

Involvement of the ophthalmic division (V1) by orbital disease is uncommon. Rose and Wright (189) identified peri-

orbital trigeminal sensory loss in 103 (3.3%) of 3,070 patients with orbital disease seen at Moorfields Eye Hospital. Of the 103 patients, 83 had sensory loss in the territory of one or more branches of V1. In almost all patients, the involved cutaneous territory was appropriate to the position of the lesion in the orbit.

In one study (226), cutaneous allodynia (pain induced by normally nonpainful stimuli) and hyperalgesia was found in 22% of patients with trigeminal postherpetic neuralgia.

Nasociliary Branch Lesions

In the series of Rose and Wright (189), only 15 of 103 patients with orbital disease had sensory loss in the infratrochlear territory, and all had additional involvement of other nerves. In contrast, 40 patients had loss of corneal sensation, and this was the only sensory deficit in 15 of these patients. Corneal sensory loss occurred equally often with benign disease and malignancy. Unlike loss of cutaneous sensation, loss of corneal sensation appeared to be unrelated to the position of the lesion in the orbit. Selective involvement of the nasociliary branch may also follow a penetrating orbital injury or extensive orbital surgery.

Frontal Branch Lesions

Hypesthesia in the territory of the supraorbital or supratrochlear nerve is the most common sensory deficit from orbital disease, occurring in 44 patients in the series of Rose and Wright (189). Isolated involvement of one or both nerves was seen in 25 patients. These lesions are very common after contusions, lacerations, surgical incisions, and fractures of the superior orbital rim. In some cases, hypesthesia in this area occurs from pressure on the forehead by an improperly positioned headrest during surgery in the prone position (e.g., during back surgery). Squamous cell carcinoma may also produce supraorbital nerve sensory loss by perineural infiltration (227).

Lacrimal Branch Lesions

Lesions of this branch cause hypesthesia over the lateral bulbar conjunctiva and skin of the lateral canthus. Because sensation in this area is seldom tested, the deficit is probably often overlooked. Of 103 patients with sensory loss from orbital disease (189), 25 had lacrimal branch involvement, and this was the only nerve affected in 10 patients. Lacrimal branch involvement was appropriate to the site of the lesion in the orbit in all but one patient. Rose and Wright (189) did not specifically analyze the causes of lacrimal branch lesions, but 19 patients in their series had lacrimal gland carcinoma, and most of these tumors likely involved the lacrimal branch. Thus, a lacrimal branch sensory deficit should be regarded with some concern, especially if associated with pain. Penetrating lateral orbital injuries and surgical procedures in the region of the lacrimal gland may also involve the sensory lacrimal nerve. A trigeminal neurinoma of the lacrimal nerve has been reported (228).

Syndromes of the Orbital Apex, Superior Orbital Fissure, and Anterior Cavernous Sinus

The ophthalmic division of the trigeminal nerve is usually involved, along with other cranial nerves and sympathetic nerves that travel close to it, in the apex of the orbit and the cavernous sinus (3,7,229–231). In its complete form, the **syndrome of the superior orbital fissure** is characterized by denervation of all branches of the 1st division of the trigeminal nerve, denervation of the sympathetic nerves, paralysis of one or more of the nerves to the ocular muscles (oculomotor, trochlear, and abducens nerves), and, in many cases, proptosis. The complete **syndrome of the orbital apex** is similar to that of the superior orbital fissure except that there is also involvement of the optic nerve. Involvement of the **anterior cavernous sinus** may produce signs that are exactly like those produced by a lesion affecting the superior orbital fissure. Although venous congestion in such cases may suggest that the cavernous sinus rather than the orbital apex is the site of involvement, we prefer to combine the syndromes and refer to them collectively as the **sphenocavernous syndrome**.

Because of the close proximity of the superior orbital fissure, the orbital apex, and the cavernous sinus, any pathologic process (e.g., tumor, inflammation, vascular disease) may begin in one of these regions and rapidly spread to the neighboring regions. Incomplete syndromes are the rule. Lesions that cause these syndromes are discussed in detail in Chapter 20, but pathologic processes include aneurysms, tumors (primary, metastatic, or locally invasive), ischemia, and both septic and aseptic inflammation. Trauma may produce sphenocavernous syndromes by direct damage or indirectly (e.g., carotid-cavernous sinus fistula). Appropriate neuroimaging studies, including CT scanning with both axial and coronal views, MR imaging, and conventional or MR angiography (MRA), usually are sufficient to identify the responsible lesion.

INVOLVEMENT OF THE MAXILLARY DIVISION OF THE TRIGEMINAL NERVE

Damage to the maxillary division (V2) of the trigeminal nerve produces anesthesia or hypesthesia of the skin lateral to the nose, the mucous membrane of the maxillary antrum and lower part of the nose, the upper teeth and gums, the palate anterior to the palatopharyngeal arch, and occasionally the lower part of the cornea (232). As detailed above, the palatine and posterior superior alveolar branches arise in the pterygopalatine fossa before the origin of the infraorbital nerve and supply sensation to the palate and the two posterior upper molars and adjacent gingiva (233). Thus, when a sensory deficit is detected over the cheek, testing sensation in these areas helps to differentiate a lesion of the infraorbital nerve from more proximal pathology (234).

Diseases of the orbit or maxillary sinus may cause hypesthesia in the territory of the infraorbital nerve. Rose and Wright (189) documented infraorbital nerve involvement in 28 of 103 patients who had trigeminal sensory loss caused by orbital disease. Most of the lesions were located along the floor of the orbit. Lesions of the maxillary sinus, including

carcinomas (233) and mucoceles (235), may erode the roof of the sinus and compress or infiltrate the infraorbital nerve. Carcinomas arising on the anterior wall of the sinus may invade the alveolar canal and the anterior superior alveolar nerve and produce localized sensory loss of the incisor and canine teeth and adjacent gingiva (233). Anesthesia or hypesthesia of the infraorbital branch is a common consequence of maxillofacial and orbital injuries.

Numbness of the cheek may result from metastatic perineural infiltration of the infraorbital nerve—the numb cheek syndrome (234) (Fig. 25.16). This syndrome may be the presenting feature or the first sign of recurrence of a basal cell or squamous cell carcinoma (232,234,236–238) or the rare amelanotic spindle cell variant of melanoma (desmoplastic malignant melanoma) (239). Brazis et al. (232) coined the term ''numb cheek-limp lower lid'' syndrome to describe the findings of a patient who developed a numb cheek followed by progressive ipsilateral weakness of lower eyelid closure and upper lip movement. MR imaging showed a subcutaneous linear band of increased signal intensity over the maxillary sinus; biopsy showed widespread infiltration of infraorbital nerve and facial nerve branches by squamous cell carcinoma.

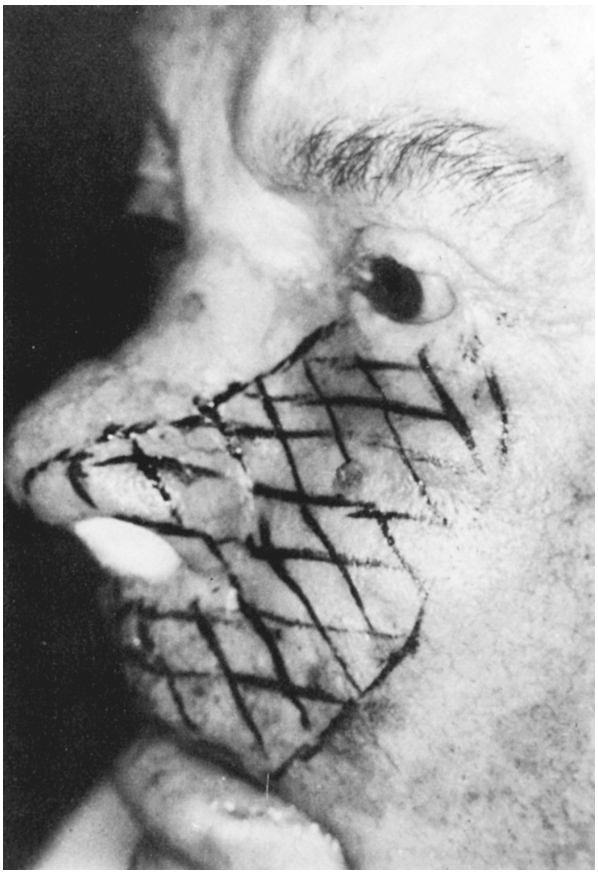


Figure 25.16. Distribution of cutaneous hypesthesia to pin and touch in a patient who developed the ''numb cheek'' syndrome from infiltrating perineural squamous cell carcinoma. Sensation also was lost over the anterior gingiva but not the posterior gingiva, localizing the lesion to the infraorbital nerve (distal to the pterygopalatine fossa). Note scarring from past surgical procedures, especially about the left eye. (From Campbell WW. The numb cheek syndrome: A sign of infraorbital neuropathy. Neurology 1986;36:421–423.)

Other tumors rarely involve V2 in isolation. Erzurum et al. (240) reported a malignant schwannoma of the infraorbital nerve. Isolated maxillary sensory loss also occurs with tumors involving the cavernous sinus or Meckel's cave, including trigeminal schwannoma (241), meningioma (242), and choristoma (243). In such cases, pain in the cheek is usually a prominent symptom.

INVOLVEMENT OF THE MANDIBULAR DIVISION OF THE TRIGEMINAL NERVE

Sensory Abnormalities

Involvement of branches of the mandibular division (V3) of the trigeminal nerve may produce sensory dysfunction, motor dysfunction, or both. Isolated sensory dysfunction can occur in patients with systemic cancer, primarily in the distribution of the inferior alveolar nerve and its terminal cutaneous branch, the mental nerve, producing a numb chin (244–253). The most common neoplasms associated with this **numb chin syndrome** are breast and lymphoproliferative disorders (254–257). Other responsible solid tumors such as prostate cancer (258) have been reported. Lymphoproliferative disorders commonly associated with the numb chin syndrome include Burkitt cell leukemia (L3 ALL) (259,260), Burkitt's lymphoma (261), and lymphoma. When due to cancer, the syndrome may result from metastatic lesions of the jaw, base-of-skull metastases, or leptomeningeal seeding (254). Chin numbness may be the initial sign of cancer, or it may be a late manifestation of malignancy in the setting of stable or progressive systemic disease.

Patients who develop a nontraumatic mental neuropathy should be questioned specifically regarding previous malignancy, including skin lesions of the face, and should undergo contrast-enhanced CT scanning or MR imaging of the head, base of skull, and mandible. Subtle perineural enhancement or effacement of fat planes may provide the only evidence of neoplastic infiltration (262). Lossos and Siegal (254) found that CT scanning and analysis of cerebrospinal fluid (CSF) together provided a diagnosis in 89% of patients. In cases where neuroimaging and CSF results are normal, nuclear bone scanning may provide evidence of bony metastases elsewhere. When the numb chin syndrome is caused by cancer, the prognosis is poor. In the series of Lossos and Siegal (254), median survival after onset of numbness was 5 months for patients with bone metastases and 12 months for those with meningeal disease.

A mental neuropathy is a rare complication of sickle cell disease (263,264). As opposed to the patients with systemic cancer, the patients evaluated by Konotey-Ahulu (263) described a burning sensation of the lower lip, followed later by numbness, and most patients with mental neuropathy in the setting of sickle cell disease also complain of severe bone pain involving the mandible. Bone scans in these patients typically show an area of increased uptake in the mandible, consistent with infarction, and it thus is assumed that the

mental neuropathy that occurs in patients with sickle cell disease is caused by infarction of either the inferior alveolar nerve or the mental nerve in their respective canals.

Dental procedures, particularly extractions of the 3rd lower molar teeth (wisdom teeth), may give rise to inferior alveolar or lingual neuropathies (265). Since the lingual nerve is joined by the chorda tympani nerve and passes medial to the roots of the 3rd molar before entering the tongue, damage at this location during extraction or from an injection of an anesthetic agent may cause loss of somatic and taste sensation to the anterior two-thirds of the tongue as well as hypesthesia of the floor of the mouth and inner surface of the lower gums (266). In elderly edentulous patients, a mental neuropathy may be produced by ill-fitting dentures (265) and possibly by age-related mandibular atrophy (267).

Other miscellaneous etiologies of sensory mandibular neuropathy have been described. Krimsky Fischoff et al. (268) reported a patient with systemic sclerosis and CREST syndrome (calcinosis, Raynaud's, esophageal stricture, and telangiectasia) who developed a painful inferior alveolar neuropathy caused by severe mandibular resorption. Perineural spread of tumor has been reported as a cause of auriculotemporal neuropathy (26). Cruccu et al. (269) studied patients with severe diabetic polyneuropathy and chronic inflammatory demyelinating polyneuropathy and found subclinical sensory mandibular nerve abnormalities in over half of them.

Motor Abnormalities

Proximal lesions of V3 may also involve the motor root, resulting in weakness and wasting of the muscles of mastication (Fig. 25.17), deviation of the jaw to that side, flaccidity of half of the floor of the mouth from paralysis of the mylohyoid and anterior belly of the digastric, and dysacusis for low-pitched sounds due to paralysis of the tensor tympani. Isolated involvement of the motor root is extremely rare. Chia (270) reported five young patients who developed unilateral weakness of masticator muscles without sensory loss and who eventually showed wasting and electromyographic evidence of denervation. CT scans were normal. Three of the five patients had acute weakness and in each case, the weakness was preceded by symptoms of the common cold and accompanied by pain in the cheek. Chia (270) suggested that viral infection may play a role in the etiology of this condition. Pure trigeminal motor neuropathy may also caused by blunt head trauma (271), meningiomas (272), and multiple sclerosis (273).

Lesions of the motor root or its branches may produce abnormal or excessive activity of masticator muscles. An example of such a disorder is **hemimasticatory spasm**, a rare idiopathic condition characterized by recurrent spasms of the masseter and temporalis muscles on one side (274–279). Trigeminal nerve function is otherwise normal, and there is no involvement of the facial nerve. It has been suggested that the nerve to the masseter muscle may be entrapped at a point in its course between the lateral pterygoid muscle and the skull, causing focal demyelination and spontaneous neural discharges (277,279).

The mylohyoid muscle and anterior belly of the digastric may also exhibit abnormal spontaneous activity. Hyperexcitability of the mylohyoid branch of the mandibular division was reported by Diaz et al. (280) as a delayed complication of radiotherapy to the base of the skull. These authors described two patients who developed episodic contraction of the muscles in the floor of the mouth on one side.

INVOLVEMENT OF THE GASSERIAN GANGLION OR THE SENSORY ROOT OF THE TRIGEMINAL NERVE

General Considerations

Paralytic lesions of the gasserian ganglion, whether ischemic, inflammatory, compressive, traumatic, toxic, or infiltrative, cannot be differentiated dependably from lesions of the sensory root (281). Involvement of both structures may cause anesthesia in one or more divisions of the trigeminal nerve as well as paralysis of the motor nerve to the muscles of mastication. Certain findings may help, however, to differentiate a lesion in the region of the cavernous sinus, involving the ganglion or root, from focal involvement of the sensory root in the perimesencephalic cistern. A trigeminal deficit associated with ophthalmoplegia usually indicates a lesion of the cavernous sinus or Meckel's cave. In the absence of a more peripheral lesion, sensory loss limited to the ophthalmic distribution signifies a lesion of the cavernous sinus or superior orbital fissure (282), as does the associated finding of paralysis of the ipsilateral oculosympathetic nerve. On the other hand, loss of facial or corneal sensation combined with paralysis of the facial and auditory nerves implies involvement of the sensory root in the basal cistern (e.g., as in the syndrome of the cerebellopontine angle).

Tumors of the middle and posterior fossa are a common cause of trigeminal nerve dysfunction. In a series of 64 patients with facial numbness as an initial or presenting symptom (281), 25% had CPA tumors, and 17% had base-of-skull tumors. Acoustic neuromas are the most common of these tumors and cause trigeminal signs in 9–30% of patients, (188,281,283–286). Hypesthesia from acoustic neuromas may be limited to the cornea but the tumor may also be heralded by hypesthesia in a distribution approximating that of V2 or V3 (287). Puca et al. (285) found masticator weakness in 17% of 30 patients with trigeminal involvement from acoustic neuroma. Acoustic neuromas are discussed further in Chapter 33.

Meningiomas that cause facial numbness arise most often from the cavernous sinus but may also arise from the dura of Meckel's cave, in the CPA (288), or from the inferior aspect of the tentorium. Puca et al. (285) found trigeminal deficits in 10 of 21 patients with ''sphenopetrosal'' meningiomas; 6 of the 10 patients had trigeminal symptoms in isolation. In the same study, only one of ten CPA meningiomas was associated with facial hypesthesia. In another series of 16 patients with meningiomas of Meckel's cave (242), trigeminal sensory loss was the only sign of disease in 3 of the 8 patients with small tumors (less than 3 cm), and occurred together with ophthalmoplegia in all 8 patients with larger tumors. Trigeminal neuralgia, typical or atypical, was the

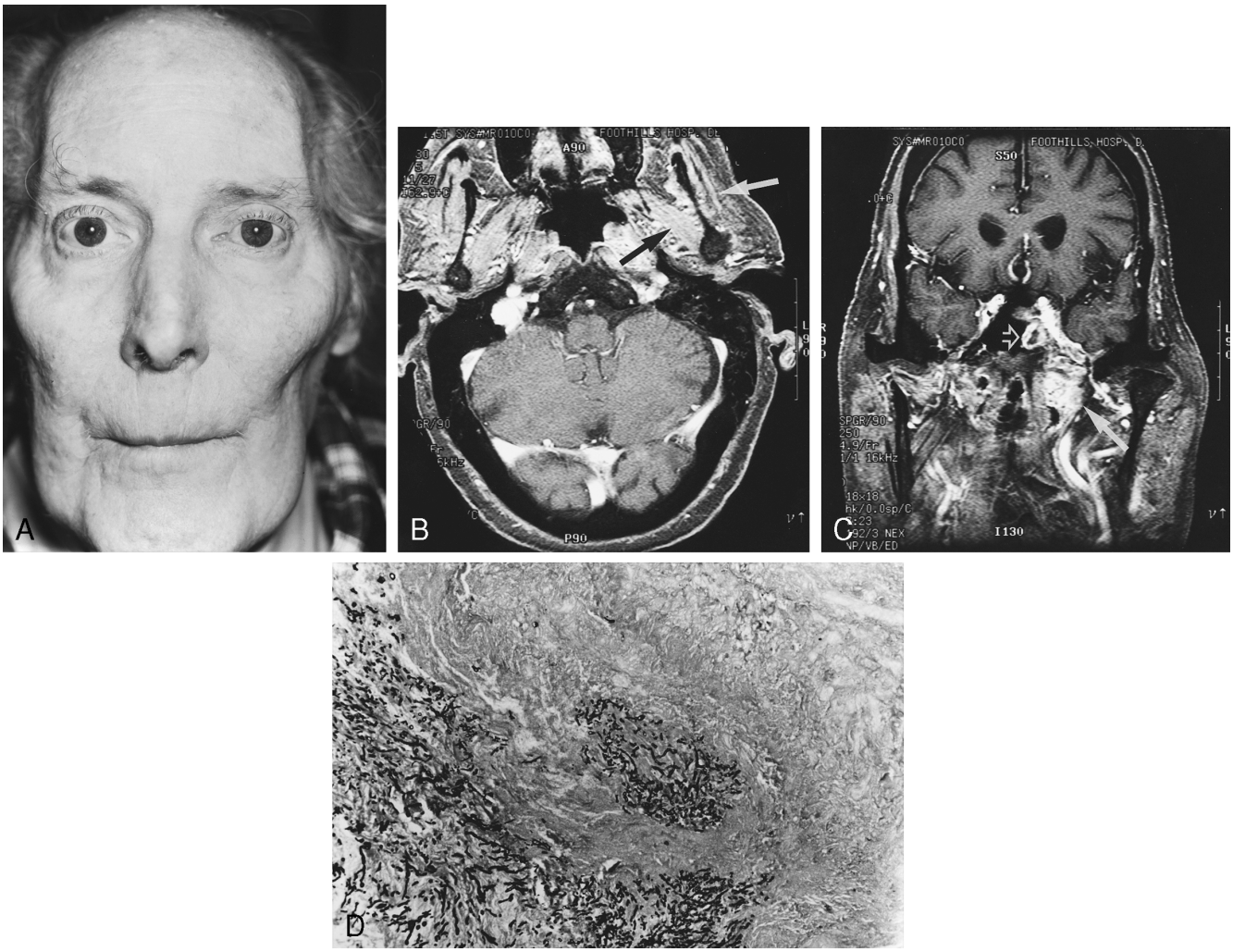


Figure 25.17. Left trigeminal motor neuropathy from invasive aspergillosis. An otherwise healthy 80-year-old man presented with a 6-month history of increasing pain in the left mandibular region. The left masseter and pterygoids were wasted and weak, and there was no sensory deficit. *A*, Photograph showing marked wasting of the left masseter. *B*, Axial MR image illustrating atrophy of the masseter (*white arrow*) and lateral pterygoid muscle (*black arrow*). *C*, Postgadolinium MR image shows irregularly enhancing lesion of infratemporal fossa on the left (*solid arrow*), which extends through the foramen ovale into the cavernous sinus. Also note thickened enhancing mucosa of left sphenoid sinus (*open arrow*). *D*, Photomicrograph of biopsy of infratemporal lesion from left nasopharynx. Multiple fungal organisms with 45° branching hyphae consistent with *Aspergillus* are invading connective tissue. (Grocott, ×40.)

initial symptom in 10 of the 16 patients. Facial pain and numbness also may herald trigeminal root involvement by tentorial meningiomas (289). The mechanism by which meningiomas compromise nerve function is not always simple compression; infiltration of the trigeminal nerve by a benign meningioma of Meckel's cave was demonstrated histologically by Larson et al. (290). Meningiomas are discussed in Chapter 30 of this text.

Schwannomas (neuromas) of the trigeminal nerve are uncommon, but a review by Samii et al. (291) of 190 cases showed that 51% presented with trigeminal symptoms, particularly pain and paresthesia in the V1 and V2 dermatomes. Symptoms often began long before presentation, with a mean duration of 34 months. The abnormal findings at presentation included facial hypesthesia in 70% of cases, decreased corneal reflex in 56% of cases, and masticator weakness in 34% of cases. Similar results were documented in other series (292–294). Hemorrhage into a schwannoma may produce the acute onset of trigeminal symptoms (295). An unusual symptom of massive trigeminal nerve schwannomas is pathological laughter, attributed in part to seizures or pontine dysfunction (294,296). Schwannomas of the trigeminal nerve are discussed in Chapter 33 of this text.

A variety of other nonmalignant mass lesions may arise from or compress the trigeminal ganglion or root and present with trigeminal symptoms and signs. These include CPA

epidermoids (285), intracavernous carotid aneurysms (297), and an assortment of rare lesions, including ependymomas (298), granular cell tumors (299), choristomas (243,300), amyloidomas (301,302), lipomas (303), aspergillomas (304), cavernous hemangiomas of Meckel's cave (305,306), juvenile xanthogranuloma, teratoma (307), and distal aneurysms of the anterior inferior cerebellar artery (308). Chang et al. (309) described a unique intracranial trigeminal lesion in a patient with chronic progressive ophthalmoplegia. MR imaging showed slight enlargement of the cavernous sinus and thickening and contrast-enhancement of the mandibular division of the trigeminal nerve. Biopsy of the lesion (confirmed later by autopsy) disclosed a localized hypertrophic process characterized histologically by periaxonal Schwann cell ''onion-bulb'' formation.

Trigeminal sensory loss is an underrecognized sign of metastatic perineural spread of orofacial neoplasms to the trigeminal ganglion and root. The development of trigeminal dysfunction often signals the recurrence of a previously treated tumor, particularly a squamous cell carcinoma of the face or oropharyngeal mucosa (237,238,310). Involvement may be limited initially to a single nerve branch, especially the infraorbital nerve (see the section, Involvement of the Maxillary Division of the Trigeminal Nerve in this chapter) (237), but spread of tumor proximally to the cavernous sinus is often present at the time of diagnosis (Fig. 25.18). A similar propensity for producing perineural cavernous sinus invasion is observed with adenoid cystic carcinoma of the lacrimal or salivary glands (311–313) (Fig. 25.19) and nasopharyngeal carcinoma (314). Perineural spread of these neoplasms is best detected by MR imaging with gadolinium enhancement (315). If V3 is involved, the study should extend inferiorly to the lower mandibular margin (282). Adenoid cystic carcinoma and nasopharyngeal carcinoma are discussed in Chapter 35 of this text.

MR imaging may also reveal leptomeningeal spread of metastases to trigeminal roots (316) or focal metastatic involvement of the trigeminal ganglion or root by melanoma, lymphoma (317,318), or carcinoma (319,320) (Fig. 25.19). Malignant lesions are suggested by enlarged, enhancing nerves with spiculated margins, whereas benign lesions usually show minimal or no enlargement and smooth margins. Sevick et al. (316) noted that overlap occurs between the MR appearance of benign and malignant lesions and suggested follow-up MR evaluation within several weeks when the diagnosis is not clear clinically. In a review of 17 patients with metastatic lesions of the cavernous sinus, Post et al. (321) noted that 9 had decreased sensation in the distribution of one or more trigeminal divisions, but only 1 had facial numbness as a presenting symptom.

A variety of nonneoplastic disorders may affect the trigeminal ganglion or the sensory or motor roots of the trigeminal nerve. **Gradenigo's syndrome** comprises the triad of trigeminal and abducens nerve palsies and otitis media (322). The trigeminal neuropathy is characterized by excruciating facial pain, and many patients also have ipsilateral facial weakness. Hardjasudarma et al. (323) reported a patient with otitis and ipsilateral facial anesthesia who developed an abducens palsy 3 days later. MR imaging showed swelling and enhancement of the trigeminal root and ganglion and inflammatory changes of the petrous apex. Other inflammatory process that may cause trigeminal neuropathy include sarcoidosis (324,325) and Wegener's granulomatosis (326).

Severe closed head trauma with basal skull fractures may rarely cause unilateral or bilateral injury of the trigeminal ganglion or root (327–330). Typically, other cranial nerves

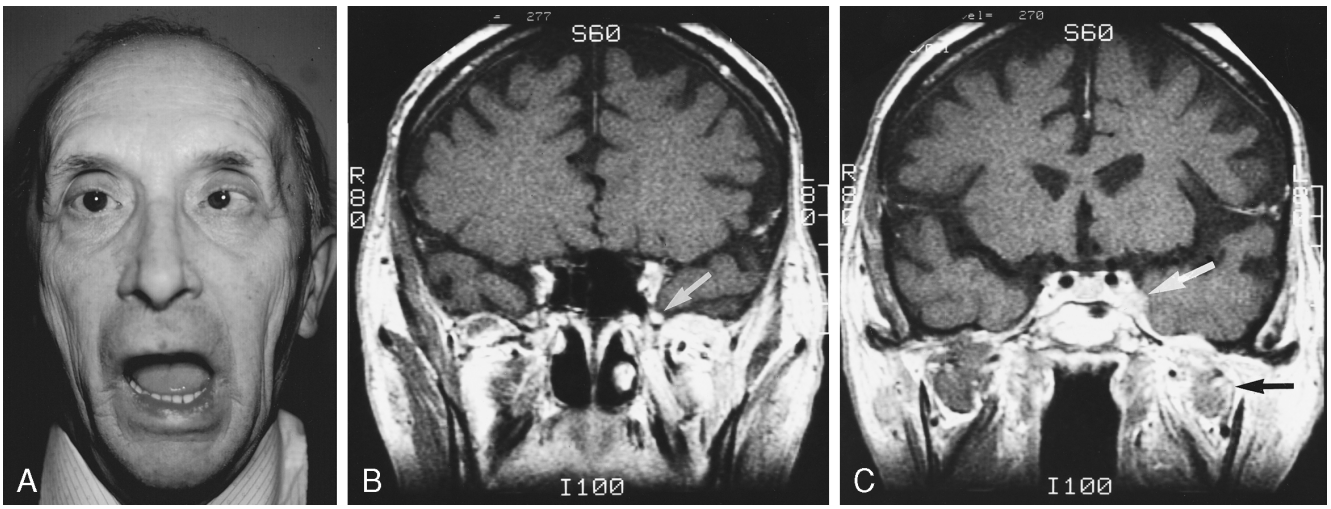


Figure 25.18. Perineural spread of squamous cell carcinoma intracranially along the trigeminal nerve. This 70-year-old man had progressive sensory loss over the left forehead and cheek over a period of 6 months, followed by horizontal diplopia and difficulty chewing. A squamous cell carcinoma was removed from his left temple 2 years earlier. *A*, Photograph showing wasting of left temporalis, deviation of the open jaw to the left, and left esotropia (due to left 6th nerve palsy). *B and C*, Postgadolinium coronal T1-weighted images showing an enlarged enhancing maxillary nerve on the left (*B, arrow*) and posterior extension of tumor into the cavernous sinus (*C, white arrow*) . Note atrophy of left lateral pterygoid muscle (*C, black arrow*).

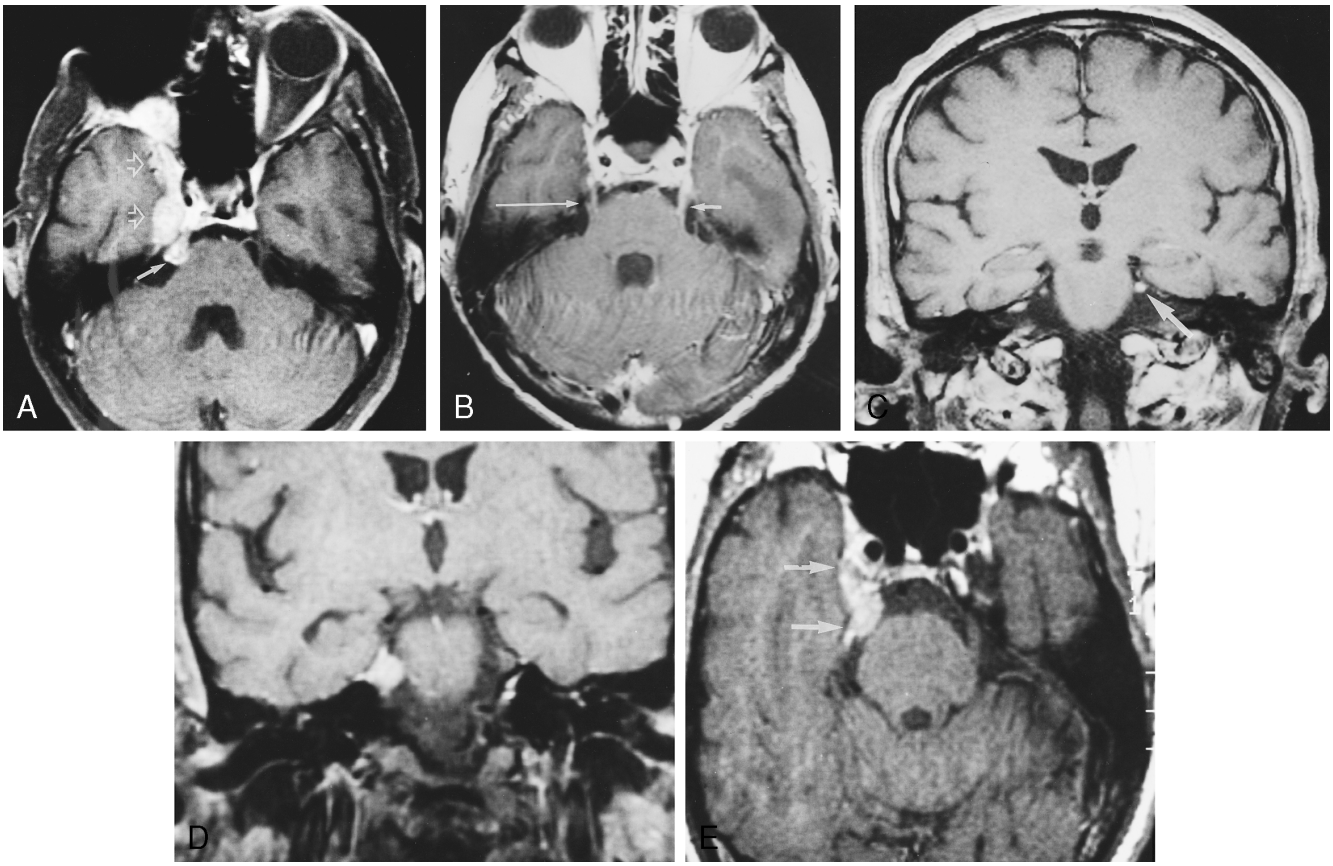


Figure 25.19. Metastatic neoplasms involving the trigeminal ganglion or nerve root. *A*, Perineural spread of adenoid cystic carcinoma originating in the orbit (previous right orbital exenteration). The T1-weighted image postgadolinium shows irregular, enhancing mass extending posteriorly from the right orbit. Mass involves the cisternal (*solid arrow*), as well as the ganglionic and postganglionic (*open arrows*) segments of the 5th nerve; *B*, Leptomeningeal spread of highly anaplastic astrocytoma. Axial T1-weighted MR image shows bilateral enhancement of trigeminal nerve roots with slight enlargement on the left (*short arrow*) and irregular contour on the right (*long arrow*). *C*, Metastatic melanoma (primary tumor involved the left side of face). The T1-weighted coronal image shows smooth contour of left trigeminal nerve root with uniform enhancement and minimal enlargement (*arrow*). *D* and *E*, Lung carcinoma metastatic to trigeminal ganglion and root. *D*, The T1-weighted coronal image shows enlargement of the cisternal portion of the right trigeminal nerve root with uniform enhancement and irregular spiculated margins. *E*, Axial T1-weighted image demonstrates a large, irregular mass involving the cisternal and ganglionic segments of the trigeminal nerve on the right (*arrows*). (From Sevick RJ, Dillon WP, Engstom J, et al. Trigeminal neuropathy: Gd-DTPA enhanced MR imaging. J Comput Assist Tomogr 1991;14:605–611.)

also suffer damage, particularly the abducens nerve. In two cases described by McGovern et al. (328) and Nelson and Kline (329), the sequelae of such an injury included an unusual trigemino-abducens synkinesis, whereby voluntary activation of the masseter or lateral pterygoid triggered abduction of the ipsilateral eye. The postulated explanation for the synkinesis is that regenerating motor fibers of the trigeminal nerve are misdirected along trigeminal channels that normally convey spindle afferent fibers from the lateral rectus. Trigeminal dysfunction may also be a feature of basilar invagination (331).

''False-localizing'' trigeminal symptoms, signs, or both may occur in the presence of an extrinsic, posterior fossa mass (332–335). The mechanism, according to O'Connell (252), is that the mass displaces the brainstem upward or, in the case of a CPA lesion, to the opposite side. This produces distortion of the sensory root and traction at the dural foramen on one or both sides. O'Connell (252) described four such patients, all of whom had sensory loss on the side opposite a posterior fossa tumor. All four of these patients also had increased intracranial pressure, however, and this may have contributed to the symptoms, because facial hypesthesia occasionally occurs in patients who have non-tumor-induced intracranial hypertension, e.g., communicating hydrocephalus (336) or idiopathic intracranial hypertension (337–339). In these patients, the sensory loss typically resolves when the intracranial pressure is lowered, suggesting that increased intracranial pressure alone may be sufficient to cause false-localizing trigeminal dysfunction. Another mechanism proposed to explain this phenomenon with CPA

lesions is that the nerve is pushed against adjacent blood vessels and suffers vascular compression (334).

Isolated trigeminal sensory neuropathy occurs in some patients with various connective tissue diseases, including systemic lupus erythematosus (340), scleroderma (341–346), dermatomyositis (344), Sjögren's syndrome (347), rheumatoid arthritis (348), and mixed connective tissue disease (344,349–351). Hagen et al. (351) found that among patients with trigeminal sensory neuropathy and connective tissue disease, the trigeminal sensory neuropathy developed before general symptoms of connective tissue disease in 7% of the patients and at the same time in 47% of the patients. The pathogenesis of this condition is unknown.

Viral infections such as hepatitis (352) and herpes simplex (353) occasionally produce isolated trigeminal sensory neuropathies.

Several investigators (354–356) have also described patients with an idiopathic acute or subacute, purely sensory, trigeminal neuropathy affecting one or more divisions of the trigeminal nerve. In some cases, there is also an impairment of taste on the affected side. The symptoms typically resolve partially or completely in most of these patients. Blau et al. (354) emphasized that most patients had intact corneal reflexes, normal trigeminal motor function, and absence of pain, although trigeminal neuralgia did develop in one of their patients, and a minority of patients complained of a burning or itching sensation (356).

The diagnosis of idiopathic trigeminal sensory neuropathy is typically one of exclusion following normal MR imaging and serologies to exclude connective tissue disorders (357,358). However, transient MR imaging abnormalities, consisting of enlargement of the trigeminal root and enhancement of the root and ganglion, were described in two patients with this condition by Rorick et al. (359). In both instances, the abnormalities spontaneously disappeared within 4 months. Biopsy-proven cases with nongranulomatous (360,361) and granulomatous (362) inflammatory changes have also been described. These findings suggest that at least some cases of idiopathic trigeminal sensory neuropathy are inflammatory in origin. On the other hand, Jannetta and Robbins (363) performed retromastoid craniectomy on four patients with ''idiopathic'' trigeminal neuropathy and found that in all cases, the superior or anterior inferior cerebellar arteries were compressing and stretching the trigeminal nerve root. Postoperatively, all patients had pain relief as well as improvement or resolution of their sensory deficit.

Trigeminal sensory neuropathy also occasionally results from ischemia. Miller (364) described an elderly patient with intermittent diplopia from presumed ischemia of the right abducens nerve. The patient later developed a transient right trigeminal sensory neuropathy, which Miller (364) attributed to ischemia of the sensory root. In support of this concept, Mokri et al. (365) described trigeminal nerve palsies in 7 (4%) of 190 patients with spontaneous dissection of the internal carotid artery. Four of the seven patients presented with a syndrome of hemicrania, oculosympathetic palsy, and trigeminal neuropathy. In addition, Rizzo et al. (366) reported ischemia of the trigeminal ganglion in a patient with a dural external carotid-cavernous sinus fistula. The simultaneous onset of ipsilateral facial and trigeminal sensory neuropathy was described in a patient with diabetes mellitus by Michelucci et al. (367). The sudden onset of a combined palsy in this setting may results from occlusion of the petrosal branch of the middle meningeal artery, and as with most ischemic cranial nerve palsies, partial or complete recovery should be expected. An argument in favor of this mechanism was also made by Lapresle and Lasjaunias (368), who noted that therapeutic embolization of the middle meningeal artery occasionally produces paralysis of both nerves.

Iatrogenic trigeminal neuropathies may occur as a result of trigeminal ablation by surgical means or injection for treatment of trigeminal neuralgia. Rarely, as a result neurotropic ulcers may occur on the face in anesthetic dermatomes (369). A mefloquine-induced trigeminal sensory neuropathy has also been reported (370).

Neuroparalytic (Neurotrophic) Keratitis

This complication of corneal denervation is mentioned here because it most frequently results from lesions (usually surgical) of the trigeminal ganglion, the sensory root, or the descending trigeminal tract in the brainstem. Cases also occur after brainstem injury (371). Magendie (372) first noted that sectioning of the trigeminal nerve causes trophic or degenerative changes in the cornea, clinically referred to as neurotrophic or neuroparalytic keratitis. Neuroparalytic keratitis from damage to the trigeminal sensory nerve root is a potential complication of both radiofrequency trigeminal rhizotomy and retrogasserian glycerol injection for trigeminal neuralgia, and it occasionally complicates operations for large CPA tumors and other posterior fossa lesions.

The earliest sign of neuroparalytic keratopathy is conjunctival hyperemia, often associated with mild corneal haze. These changes may be apparent in severe cases within 24 hours after the operation, at which time the patient may complain of blurred vision in the affected eye. In mild cases, the changes are discernible only with the slit lamp; in such cases, the patient is usually asymptomatic. Very rarely, the earliest changes occur in the iris; there may be iritis with posterior corneal deposits for several days before there is definite evidence of anterior corneal and conjunctival involvement.

In cases of neuroparalytic keratitis in which only the cornea is affected, the appearance of punctate keratitis or of widespread loss of epithelium associated with conjunctival congestion, may not progress further if treatment is instituted immediately. In some cases, secondary infection develops, and the eye is rapidly lost through perforation; however, the disease is essentially a chronic one without acute sensory symptoms because of the patient's inability to perceive pain. Even in severe cases, the institution of proper treatment may serve to retain a useful eye.

Various theories have been advanced regarding the pathogenesis of neuroparalytic keratitis, including trophic disturbances, corneal desiccation, irritative effects, and abnormal cellular metabolism. Although the actual cause probably reflects a combination of factors, it is clear that the trigeminally innervated corneal nerves play an important role in maintain-

ing the anatomical integrity and function of the cornea, particularly the epithelium (373). Diminished secretion of tears likely encourages corneal involvement (374). Reflex tearing is evoked by afferent impulses transmitted through the trigeminal nerve. The same lesions that damage this nerve at the pontine angle, petrous tip, and Meckel's cave frequently affect the efferent nerve of tearing, the nervus intermedius, and the greater superficial petrosal nerve. Heigle and Pflugfelder (374) measured tear production in nine patients with previous herpes zoster ophthalmicus, five of whom had neuroparalytic keratitis. In the latter group they found a tenfold decrease in tear production compared with the group without keratitis. Nasal sensation and the nasal-lacrimal reflex were lost only in the patients with keratitis, and the authors suggested that this finding may portend the development of neuroparalytic keratitis. It is also possible that some humoral agent plays a role in the development of neuroparalytic keratitis.

Lewis et al. (193,194) examined 15 patients with intentional or unintentional V1 lesions 1–5 years after percutaneous radiofrequency trigeminal rhizotomy. Although five patients had a quantitative decrease in sensation in the eye ipsilateral to the rhizotomy compared with the contralateral eye, none had any symptoms or signs of corneal dysfunction. These investigators postulated that intact corneal sensation implies intact axonal mechanisms essential for maintenance of corneal metabolism and function, and that when sensation is absent, these mechanisms may or may not be adequate to preserve corneal integrity. This theory is consistent with the findings in patients with congenital corneal anesthesia or hypesthesia studied by Purcell and Krachmer (210), many of whom had no corneal abnormalities.

Resection of the superior cervical or stellate ganglion may prevent or reduce the risk of the development of neuroparalytic keratitis (375). The exact role of the sympathetic nerves in the production of keratitis is unknown, but sympathectomy may act by eliminating the inhibitory effect of norepenephrine on corneal epithelial mitosis (376).

Treatment of neuroparalytic keratitis is directed toward preventing corneal desiccation and secondary bacterial infection. The use of an airtight shield over the affected eye creates a moist atmosphere over the surface of the cornea and, in our experience, quickly arrests the keratitis. Epithelization of eroded areas usually follows promptly. Tarsorrhaphy has a similar beneficial effect but is often unnecessary if the patient understands that drying of the eye is dangerous and uses a semipressure patch to avoid this complication. Although the use of a topical artificial tear solution or ointment may aid patients with minimal corneal changes, it does not provide adequate protection for patients with severe disease.

INVOLVEMENT OF THE TRIGEMINAL PATHWAYS IN THE BRAINSTEM

The location of a brainstem lesion is usually indicated by distinctive combinations of cranial nerve palsies and long tract signs. We are concerned in this section with the diagnostic features of facial hypalgesia and hypesthesia that accompany some of these brainstem syndromes. In most instances, facial sensation is impaired on the side of the lesion, but occasionally, sensory loss is present on the side opposite the lesion. In contrast to peripheral involvement of the trigeminal nerve, sensory loss from brainstem lesions is commonly dissociated. Thus, perception of pain and temperature may be profoundly affected whereas modalities such as light touch and pressure are spared. Sensory defects with peripheral lesions correspond precisely with the distribution of various divisions and branches of the trigeminal nerve, whereas sensory defects from trigeminal lesions in the brainstem may not adhere strictly to these classic subdivisions. Thus, in brainstem lesions, the sensory loss might involve one small area of the mandibular region or extend into an adjacent region subserved by the maxillary nerve. Correlation of these ''unorthodox'' sensory defects with the size and location of the lesion is far from exact, but certain guidelines have emerged from pathologic studies of acquired disease as well as from tractotomies performed for the relief of facial pain.

Lesions of the Medulla

Lateral Medullary Infarction

Clinically, the classic lesion involving the descending tract and nucleus is a lateral medullary infarct produced by occlusion of a vertebral or posterior inferior cerebellar artery (Wallenberg's syndrome) (377–379). Trigeminal signs include analgesia for pain and temperature on the same side of the face or head and decreased corneal sensation. The modalities of light touch and pressure are usually intact but may be perceived as less intense or having a different quality. In patients with lateral medullary syndrome from vascular lesions, sensory loss is either in a segmental ''onionskin'' pattern or in a divisional distribution of V1 or both V1 and V2 . It should be noted, however, that sparing of intraoral and perioral sensation was described in a patient with Wallenberg's syndrome who otherwise had complete involvement of all three divisions (74). Because intraoral sensation is not often tested routinely, it may be spared more often than is reported with lateral medullary lesions.

Currier et al. (380) noted that the corneal reflex was absent in the lateral medullary syndrome whenever the loss of sensation included the upper face. Corneal sensation may improve following a lateral medullary infarct but always remains defective if careful testing is performed, and neuroparalytic keratitis can occur (364). Chronic facial pain, due to involvement of the lower spinal trigeminal tract, may be a sequela of lateral medullary infarction (381).

Medullary Tractotomy of the Descending Trigeminal Root

In 1938, Sjöquist reported that the descending trigeminal root could be readily cut in the posterolateral aspect of the medulla, with loss of facial pain and thermal anesthesia but with preservation of tactile and position sensibility. This discovery provided a new approach to the problem of intractable facial pain and stimulated further studies of trigeminal pathways in the human brainstem.

As alluded to earlier in this chapter, fibers from the middle of the face and oral mucosa tend to terminate at more rostral brainstem levels than do the fibers from more peripheral areas of the face, even within the same trigeminal region. Thus, medullary tractotomies at or below the level of the obex may fail to produce analgesia of the oral mucosa (96) or teeth (382). Furthermore, although medullary tractotomy initially abolishes trigeminal pain sensation, partial recovery may occur in the perioral and midline regions of the face (382).

Medullary tractotomies, while producing analgesia of the face and cornea, may not produce complete anesthesia. Thus, awareness of the position of the tongue is retained, and food in the mouth is not lost. The corneal sensation of touch is typically preserved. Often in tractotomies at lower medullary levels, the patient may still show a rather slow corneal reflex on stimulation of the cornea although all appreciation of pain stimuli on the face is lost. There are at least two possible explanations for this. The cornea may be stimulated by tactile stimuli that are known to project to the nucleus of the spinal trigeminal tract at upper, as well as lower, brainstem levels. Another possible explanation is that some of the impulses set up by painful stimulation of the cornea project more rostrally on the nucleus of the spinal trigeminal tract, perhaps at or near the level of the motor nucleus of the facial nerve.

Syringobulbia

Syringomyelia, a chronic disease characterized by proliferation of glial tissue and cavity formation in the central portion of the spinal cord, may extend upward to the medulla. Because of the concentric, onionskin organization of the face for pain (Fig. 25.11), involvement of the nucleus of the spinal tract in the lower cervicomedullary area will first cause defective pain and temperature sensation on the outside of the face. As the destructive process ascends in the brainstem **(syringobulbia),** the spared area in the center of the face shrinks in a radial fashion. Herniation of the cerebellar tonsils into or below the foramen magnum (Chiari I malformation) is one of the most common causes of syringomyelia (383).

Lesions of the Pons

Lesions in the lateral tegmentum of the pons may damage any of the brainstem trigeminal nuclei or the nerve fibers entering the brainstem from the trigeminal root, producing signs that are indistinguishable from those caused by damage to the gasserian ganglion or peripheral root, including neuroparalytic keratitis. Involvement of the main sensory nucleus of the trigeminal nerve causes ipsilateral loss of epicritic sensation in the face (two-point discrimination, light touch, etc.). Proper localization of the lesion in such cases is facilitated when there are associated signs of intrinsic pontine disease (e.g., abducens nerve palsy, horizontal gaze palsy, ocular myoclonus, facial myokymia and/or contracture, peripheral facial palsy, ataxia, pyramidal signs). However, small lesions in the lateral pontine tegmentum may present as an isolated trigeminal sensory neuropathy (305,384–388). In such cases, localization of the lesion may be impossible without neuroimaging, and even thin-section MR imaging may fail to detect the lesion.

Lateral pontine lesions that produce isolated facial numbness include infarction (389,390), demyelination (127, 358,391), infiltration by a neoplasm, and a small hemorrhage, such as that which occurs in patients with a vascular malformation. Holtzman et al. (384), Berlit (385), and Kim et al. (388) each described a young patient who experienced sudden numbness of the face without other symptoms. Each patient was found to have a small hemorrhage in the dorsolateral tegmentum adjacent to the middle cerebellar peduncle. In two of the patients, V2 and V3 dermatomes were preferentially affected, and the third patient later developed masseter weakness.

Like lateral medullary lesions, lateral pontine lesions may interrupt the lateral spinothalamic tract as well as the more medially situated ventral secondary ascending tract of the trigeminal nerve. Such lesions may cause contralateral hemianalgesia of the both the body and face.

Patients with medial pontine lesions may present with prominent trigeminal motor weakness, with or without sensory loss. Three patients with this syndrome were described by three separate groups (392–394). Two patients also exhibited contralateral ataxic hemiparesis. In all three cases, CT scanning showed vascular lesions involving the basis pontis. The mechanism by which basal pontine lesions selectively affect the trigeminal motor nucleus or fascicle is unclear, although the motor nucleus is slightly ventral and medial to the main sensory nucleus.

A unilateral cheiro-oral syndrome, a sensory disturbance involving the contralateral corner of the mouth and palm of the hand, is caused by a lesion either in the paramedian pontine tegmentum, mesencephalon, ventral posterior thalamus, or the postcentral gyrus of the parietal lobe (see below). Matsumoto et al. (395) described two patients with small lesions of who had the bilateral cheiro-oral syndrome, with symptoms on **both** sides of the mouth. The authors suggested that the hand and perioral symptoms on one side were caused by damage to the medial portions of the medial lemniscus and adjacent ventral secondary ascending tract, whereas the perioral symptoms on the other side were related to extension of the lesion across the midline to the medial part of the other ascending tract (395). Pontine lesions are the usual cause of bilateral cheiro-oral syndrome because of the proximity of the both somatic and facial sensory pathways (396). In addition, Yasuda et al. (397) reported a case with numbness in the contralateral foot in addition to the hand and corner of the mouth—the cheiro-oral-pedal syndrome.

Dorsomedial lesions in the lower pons rarely may produce sensory loss only inside the mouth. In such cases, the lesion is thought to damage the spinal trigeminal nucleus while sparing the adjacent trigeminal tract (74) (Fig. 25.20).

Although bilateral facial analgesia or anesthesia is a rare sign, Miller (364) observed it in a 4-month-old infant with congenital facial diplegia, bilateral horizontal gaze palsies, bulbar paralysis, and hypotonia. The infant also had bilateral neuroparalytic keratitis. It was assumed that the child had

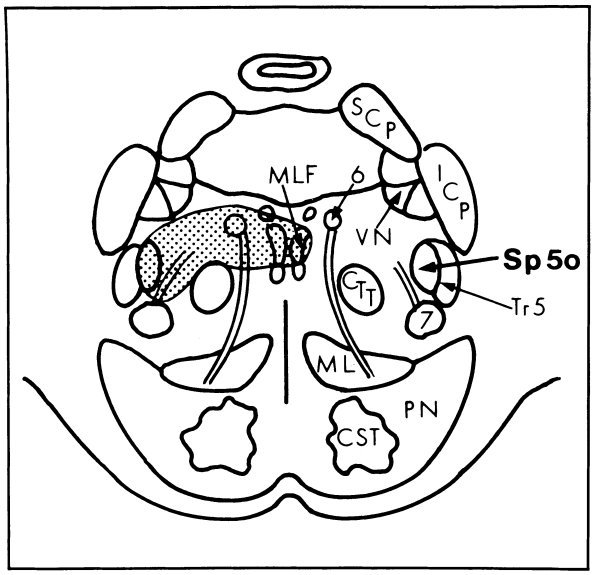


Figure 25.20. Schematic diagram of dorsal lesion (*hatched area*) in lower pons, causing ipsilateral loss of intraoral sensation with intact facial sensation. Note sparing of the descending tract of the trigeminal nerve. The patient also had an ipsilateral facial nerve palsy and one-and-a-half syndrome. SCP, superior cerebellar peduncle; ICP, inferior cerebellar peduncle; VN, vestibular nuclei; Sp5o, spinal nucleus (pars oralis) of trigeminal nerve; Tr5, descending tract of trigeminal nerve; MLF, medial longitudinal fasciculus; CTT, central tegmental tract; ML, medial lemniscus; PN, pontine nuclei; CST, corticospinal tract. (From Graham SH, Sharp FR, Dillon W. Intraoral sensation in patients with brainstem lesions: Role of the rostral spinal trigeminal nuclei in pons. Neurology 1988;38:1529–1533.)

congenital aplasia or hypoplasia of several motor and sensory brainstem nuclei.

Unilateral Spasm and Contracture of the Masseter Muscle: A Sign of Intrinsic Dorsal Pontine Pathology

In Leningrad in 1935, Rasdolsky (398) called attention to a sign of trigeminal involvement that he considered typical of involvement of the dorsal pontine tegmentum by tumor. He reported ipsilateral masseter spasm in five patients with dorsal pontine tumors. All patients had a slowly progressive syndrome characterized by ipsilateral hearing impairment, numbness along the distribution of the trigeminal nerve, loss of the corneal reflex, weakness of the face and forehead, pupillary miosis, ataxia, and progressive spastic contracture of the masseter. His patients were barely able to open their jaws, and their speech was typical in that they were forced to speak ''through their teeth.'' Palpation of the jaw muscles revealed a knotty firmness on the affected side, and the temporalis muscle was obviously wasted as evidenced by concavity of the temporal fossa. Rasdolsky (398) also stressed the peculiar contracted facial musculature on the affected side. Autopsy confirmed that in each case a tumor involved the masticator nucleus, the motor roots of the trigeminal nerve, and all surrounding structures. Many similar cases have been subsequently reported (399–401), although not all of the patients reported have the so-called ''masseter sign.'' Although neoplasms are the most common cause of spastic paretic facial contracture, this sign also occurs in patients with multiple sclerosis (402), and in patients with other intrinsic lesions of the brainstem, such as tuberculomas (403). Spasms of the masseter muscle also occur in patients with hemimasticatory spasm, but there is no associated contracture of facial muscles and hemimasticatory spasms are paroxysmal (see Involvement of the Mandibular Division of the Trigeminal Nerve in this chapter).

Lesions of the Mesencephalon

Superior lateral lesions of the mesencephalon may involve the trigeminal and spinothalamic pathways (medial lemniscus). For instance, occlusion of the superior cerebellar artery may cause an infarction of the superior lateral portion of the pontomesencephalic tegmentum, resulting in contralateral hemianesthesia of the face and body, cerebellar hypotonia, intention tremor and, occasionally, paresis of vertical gaze (404). Kim (405) described three patients who presented with diplopia and numbness or painful paresthesia on one side of the face. Examination revealed facial hypesthesia on the affected side in two patients and hyperpathia in one. Two patients had contralateral partial oculomotor nerve palsies, and one had an ipsilateral trochlear nerve palsy. MR imaging in each case showed a small lesion involving dorsal midbrain tegmentum, which was postulated to involve the ventral ascending tract and the neighboring oculomotor or trochlear nerve fascicle. One patient also had numbness of the hand on the same side as the facial symptoms, suggesting extension of the lesion laterally to involve the medial lemniscus. Other similar clinical presentations have been described, including a cheiro-oral syndrome without diplopia, resulting from a midbrain hemorrhage (406) or stroke (407), and a cheiro-oral-pedal syndrome with ataxic hemiparesis from a ventrolateral midbrain infarction (408).

INVOLVEMENT OF THE THALAMUS AND THALAMOCORTICAL PROJECTIONS

The thalamogeniculate artery, a proximal branch of the posterior cerebral artery, supplies the posterior part of the lateral nuclear mass of the thalamus. Occlusion of the thalamogeniculate artery produces the classic **thalamic syndrome of Déjerine and Roussy** (409), characterized by complete contralateral hemianesthesia with slight or transient hemiparesis and hemiataxic or choreoathetotic movements of the affected side. The hemianesthesia is usually transitory, but the patient is often left with a ''burning'' or ''ripping'' pain and dysesthesia (410). These sensations are often most pronounced in the face. Homonymous hemianopia is commonly associated with the thalamic syndrome and signifies occlusion of the posterior cerebral artery proximal to the thalamogeniculate artery. The Déjerine Roussy syndrome is rarely seen in its complete form in patients with thalamic tumors (411), but it occurs frequently with vascular lesions.

Because the nucleus ventralis posteromedialis (VPM) of the thalamus receives crossed sensory fibers from the opposite side of the face, acute lesions in this nucleus cause anal-

gesia of the face. Touch and vibration sensation may or may not be affected. Iwasaki et al. (412) described a patient with isolated loss of pain and temperature sensation in the left perioral region from a small right thalamic infarction. More commonly, small ventral posterior infarcts cause the cheiro-oral syndrome, characterized by contralateral paresthesia involving the corner of the mouth (especially the upper lip) and the thumb and fingers (especially the index and middle finger). Small hemorrhages may also be responsible (413). The degree of objective sensory loss is variable (414–419). Kim (418) described 10 patients with perioral involvement from thalamic vascular lesions; all 10 had associated paresthesia in the fingers, 4 had numbness in the palm of the hand, and 5 had milder paresthesia in the foot or toes (especially those on the medial side). Two patients developed uncomfortable, often burning, paresthesia in the affected areas.

Autopsy studies of patients with the thalamic cheiro-oral syndrome show localized lesions of the lateral posterior portion of the VPM nucleus and the medial posterior portion of the ventralis postero-lateralis (VPL) nucleus (420,421). Kim (418) and others (415,416) have emphasized that the areas representing the face, hand, and foot, and in particular the upper lip and radial fingers, are contiguous and proceed medially to laterally within the ventral thalamic region. These areas are relatively large compared with the more dorsal projection areas from proximal limbs and trunk. Thus, the pattern of the sensory disturbance in the thalamic cheiro-oral (-pedal) syndrome may be explained by the somatotopic organization of VPL and VPM.

A similar cheiro-oral sensory syndrome, usually associated with a mild hemiparesis, may occur with a lesion of the thalamocortical projections (418,422–424). The typical lesion is an infarction of the posterior limb of the internal capsule at its posterior and superior boundary in the territory of the lateral lenticulostriate arteries. The infarction often extends into the corona radiata and may involve the lenticular nucleus. The sensory disturbance is indistinguishable from that of the thalamic cheiro-oral syndrome, but lesions involving the thalamocortical pathway more often produce hemiparesis and may also affect taste sensation on the opposite side of the tongue (423).

INVOLVEMENT OF THE SENSORY CORTEX (POSTCENTRAL GYRUS)

Although ocular sensation is represented in the midportion of the precentral gyrus, lesions in this area typically do not affect corneal sensitivity. However, as alluded to earlier in this chapter, cerebral lesions in some instances may reduce the contralateral corneal reflex.

Clinically, irritative lesions of the somatic sensory area produce irritative symptoms (numbness, tingling, or a sense of movement) in the corresponding part of the surface of the body, but they rarely cause pain. Focal destruction of cortex leads initially to a localized and complete anesthesia affecting all sensory modalities, but much of this loss is transitory, and a considerable degree of sensibility returns. Complete and lasting anesthesia suggests a lesion at a lower level in the brain. The return of sensation involves those sensations that are most effectively interpreted by the thalamus. It is interesting that in the process of recovery, the most rapid and complete return of sensation occurs in the area supplied by the trigeminal nerve. Pain returns first, the sense of temperature is largely restored, and an appreciation of tactile stimuli is partly regained. The senses of position and discrimination are severely and permanently affected. The greatest loss occurs in the stereognostic sense. It seems, therefore, that the sensory cortex is essential for finer spatial and discriminatory function, whereas the thalamus can analyze and appreciate only the cruder forms of sensation.

Because of the proximity of the face and hand areas in the inferior postcentral gyrus (103), brief episodes of numbness or tingling in the contralateral face and hand often occur together with transient ischemia in the territory of the middle cerebral artery. Migraine sensory auras often are characterized by ipsilateral sensory changes in the face and head. More sustained sensory symptoms in a cheiro-oral distribution occur with parietal lobe tumors (415) and rarely with small infarctions in the parietal operculum (425) or superior postcentral gyrus (426).

CONGENITAL INSENSITIVITY TO PAIN

Most of the patients with congenital insensitivity to pain have a type of hereditary sensory and autonomic neuropathy (HSAN) (427). Some of the HSANs are characterized by distal loss of pain, temperature, light touch, and proprioceptive sensation. However, HSAN III (Riley-Day syndrome, familial dysautonomia) and HSAN IV (congenital pain insensitivity with anhidrosis due to a mutation in the TRK-A gene) have diffuse pain and thermal insensitivity (428). In addition, Donaghy et al. (429) described three members of a consanguinous family who likely had HSAN V (congenital insensitivity to pain with selective loss of small myelinated fibers). A unique feature of this pedigree was that all three affected individuals developed bilateral neurotrophic keratitis in infancy and required corneal transplants. Donaghy et al. (429) pointed out the rarity of corneal opacification in previous reports of hereditary sensory neuropathy, but Miller (364) noted corneal scars in two of five patients with congenital insensitivity to pain, and other authors subsequently described similar patients (430,431).

HYSTERICAL (NONORGANIC) HEMIANESTHESIA

Hysterical hemianesthesia is a conversion reaction that usually involves the entire left side of the body (432,433). It is regularly associated with loss of all types of sensation on the involved side, including the special senses. More important is the characteristic affect on the patient, who invariably displays complete indifference to severe, often absolute, sensory loss. The patient may deny any corneal sensation, even though the corneal blink reflex is normal and symmetric on the two sides. All modalities of sensation are reduced or absent over the side of the face and the corresponding side of the body. The grossness of the sensory loss often helps to distinguish hysterical hemianesthesia from organic disease of the brain.

Two sensory findings that are widely accepted as proof of a hysterical presentation are (*a*) hemianesthesia that splits the midline; and (*b*) unilateral loss of vibratory sensation when the two sides of the forehead are stimulated 1–2 cm from the midline. Both signs, however, are unreliable indicators of hysteria. Rolak (434) tested 100 consecutive patients with hemifacial sensory loss, including 20 patients with psychogenic sensory loss and 80 with structural lesions. Exact splitting of the midline occurred in 20% of those with psychogenic loss and in 8% of those with structural lesions, whereas unilateral loss of vibration sensation was demonstrated in 95% and 86% of patients, respectively. Similarly, Gould et al. (435) found that 21 of 30 patients with acute lesions (mostly strokes) had midline splitting of pain or vibration sensation.

Patients with hysterical hemianesthesia may also claim to have lost one or more of the special senses on the involved side, including hearing, vision, and the sense of smell. Hearing loss is a common finding, but the patient does not complain of it until hearing is tested during the examination. Ipsilateral loss of vision may comprise complete or partial blindness in one eye or a homonymous hemianopia, typically with nonphysiologic features (see Chapter 27). Keane (436) reported ten patients with hysterical hemianopias, eight of whom complained of ipsilateral neurologic symptoms, usually numbness.

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