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Neuro-Ophthalmology

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Neuroanatomy and neuro-ophthalmologic examination

Neuro-ophthalmologic disorders arise from all areas of the neuro-ophthalmologic tract. They may be expressed simply as loss of vision or double vision, or as complex syndromes or systemic illnesses, depending on the location and type of lesion. Problems may occur anywhere along the visual pathway, including the brainstem, cavernous sinus, subarachnoid space, and orbital apex, and may affect adjacent structures also. A firm understanding of the neuroanatomy and neurophysiology of the eye is essential to correct diagnosis [1–3].

The visual pathway

Functionality of the visual pathway requires the afferent innervation of the optic nerve, cranial nerve (CN) II. A lesion can occur anywhere along the pathway and is manifested according to distinct location and fiber involvement. An adequate understanding of the visual pathway from the retina, through the optic nerve and chiasm, with projection dorsally to the occipital lobe, allows for localization of the insult (Fig. 1). The fibers from the temporal retina (capturing the images from the nasal visual field) and nasal retina (capturing images from the temporal visual field) converge at the optic disc and proceed dorsally to form the optic nerve. The ophthalmic artery supplies the retina and optic nerve. It is the first intracranial division off the internal carotid artery. The optic nerve is subject to ischemic, compressive, infiltrative, or inflammatory damage because of its vulnerability to increased

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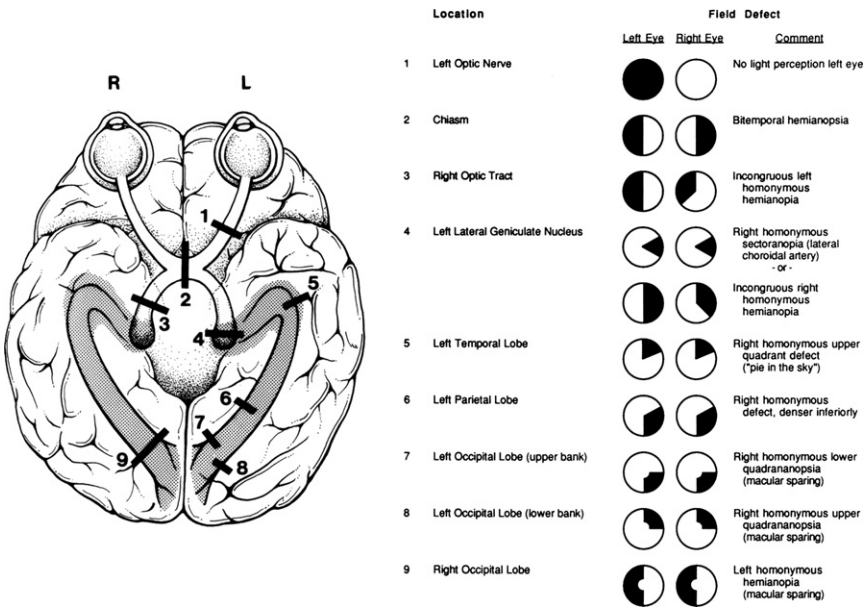


Fig. 1. Lesions of the afferent visual pathway and their corresponding visual field defects. The term hemianopsia (or hemianopia) refers to a visual field defect that respects the vertical meridian. Homonymous indicates that the defect involves the same side of the visual field in both eyes. An incongruous defect is that for which the extent of visual field loss is asymmetric between the two eyes. (*Adapted from* Mason C, Kandel ER. Central visual pathways. In: Kandel ER, Schwartz JH, Jessell T, editors. Principles of neural science. 3rd edition. Norwalk (CT): Appleton & Lange; 1991. p. 437; with permission.)

intraocular pressure or papilledema. An optic nerve deficit may result in unilateral, complete vision loss, without macular sparing.

As the fibers approach the optic chiasm intracranially, the temporal fibers remain ipsilateral and the nasal fibers cross within the chiasm to join the contralateral optic tracts. The optic chiasm is located directly above the pituitary fossa, anterior to the pituitary stalk, and inferior to the hypothalamus and third ventricle. Infarction of the optic chiasm is extremely rare because of its collateral blood supply. The superior hypophyseal arteries perfuse the chiasm inferiorly, which are fed by the internal carotid, posterior communicating, and posterior cerebral arteries. Superiorly the optic chiasm is perfused by the branches of the anterior cerebral arteries. A lesion in the chiasm classically presents as bitemporal hemianopsia, although this can vary depending on the specific area of the chiasm that is affected (see Fig. 1).

Posterior to the chiasm, the optic fibers course superiorly and around the infundibulum, below the third ventricle. They contain fibers from the ipsilateral temporal retina and the contralateral nasal retina. Most of the blood supply is from the thalamic perforators of the posterior cerebral artery and branches of the anterior choroidal artery. Most of the fibers synapse

in the lateral geniculate nucleus (LGN), whereas those axons that are responsible for the pupillary light reflex branch off before the LGN and synapse in the pretectal nuclei of the midbrain.

The optic radiations that emerge from the LGN are called the geniculocalcarine fibers. These separate into superior and inferior bundles, containing the afferent signal from the contralateral inferior visual fields and the contralateral superior visual fields, respectively. The superior bundles that pass through the parietal lobe project back to the upper bank of the calcarine cortex of the occipital lobe, thus receiving the image from the contralateral inferior visual field. The inferior bundles pass through the temporal lobe to form the Meyer loop and project back to the lower bank of the calcarine cortex of the occipital lobe, thus receiving the image from the contralateral superior visual field. The optic radiations receive blood supply from the middle cerebral arteries and anterior choroidal arteries. The macular area of the visual cortex, which represents the central 30° of vision, is processed by one half of the visual cortex. The fovea, or very center of the visual field, is represented within the tips of the occipital poles and has a dual blood supply, including branches of the posterior and middle cerebral arteries, providing the basis for macular sparing in the setting of occipital lobe infarct.

Efferent and afferent pupillary innervation

The efferent innervation of the pupil, which is responsible for pupillary constriction and dilation, involves parasympathetic and sympathetic fibers. Afferent pupillary innervation involves the retina, optic nerve, chiasm, optic tract and optic radiations.

The parasympathetic preganglionic fibers originate in the Edinger-Westphal subnucleus, adjacent to the oculomotor nucleus in the periaqueductal midbrain. The fibers travel on the superficial aspect of the oculomotor nerve (CN III) until it synapses in the ciliary ganglion in the orbit. The superficial location of the parasympathetic fibers explains why a blown pupil is an early sign of a compression lesion, including aneurysm or uncal herniation. From the ciliary ganglion, the postganglionic nerve fibers travel to the ciliary muscle and the iris sphincter and provide the tone for pupillary constriction. The pupillary light reflex pathway, allowing the pupil to constrict when exposed to light, consists of four neurons (Fig. 2). The image obtained from the retinal ganglionic cells travels through the optic nerve and follows the nasal retinal fibers across the chiasm, where they synapse in both of the pretectal nuclei of the dorsal midbrain. Each pretectal nucleus sends axons bilaterally to the two Edinger-Westphal nuclei, which contain the parasympathetic preganglionic fibers. These fibers travel with the third nerve to the ciliary ganglion within the orbit, which then sends parasympathetic postganglionic fibers to the pupillary sphincter muscle and ciliary muscle for lens accommodation. The projections to bilateral pretectal and Edinger-Westphal nuclei explain consensual pupillary constriction to light. Near inputs, such as

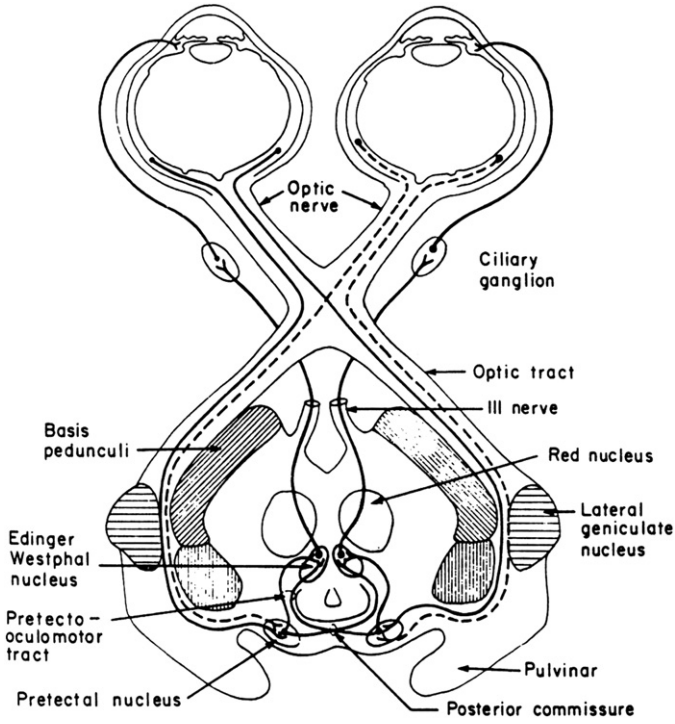


Fig. 2. The pupillary light reflex pathway. (*Adapted from* Walsh FB, Hoyt WF. The autonomic nervous system. In: Clinical neuro-ophthalmology. 3rd edition. Baltimore (MD): Williams & Wilkins; 1969. p. 473; with permission.)

an object placed directly in front of a patient being examined, project directly to both Edinger-Westphal nuclei, bypassing the pretectal area, which can serve to distinguish some forms of light-near dissociation in which the dorsal midbrain is involved. Adie syndrome, or Adie tonic pupil, is an example of light-near dissociation.

The sympathetic pathway originates in the posterolateral hypothalamus and descends along the lateral brainstem to synapse at the ciliospinal center of Budge-Waller, at the level of C8-T2 (Fig. 3). The preganglionic fibers exit the spinal cord with the ventral rootlets at this level and travel across the apex of the lung before ascending the neck to synapse in the superior cervical ganglion. The postsympathetic fibers form a plexus around the cervical internal carotid artery and reenter the skull. The oculosympathetic fibers leave the carotid artery in the cavernous sinus and enter the orbit with the ophthalmic division of the trigeminal nerve. The sympathetic fibers continue with the long ciliary nerves to the radial iris muscle, causing pupillary dilatation. There are also fibers that innervate the smooth muscle in the upper and lower eyelids (Mueller muscle) and the blood vessels in the skin and conjunctiva. Classic symptoms of sympathetic dysfunction, Horner

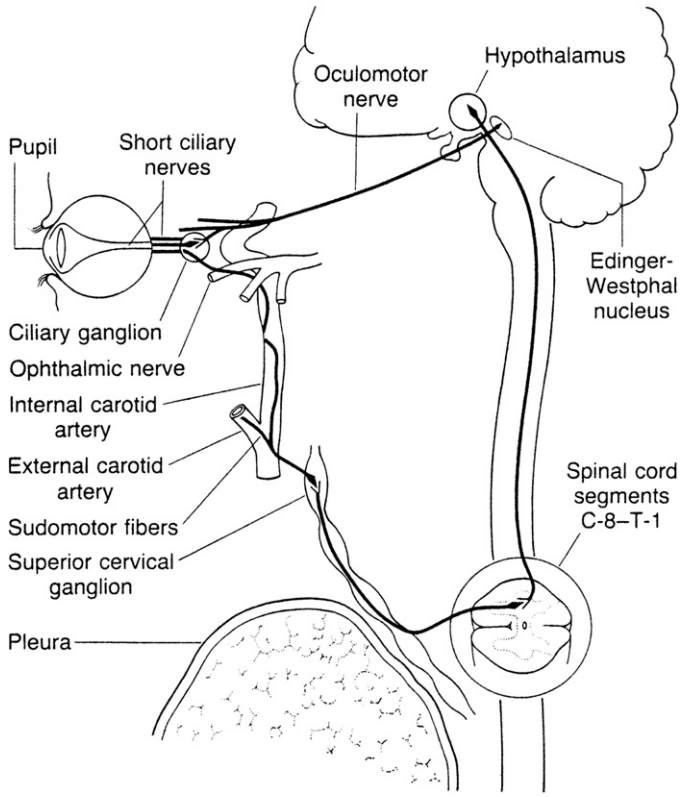


Fig. 3. The autonomic innervation of the pupil. The two-neuron parasympathetic pathway begins in the Edinger-Westphal nucleus of the midbrain and synapses in the ciliary ganglion in the orbit. Short ciliary nerves innervate the iris sphincter. The three-neuron sympathetic pathway begins in the hypothalamus, synapses in the lower cervical cord, ascends the neck on the carotid artery, and synapses again in the superior cervical ganglion to innervate the pupillodilator. (*From* Selhorst J. The pupil and its disorders. Neurol Clin 1983;1:861; with permission.)

syndrome, occur ipsilateral to the side of the lesion and include mild ptosis, papillary miosis, and inconsistently anhidrosis (Fig. 4). There is a small area of sweat glands above the eyebrows innervated by branches directly from the superior cervical ganglion, which explains why some third-order neuron Horner syndromes do not involve anhidrosis.

The cranial nerves

The five cranial nerves that innervate the eye are the optic nerve (CN II), the oculomotor nerve (CN III), the trochlear nerve (CN IV), the abducens nerve (CN VI), and the first division of the trigeminal nerve (CN V_1). A review of the course of these cranial nerves is important for understanding ocular pathology.

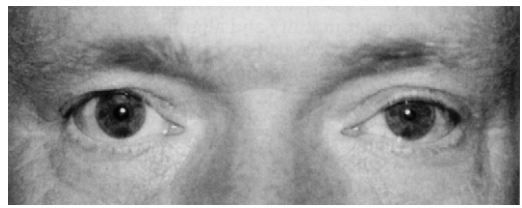


Fig. 4. A patient who had a left Horner syndrome secondary to an apical lung tumor. (*From* Balcer LJ, Galetta SL. Pancoast's syndrome. N Engl J Med 1997;337:359; with permission. Copyright © 1997, Massachusetts Medical Society.)

Ocular motility

Eye movement is controlled by a group of muscles innervated by the oculomotor nerve (CN III), the trochlear nerve (CN IV), and the abducens nerve (CN VI). The coordinated action of these muscles is accomplished by supranuclear control and is what allows for conjugate gaze of both eyes (Fig. 5).

Cranial nerve III. The oculomotor nerve (CN III) innervates the superior rectus muscle, inferior rectus muscle, medial rectus muscle, inferior oblique, levator palpebrae, and ciliary ganglion, providing motor and parasympathetic innervation to the eye. Partial dysfunction is common but a classic dysfunction of the entire nerve results in ptosis (attributable to loss of levator palpebrae function), papillary dilation (with loss of parasympathetic tone of ciliary ganglion), and the eye deviated down and out (attributable to the sole action of superior oblique and lateral rectus muscles) (Fig. 6). The origin

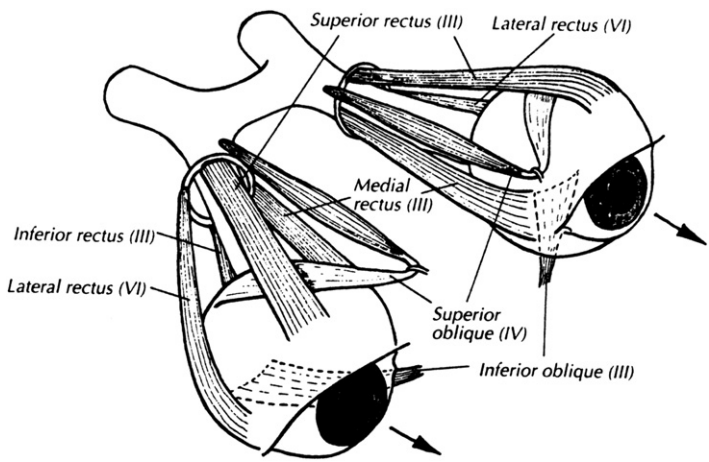


Fig. 5. The extraocular muscles. The medial rectus, superior rectus, inferior rectus, and inferior oblique are innervated by the third nerve (III); the superior oblique is innervated by the fourth nerve (IV); the lateral rectus is innervated by the sixth nerve (VI). (*From* Patten J. Vision, the visual fields, and the olfactory nerve. In: Patten J, editor. Neurological differential diagnosis. 2nd edition. New York: Springer-Verlag; 1996; with permission.)

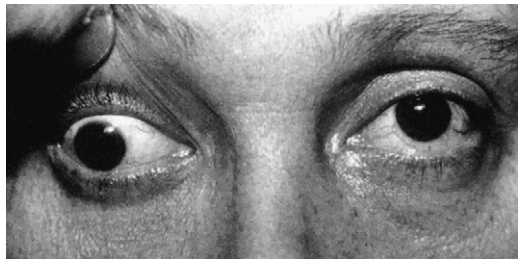


Fig. 6. Complete right third nerve palsy resulting in hypotropia, exotropia, and pupillary mydriasis. The ptotic eyelid is elevated manually. (*From* Bennett JL, Pelak VS. Palsies of the third, fourth, and sixth cranial nerves. Ophthalmol Clin North Am 2001;14(1):169–85; with permission.)

of the oculomotor nerve is in the periaqueductal midbrain, from a paired nuclear complex (Fig. 7). Within the complex are several paired subnuclei that send projections ipsilaterally to its target organ. The two exceptions to this are the axons originating from the unpaired midline central caudal nucleus, which innervate the levator palpebrae muscles, and the axons innervating the superior rectus muscles, which travel from the contralateral subnucleus. The parasympathetic preganglionic axons originate from the Edinger-Westphal nuclei, then travel to innervate the ciliary ganglion.

The fascicles that form from the oculomotor nuclei project anteriorly through the midbrain, passing through the red nucleus, then run adjacent to the substantia nigra and cerebral peduncle. The oculomotor nerve emerges from the ventral surface of the midbrain, where it passes between the superior cerebellar artery and the posterior cerebral artery. It is at this point that it is vulnerable to aneurysmal compression. Within the subarachnoid space, the nerve travels adjacent to the posterior communicating artery and the tip of the basilar artery, making a CN III deficit one of the ominous signs of aneurysm in this area. The oculomotor nerve continues to track anteriorly and enters the cavernous sinus and runs along the wall where it lies superior to CN IV. As the nerve exits the cavernous sinus, it passes through the superior orbital fissure and divides into superior and inferior branches. The superior branch provides motor function to the superior rectus and levator palpebrae, whereas the inferior branch provides motor function to the inferior rectus, medial rectus, inferior oblique, and the parasympathetic fibers for the ciliary ganglion.

Cranial nerve IV. The trochlear nerve (CN IV) innervates the superior oblique muscle (see Fig. 5). The dysfunction of this muscle is the most common cause of vertical strabismus. The superior oblique muscle depresses the eye in adduction and intorts the eye in abduction, making the deficit more apparent and exaggerating symptoms when the gaze is deviated downward and inward toward the affected side (Fig. 8). The nucleus is dorsal to the medial longitudinal fasciculus and inferior to the oculomotor nuclear

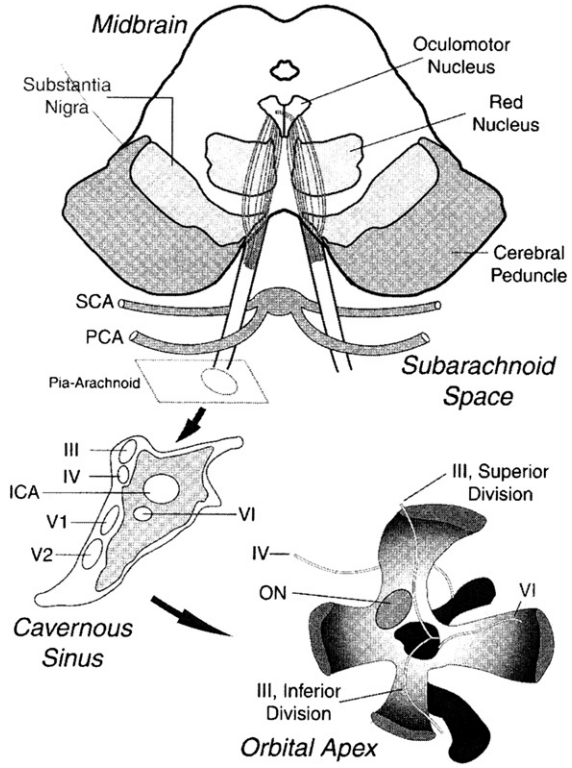


Fig. 7. Anatomy of the oculomotor nerve. The dotted lines depict the crossed fibers emanating from the superior rectus subnucleus. ICA, internal carotid artery; III, oculomotor nerve; IV, trochlear nerve; ON, optic nerve; PCA, posterior cerebral artery; SCA, superior cerebellar artery; VI, abducens nerve; V1, trigeminal nerve, ophthalmic division; V2, trigeminal nerve, maxillary division. (*From* Bennett JL, Pelak VS. Palsies of the third, fourth, and sixth cranial nerves. Ophthalmol Clin North Am 2001;14(1):169–85; with permission.)

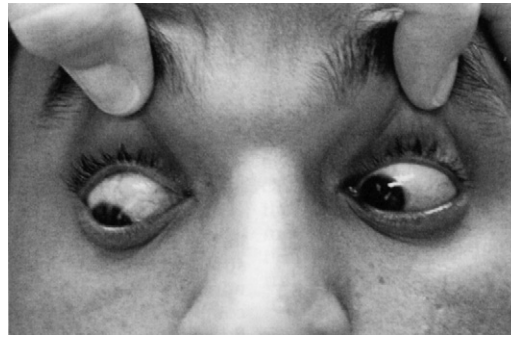


Fig. 8. Left fourth nerve palsy in a patient who had head trauma. There is a significant left hypertropia in down and right gaze. (*From* Bennett JL, Pelak VS. Palsies of the third, fourth, and sixth cranial nerves. Ophthalmol Clin North Am 2001;14(1):169–85; with permission.)

complex within the midbrain (Fig. 9). As the fascicles leave the nucleus, they course posteriorly and inferiorly, where they decussate in the superior medullary velum of the dorsal midbrain. It emerges at this point at the level of the inferior colliculus and runs within the subarachnoid space anteriorly, between the lateral midbrain and the tentorium cerebelli, between the superior cerebellar and posterior cerebral arteries. The trochlear nerve has the longest course outside of the midbrain. It courses around the cerebral peduncle as it enters the cavernous sinus, which makes it the most vulnerable cranial nerve to injury. Within the cavernous sinus, the trochlear nerve holds a position that is inferior to the oculomotor nerve and superior to the first division of the trigeminal nerve. The trochlear nerve then passes through the superior orbital fissure to enter the orbit and innervate the superior oblique muscle.

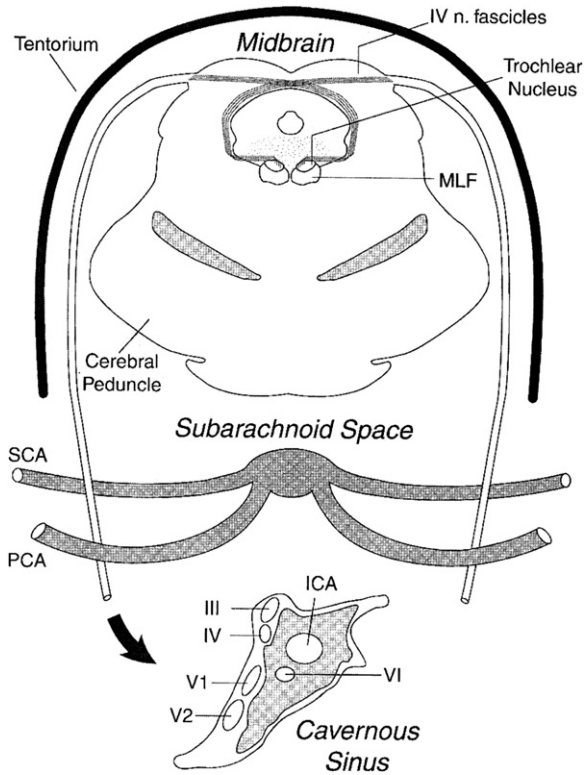


Fig. 9. Anatomy of the trochlear nerve. The speckled area demarcates the descending preganglionic sympathetic fibers. ICA, internal carotid artery; III, oculomotor nerve; IV, trochlear nerve; MLF, medial longitudinal fasciculus; PCA, posterior cerebral artery; SCA, superior cerebellar artery; VI, abducens nerve; V1, trigeminal nerve, ophthalmic division; V2, trigeminal nerve, maxillary division. (*From* Bennett JL, Pelak VS. Palsies of the third, fourth, and sixth cranial nerves. Ophthalmol Clin North Am 2001;14(1):169–85; with permission.)

Cranial nerve VI. The abducens nerve (CN VI) innervates the lateral rectus muscle (see Fig. 5). Paresis of this muscle results in binocular, horizontal diplopia that is worse in the direction of the affected side. Examination reveals an inability to abduct the affected eye on lateral gaze (Fig. 10). The abducens nerve fascicles originate in the dorsal pons, on the floor of the fourth ventricle, adjacent to the medial longitudinal fasciculus (MLF), paramedian pontine reticular formation (PPRF), and the fascicles of the facial nerve (CN VII). These fascicles are grouped to innervate the ipsilateral lateral rectus muscle and another group to innervate the contralateral medial rectus subnucleus by way of the MLF. The fascicles that course to the lateral rectus muscle project ventrally from the abducens nucleus and course through the tegmentum of the pons, where it emerges caudally. The nerve courses superiorly along the clivus to the level of the petroclinoid (Gruber) ligament, where it leaves the subarachnoid space and enters the Dorello canal and into the cavernous sinus. Within the cavernous sinus, the abducens nerve courses freely along with the carotid artery ventrally until it leaves the cavernous sinus and enters the orbit through the superior orbital fissure (Fig. 11). The abducens nerve is often the first deficit to be seen with cavernous sinus pathology because of its vulnerable position within the space.

Corneal reflex. The corneal reflex is accomplished by the afferent action of the ophthalmic branch of the trigeminal nerve (CN V_1) and the efferent action of the facial nerve (CN VII). When the cornea is touched, an impulse is sent by way of CN V_1 to the chief sensory nucleus of CN V, which is located in the rostral pons. Axons then project bilaterally to motor nucleus of CN VII, leading to coordinated eye closure with touch stimulation of CN V_1.

Conjugate eye movements. The coordination of eye movements in a determined direction is orchestrated by a supranuclear and internuclear pathway between the frontal eye fields and the contralateral side of the body. The

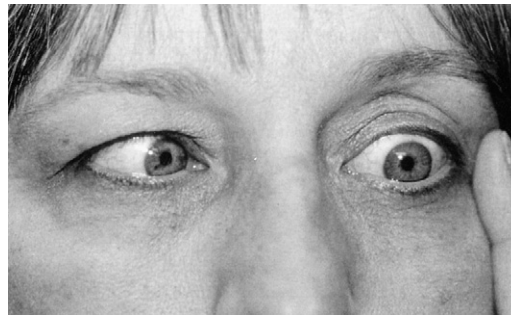


Fig. 10. Left abducens palsy caused by vasculopathic injury. There is a large angle esotropia in left lateral gaze. (*Data from* Bennett JL, Pelak VS. Palsies of the third, fourth, and sixth cranial nerves. Ophthalmol Clin North Am 2001;14(1):169–85.)

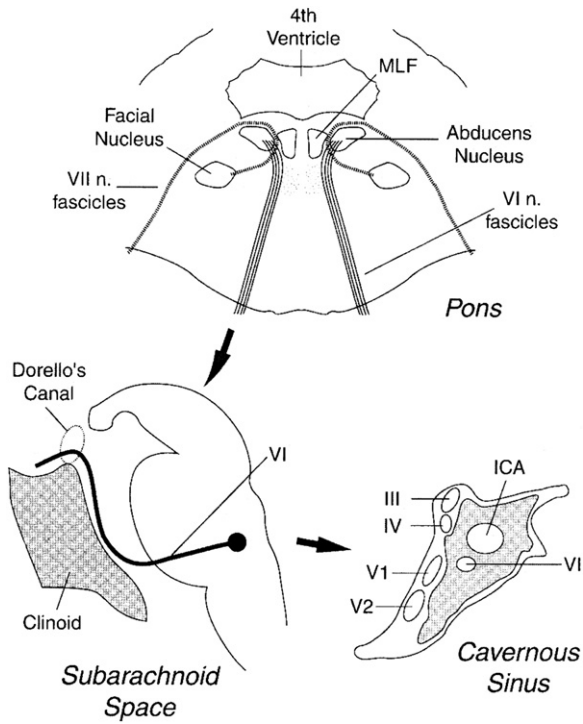
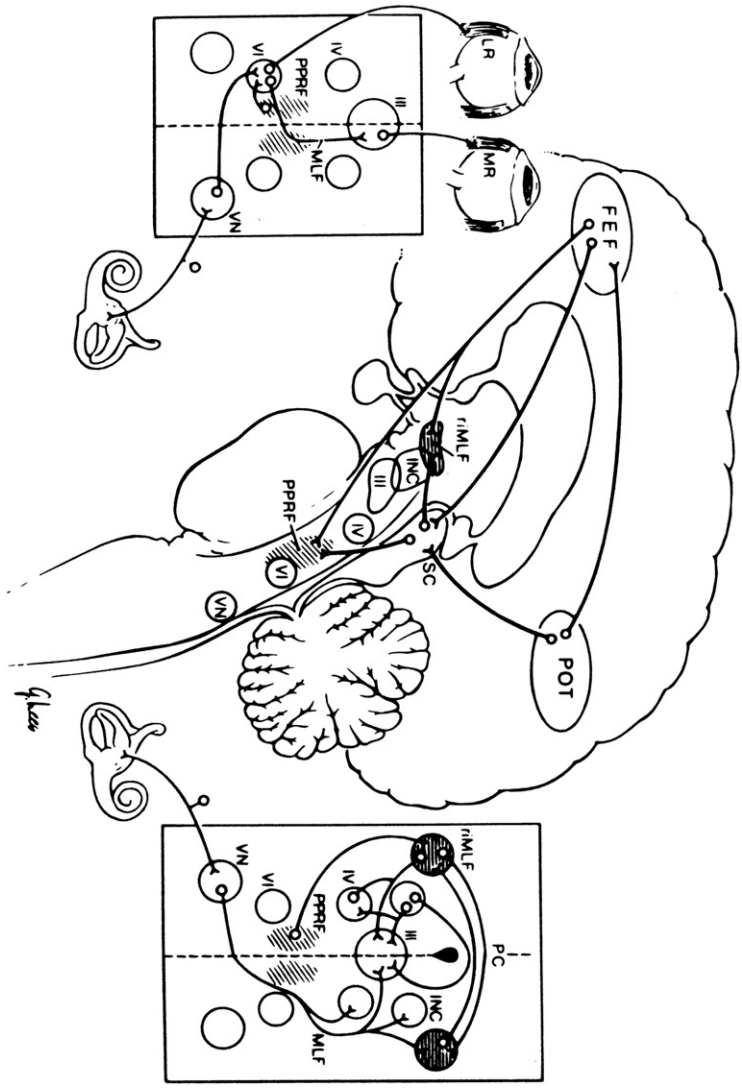


Fig. 11. Anatomy of the abducens nerve. The speckled area demarcates the paramedian pontine reticular formation. ICA, internal carotid artery; III, oculomotor nerve; IV, trochlear nerve; MLF, medial longitudinal fasciculus; VI, abducens nerve; V1, trigeminal nerve, ophthalmic division; V2, trigeminal nerve, maxillary division. (*Data from* Bennett JL, Pelak VS. Palsies of the third, fourth, and sixth cranial nerves. Ophthalmol Clin North Am 2001;14(1):169–85.)

frontal eye fields send a signal to the superior colliculus, the contralateral PPRF, and the rostral interstitial nucleus of the MLF (Fig. 12). Axons from the cell bodies in the PPRF project to the ipsilateral sixth nerve nucleus and synapse. Axons of the abducens motor nucleus travel to the ipsilateral lateral rectus muscle and axons from the abducens internuclear neurons cross over and ascend the contralateral MLF to the medial rectus subnucleus of the third cranial nerve. This internuclear connection between the PPRF of CN VI and the contralateral third nerve nucleus by way of the MLF allows for horizontal conjugate gaze. Distinction between sixth nerve palsies and lesions of the PPRF, or internuclear ophthalmoplegia (INO), can be distinguished by performing the oculocephalic (doll's eyes) maneuver or caloric testing. One of these maneuvers will overcome the ipsilateral horizontal gaze palsy if the sixth nerve is intact, whereas a PPRF lesion prevents the voluntary movement of the eye past midline.

The vestibulo-ocular system allows for stabilization of conjugate vertical and horizontal gaze. Inputs from each vestibular nucleus produce conjugate

horizontal gaze by sending signals to the contralateral sixth nerve nucleus, serving the lateral rectus muscle. Interneurons then cross back by way of the MLF ipsilateral to the vestibular nucleus to allow for horizontal gaze toward the contralateral size of the body (Fig. 13). Vertical gaze holding occurs through the contralateral fourth nerve nucleus, third nerve nucleus, INO, and MLF. Vertical alignment is maintained by coordination through the fourth nerve nucleus (contralateral superior oblique muscle) and the third nerve subnuclei (contralateral superior rectus muscle, ipsilateral inferior oblique muscle, and inferior rectus muscle).



Neuro-ophthalmologic examination

Visual acuity

Visual acuity is a vital part of the neuro-ophthalmologic examination. Any change in visual acuity should be noted. Please refer to the article by Robinett and Kahn elsewhere in this issue.

Visual fields

Testing the visual field is essential for the neuro-ophthalmology evaluation. The visual field of each eye should be assessed individually. The patient begins by covering one eye and fixating on the nose of the examiner. The patient should note any obvious differences in upper and lower face. Hemianopic defects can be detected in this manner. If the nose is not clear to the patient, he or she likely has a central scotoma. The patient should then count fingers in the four quadrants. Simultaneous presentations of fingers in two separate quadrants can increase the sensitivity of finding a visual field defect. If a defect is found, the hand should be moved from the defected field to the normal one to establish the boundaries of the defect. Recordings of the visual fields are taken from the patient's perspective. If the cap held off midline is a clearer red, a central scotoma is suggested. By mapping out the visual field defect, the location of the lesion can be isolated using the anatomy of the neuro-ophthalmic pathways (see Fig. 1).

Visual field defects may be associated with higher cortical functioning, such as neglect (parietal lesion) or visual agnosia. Neglect is present if a patient can perceive a single stimulus (such as a finger), but on introduction of a second stimulus, one stimulus is neglected. An example of visual agnosia is prosopagnosia, which is a condition in which the patient cannot recognize familiar faces. These defects should be distinguished from pure visual field defects.

Fig. 12. Summary of eye movement control. The center shows the supranuclear connections from the frontal eye fields (FEF) and the parieto-occipital-temporal junction region (POT) to the superior colliculus (SC), rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF), and the paramedian pontine reticular formation (PPRF). The FEF and SC are involved in the production of saccades, whereas the POT is believed to be important in the production of pursuit. The left shows the brainstem pathways for horizontal gaze. Axons from the cell bodies located in the PPRF travel to the ipsilateral sixth nerve (abducens) nucleus (VI) where they synapse with abducens motoneurons whose axons travel to the ipsilateral lateral rectus muscle (LR) and with abducens internuclear neurons whose axons cross the midline and travel in the medial longitudinal fasciculus (MLF) to the portions of the third nerve (oculomotor) nucleus (III) concerned with medial rectus (MR) function (in the contralateral eye). The right shows the brainstem pathways for vertical gaze. Important structures include the riMLF, PPRF, the interstitial nucleus of Cajal (INC), and the posterior commissure (PC). Note that axons from cell bodies located in the vestibular nuclei (VN) travel directly to the sixth nerve nuclei and, mostly by way of the MLF, to the third (III) and fourth (IV) nerve nuclei. (*From* Miller NR. Neural control of eye movements. In: Miller RN, editor. Walsh and Hoyt's Clinical Neuro-Ophthalmology. 4th edition. Baltimore (MD): Williams & Wilkins; 1985. p. 627; with permission.)

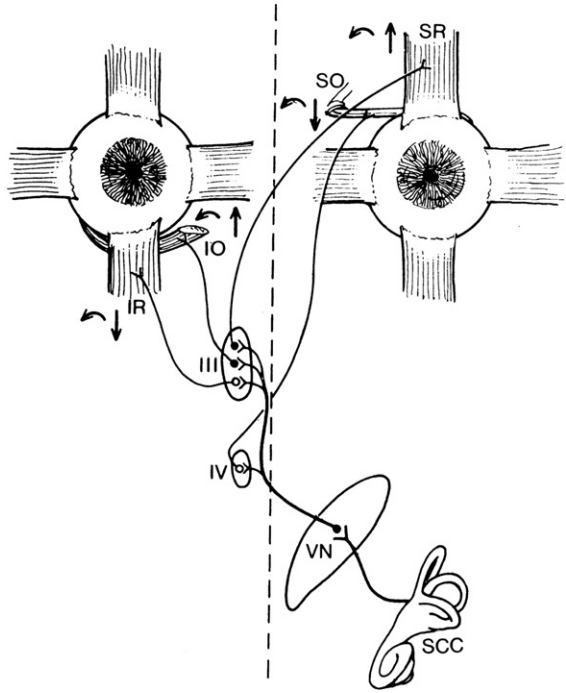


Fig. 13. The main excitatory vestibulo-ocular connections from the vertical semicircular canals. Dashed line, midline of the brainstem; arrows, directions of eye movement when individual extraocular muscles are stimulated; solid circles, receivers of the anterior canal projection; open circles, receivers of the posterior canal projection. Lesions occurring within these vestibulo-ocular pathways result in skew deviation. III, third nerve (oculomotor) subnuclei; IV, fourth nerve (trochlear) nucleus; IO, inferior oblique muscle; IR, inferior rectus muscle; SCC, semicircular canals; SO, superior oblique muscle; SR, superior rectus muscle; VN, vestibular nuclei. (*Adapted from* Zee DS. The organization of the brainstem ocular motor subnuclei. Ann Neurol 1978;14:384; with permission. Copyright © 1978. Reprinted with permission of John Wiley & Sons, Inc.)

Funduscopic examination

Evaluation of the visual pathway is not complete without a funduscopic examination. A swollen and elevated optic disc may be present in a patient who has papilledema. In other conditions, the optic disc may be pale and atrophic. The presence of spontaneous venous pulsations should be noted, which suggests that the intracranial pressure is not elevated. Getting a general sense of the condition of the retina can help guide a differential diagnosis for visual complaints (see the article by Robinette and Kahn elsewhere in this issue for a more complete discussion of the funduscopic examination).

Testing efferent and afferent pupillary innervation

Pupillary size is determined by the efferent dilating tone of the sympathetic nervous system and the efferent constricting tone of the parasympathetic

nervous system. The pupils should be assessed for size and reactivity to light with the patient's vision fixated on an object in the distance. The pupils should be round and equal in diameter, although 1 mm of inequality may be a normal variation. Direct response to light is assessed one eye at a time by bringing the light source from below to avoid triggering near reaction.

Near response is tested by having the patient look at an object, such as a pen, starting at 14 in away. The examiner should note the pupillary change as the object is drawn closer. Pupillary constriction indicates a response to convergence. An absent response to light with normal response to convergence suggests the presence of light-near dissociation. Argyll Robertson pupil is an example of this and is often seen in patients who have untreated syphilis or encephalitis that has damaged the pretectal area of the dorsal midbrain. These pupils also dilate with anticholinergic eye drops but do not constrict with light because of the damaged pretectal area.

Afferent pupillary defects (APD) are examined using the swinging flashlight test. Marcus Gunn pupil is an example of an APD in which the pupils do not react equally to light, indicating a disturbance in the anterior afferent visual pathway, including retina, optic nerve, chiasm, or optic tract. Ask the patient to fixate on an object at a distance. A light is directed in the pupil for 1 to 2 seconds and the light is moved rapidly across the bridge of the nose to the other eye and moved back in a rhythmic fashion to equally stimulate both eyes (Fig. 14). The pupillary size should be compared bilaterally. In the presence of an afferent pupillary defect, there is a paradoxic dilation in the affected eye as light is directed into it, despite a normal consensual response (Fig. 15). Afferent pupillary defects can also be uncovered indirectly in the setting of a third nerve palsy with a dilated pupil by shining a light in the affected eye and observing the response in the opposite eye. Adequate constriction in the opposite eye indicates an intact optic nerve in the interrogated eye, despite its lack of direct response. Another example of a tonically dilated pupil with intact optic nerve is Adie tonic pupil, a lesion of the ciliary ganglion, which holds the cell bodies for the postsynaptic parasympathetic fibers that allow pupillary constriction. The lesion is often unilateral and in the setting of a traumatic or postviral injury. At about 8 weeks past the initial insult, the accommodating fibers can regenerate and the pupil begins to act like a light-near dissociation with improvement in the patient's near vision.

The corneal reflex can be tested by touching the cornea lightly with the edge of a sterile piece of gauze. A lack of response indicates a deficit in the afferent fibers of CN V_1 or the efferent fibers of CN VII. Testing both corneas is important to reveal direct and consensual reflexes.

Testing ocular motility

The motility examination assesses the integrity of the supranuclear pathways, ocular motor nuclei and nerves, and the muscles they innervate. The examination should begin with eyelid examination, observing for asymmetry and lid retraction, which could suggest CN III palsy or thyroid disease,

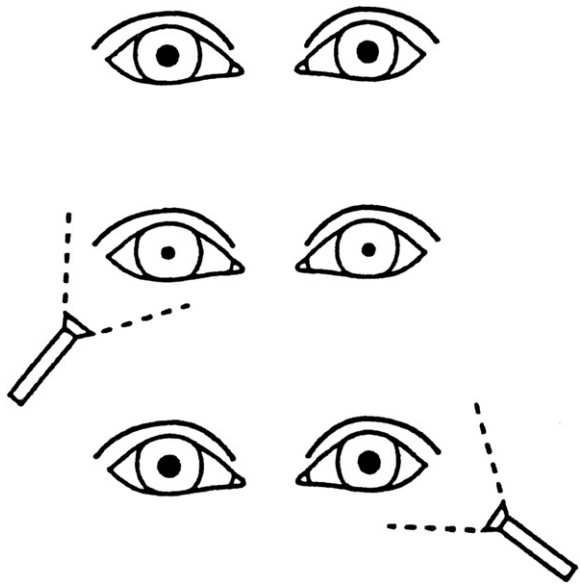


Fig. 14. The swinging flashlight test is used to test the integrity of the afferent visual pathway. In this example, the left optic nerve is not functioning properly, and there is a paradoxic dilation of the left pupil as the light is directed into it (left relative afferent pupillary defect). (*From* Wilhelm H. Neuro-ophthalmology of pupilary function–practical guidelines. J Neurol 1998;245:573–83; with permission.)

respectively. Myasthenia gravis is suggested when fatigable ptosis or Cogan lid twitch sign (transient improvement of lid function after sustained down gaze) is present. Ocular deviation is assessed from the neutral position and is classified as esotropia with inward displacement, exotropia with outward displacement, or hypertropia with vertical displacement. Corneal light reflex, in which a penlight is held directly in front of the patient, can be used to compare position as the light reflects off the cornea. Deviation is suggestive of strabismus, extraocular muscle dysfunction, or oculomotor nerve dysfunction.

Diplopia is often binocular, although monocular diplopia can be caused by early cataract formation or astigmatism and can be relieved by viewing through a pinhole device. Palsies of the third, fourth, or sixth cranial nerves or the muscles they innervate result in binocular diplopia, typical of paretic strabismus. In assessing a patient who has complaints of diplopia, it is important to establish whether the double vision is vertical, horizontal, or oblique, and determine in which direction the two images are most widely separated. The patient is then taken through the six cardinal fields of gaze to localize any involved nerve or muscle. This examination is usually done by asking the patient to follow an object, usually the examiner's finger, to the patient's upper right, upper left, lower left, lower right, right, and left,

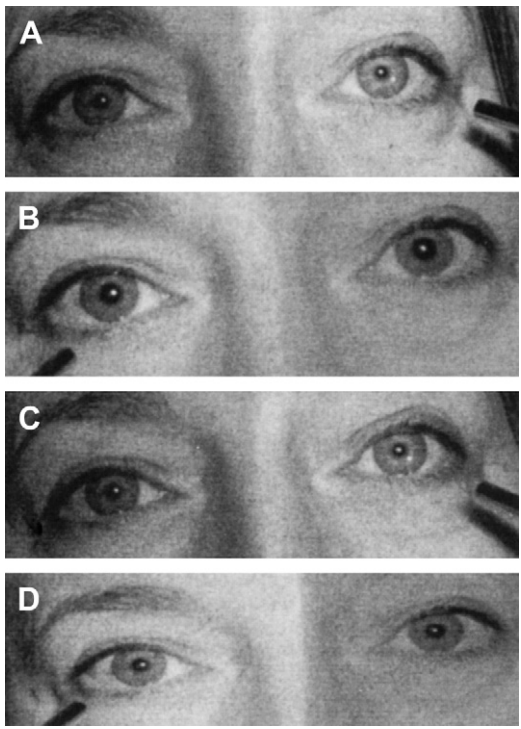


Fig. 15. The alternating light test in a patient who had a right optic neuropathy. (*A*) Patient is fixating a distant target while in dim room light. Light stimulation of the good left eye produces brisk, strong pupilloconstriction in both eyes. Clinically, the observer watches only the reaction of the illuminated pupil. (*B* and *C*) Light stimulation of the right eye produces lesser pupilloconstriction compared with light stimulation of the good left eye. (*D*) Rapid alternation of the light stimulus back to the bad right eye results in pupillodilation because that eye "sees" a relative decrement in light intensity. There is thus a relative afferent pupillary defect in the right eye. (*From* Kawasaki A, Kardon R. Disorders of the pupil. Ophthalmol Clin North Am 2001;14(1):149–68; with permission.)

returning to midline between each field. Any paralysis or weakness of the extraocular muscles can be isolated in this manner. Nystagmus is also observed if present in any of these six cardinal positions. Horizontal nystagmus usually indicates a lesion in the cerebellar or vestibular pathways, whereas downbeat nystagmus localizes to the cervicomedullary junction.

Saccades or fast eye movements are assessed by having the patient fixate on two targets, usually the examiner's nose and an eccentrically placed finger. Have the patient follow a swinging reflex hammer from side to side to test pursuit. Pursuit can also be assessed vertically by moving the reflex hammer up and down in a constant manner. Lastly, the vestibular ocular reflex (VOR) can be tested by having the patient fixate on the examiner's finger while rotating the head from side to side. A defective VOR results in catch-up saccadic eye movements.

Finally, a complete neurologic examination should be done on any patient in whom a neuro-ophthalmologic problem is suspected. Most lesions involving the optic tract, cranial nerves, or occipital lobe affect adjacent structures. These are manifest in physical examination findings consistent with pathology in those areas.

Pupillary disorders

Neurologic dysfunction of the pupils may be classified as an afferent or efferent defect based on the neuroanatomic site of the lesion. An afferent pupillary lesion refers to the retina, the optic nerve, chiasm, and tract, and the optic radiations. An efferent pupillary lesion refers to lesions of parasympathetic and sympathetic innervation, controlling constriction and dilation, respectively (see Fig. 3). Disorders of the pupils may also be defined by a clinical presentation, such as asymmetry of pupils, bilaterally abnormal pupil size, abnormal light reactivity, or deficits with other associated neurologic abnormalities. For the purposes of this article, we describe pupillary disorders by the defect and clinical presentation.

Pupil size and reactivity

Anisocoria

Anisocoria is defined as asymmetry of pupillary size. Physiologic, or simple, anisocoria occurs in about 20% of people [4,5]. The asymmetry is more prominent in dim light and rarely more than 1 mm. On examination, there is symmetric, rapid papillary constriction and dilatation. There has been no clear physiologic explanation, but it is believed to be attributable to an asymmetric supranuclear inhibition of the Edinger-Westphal parasympathetic nuclei in the pupilloconstrictor pathway [5].

Horner syndrome

Horner syndrome is classically described as ptosis, miosis, and anhidrosis. Ptosis and anhidrosis may be present to varying degrees, however, and may be clinically subtle (Fig. 16). When anisocoria is present and there is sluggish dilation of the miotic pupil, one should suspect Horner syndrome. The pupillary lag in dilation takes about 15 to 20 seconds, with the most prominent asymmetry at 4 to 5 seconds [5,6]. Normally, or in the case of physiologic anisocoria, there is no such lag and the pupils dilate with equal speed. Pupillary lag is present in about 50% of those who have Horner syndrome [5]. Ptosis is attributable to denervation of the tarsal muscles. The degree of ptosis is usually mild, partly because of compensation of the levator palpebrae and frontalis muscles. Anhidrosis is not always present, although its presence can be helpful diagnostically and usually implies an acute cause, because there is reinnervation of sweat glands in chronic cases. If Horner syndrome is present, localization of the lesion is the next step because the

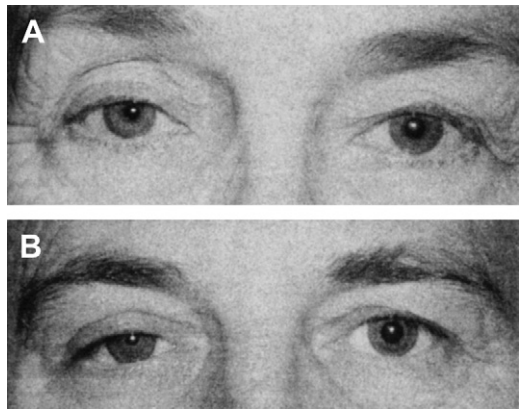


Fig. 16. (*A*) Right upper lid ptosis and ipsilateral miosis in a patient who had pseudo-Horner syndrome (levator dehiscence and simple anisocoria). (*B*) Right upper and lower lid ptosis and ipsilateral miosis in a patient who had true Horner syndrome (oculosympathetic defect). (*From* Kawasaki A, Kardon R. Disorders of the pupil. Ophthalmol Clin North Am 2001;14(1):149–68; with permission.)

differential is broad and ranges from benign to serious (Box 1). There should be a search for associated signs and symptoms to help localize the lesion. For instance, if anhidrosis is present over the entire body, this indicates a central lesion. If anhidrosis affects the face, neck, and arm only, there is a cervical lesion. Consultation with neurology or ophthalmology for pharmacologic tests (cocaine or hydroxyamphetamine provocation) may be necessary. For further localization, imaging is usually indicated.

Tonic (Adie) pupil

Another cause of a unilateral sluggishly reactive pupil is Adie, or tonic, pupil. Adie pupil is caused by degeneration of the ciliary ganglion, followed by aberrant reinnervation of the pupilloconstrictor muscles. On slit-lamp examination, segmental pupillary sphincter palsies may be appreciated. Most cases are idiopathic, with a minority of cases caused by ocular trauma or surgery, infections such as zoster, neoplasm, or ischemia from temporal arteritis. In general, a finding of a tonic pupil requires no further evaluation. In the elderly, however, giant cell arteritis should be considered because prompt therapy can slow visual loss, reduce the risk for contralateral eye involvement, and may restore vision [7]. Although corticosteroids have been the mainstay of treatment, a small, randomized, double-blinded trial showed that combination oral methotrexate and oral prednisone significantly reduces disease relapse compared with prednisone alone (Fig. 17) [8].

Pharmacotherapy and pupils

The sympathetic and parasympathetic innervation of the pupil (see Fig. 3) makes the response to certain pharmacologic agents predictable.

Box 1. Etiologies of Horner's Syndrome

Central
Hypothalamus/brainstem
- Ischemia
- Hemorrhage
- Demyelination

Cervical Cord
- Trauma
- Tumor
- Syrinx

Arteriovenous malformation

Preganglionic
Cervicothoracic Cord
- Trauma
- Intramedullary paravertebral tumor
- Syrinx
- Cord arteriovenous malformation
- Cervical spondylosis
- Epidural anesthesia

Lower brachial plexus
- Birth trauma
- Acquired trauma

Pulmonary apex/mediastinum
- Vascular anomalies of ascending aorta or subclavian artery
- Apical lung tumor (Pancoast)
- Mediastinal tumors
- Cervical rib
- Iatrogenic (eg, chest tube, cardiothoracic surgery)
- Infection (eg, apical tuberculosis)

Anterior neck
- Iatrogenic (eg, neck surgery, internal jugular/subclavian catheter)
- Trauma
- Tumor (eg, thyroid, lymphoma)

Postganglionic
Superior cervical ganglion
- Trauma
- Jugular venous ectasia
- Iatrogenic (eg, ganglionectomy, tonsillectomy)

Internal carotid artery
- Dissection
- Trauma

Thrombosis
Tumor
Migraine/cluster
Skull base/carotid canal
Trauma
Tumor (eg, nasopharyngeal carcinoma)
Cavernous sinus
Tumor (eg, meningioma, pituitary adenoma)
Inflammation
Carotid aneurysm
Carotid-cavernous fistula
Thrombosis

Data from Kawasaki A, Kardon R. Disorders of the pupil. Ophthalmol Clin North Am 2001;14(1):158.

Pharmacologic dilation can result with sympathomimetics and with parasympatholytics. Mydriasis by way of sympathomimetics occurs through alpha-adrenergic stimulation with agents, such as phenylephrine, ephedrine, and naphazoline, found in over-the-counter and prescription eye drops. Parasympatholytics, mainly anticholinergic agents, such as scopolamine, tropicamide, cyclopentolate, and bronchodilating inhalers, also cause pharmacologic mydriasis. These give anisocoria that is most pronounced in bright light in the case of ophthalmic application. There may still be

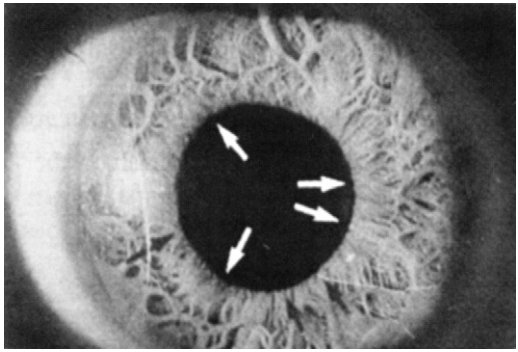


Fig. 17. A slit-lamp view of a 33-year-old man who had Adie tonic pupil. The white arrows are pointing to sectors of the sphincter that are contracting well, and the dark arrows indicate areas in which the iris sphincter is weak. Notice that the curvature of the pupillary margin is usually tighter in the sections that are functional and flatter in the palsied parts. (*From* Kardon RH, Thompson HS. The pupil. In: Rosen ES, Eustace P, Thompson HS, et al, editors. Neuro-ophthalmology. London: Mosby International Limited; 1998. p. 13.1–9; with permission.)

constriction to bright light with these agents. Pharmacologic constriction mainly occurs through cholinergic drugs, such as pilocarpine. Glaucoma ophthalmic drops, such as brimonidine, also cause pupillary constriction. There is more pronounced anisocoria in dim light in these instances.

Relative afferent pupillary defect

Any unilateral or asymmetric decreased afference of the optic nerve may manifest as a relative afferent pupillary defect (RAPD). An RAPD should not be assumed to be caused by a media disturbance (ie, cataracts) because light flashed directly into the pupil is still scattered onto the macula [6]. One exception may be a dense intraocular hemorrhage, which is generally not diagnostically elusive. Optic nerve disease also presents as a deficit in visual sensory function and possibly a change in the appearance of the optic disc. Optic neuropathies are caused by a myriad of processes and differentiating these causes is difficult (Table 1). The history may be the most helpful tool in narrowing the differential.

Preservation of visual acuity or preventing further visual loss is the goal of management. Determining which patients need emergent intervention may require further testing and consultation with an ophthalmologist, depending on the history and physical examination findings.

Traumatic optic neuropathy

Patients who present with an RAPD after trauma must be presumed to have optic nerve injury. Penetrating trauma requires prompt ophthalmologic evaluation and consultation for possible surgical intervention and

Table 1
Conditions producing relative afferent pupillary defect

Condition	Site
Intraocular hemorrhage	Anterior chamber or vitreous (dense or diffuse)
Intraocular hemorrhage	Preretinal
Central serous retinopathy	Retina (fovea)
Cystoid macular edema	Retina (fovea)
Central or branch retinal vein occlusion	Inner retina
Central or branch retinal artery occlusion	Inner retina
Retinal detachment	Outer retina
Anterior ischemic optic neuropathy	Optic nerve head
Optic neuritis—acute	Optic nerve
Optic neuritis—recovered	Optic nerve
Compressive optic neuropathy	Optic nerve
Chiasmal compression	Optic chiasm
Optic tract lesion	Optic tract
Postgeniculate damage	Visual radiations, visual cortex
Midbrain tectal damage	Olivary pretectal area of pupil, midbrain

Data from Kawasaki A, Kardon RH. Disorders of the pupil. Ophthalmol Clin North Am 2001;14(1):166.

a search for foreign bodies. In addition to careful examination, these patients should undergo CT scanning and tetanus prophylaxis, and be placed on systemic antibiotics [9,10]. Indirect trauma, from concussive forces, can result in shearing forces that result in mechanical and ischemic damage to the optic nerve. This type of traumatic optic nerve injury is much more common. The treatment of this type of injury is less well studied. In the International Optic Nerve Trauma Study, there was no clear benefit on visual acuity for treatment with corticosteroids, decompression surgery, or observation alone [11]. This conclusion should be taken in the context of the study design, however. This study was non-randomized, uncontrolled, unblinded, and retrospective, making the conclusions weakly generalizable.

Optic neuritis

Optic neuritis refers to inflammatory optic neuropathies, but more specifically to those neuropathies in which demyelination is predominant (idiopathic or secondary to multiple sclerosis [MS]). Optic neuritis is mainly a clinical diagnosis. Patients generally present with monocular visual deficits associated with periorbital or ocular pain. The pain may precede or present concurrently with the vision loss. Eye pain is present in 92% of patients and is almost universally worsened by eye movement [12–14]. There may also be decreased color perception or central scotoma. The optic disc has a normal presentation in about 70% of patients initially, because the inflammatory process is usually posterior to the optic disc [4,13]. Optic disc swelling and, less commonly, flame-shaped hemorrhages at or near the disc may be present, however. RAPD is usually seen, but may be subtle, requiring advanced ophthalmologic evaluation. MRI imaging of the brain is helpful diagnostically and prognostically but is not always needed emergently. In those who have monocular optic neuritis, there is a 50% incidence of MS if the initial MRI shows at least three typical white matter lesions. Conversely, the 5-year incidence of MS drops to 15% if the MRI is normal [14]. Consultation with an ophthalmologist is important. If the examination shows a macular star figure, this represents an infectious cause. In general, further investigation with chest radiograph, anti-nuclear antibody, or testing for syphilis are generally noncontributory in the emergency department setting and not recommended for evaluation in the patient who has typical optic neuritis [12,14]. Emergency physicians should be aware of more recent treatment recommendations based on the Optic Neuritis Treat Trial data [14–16]. Oral prednisone was associated with an increased incidence of recurrent optic neuritis in a 5-year follow-up period and was no better than placebo in improvement of visual outcomes. Intravenous methylprednisolone (over 3 days followed by a prednisone taper) was associated with faster recovery in visual function if given within 8 days of symptom onset. The difference in benefit seems to wash away after about 6 months. There is no current convincing data on the use of immunoglobulin or plasma exchange therapy in optic neuritis [13].

Oculomotor nerve palsy

Pupillary disorders may occur in the context of a third nerve lesion as discussed in the next section.

Extraocular movement disorders

Cranial nerve palsies and binocular diplopia

There are three cranial nerves involved in controlling the six extraocular muscles, the oculomotor nerve (III), the trochlear nerve (IV), and the abducens nerve (VI). The eyes have equal and opposed actions of the muscles of extraocular movement, which are in turn coordinated by supranuclear control to produce conjugate and divergent gaze. These supranuclear controls consist of brainstem gaze centers and cortical input. When there is a disruption of extraocular muscle function, the eye is unable to move in the direction of the action of the affected muscle (ie, ophthalmoplegia). Palsies of the extraocular muscles commonly present as binocular diplopia because the images fall on a different region of each retina. It is important to identify associated signs and symptoms and establish in which gazes double vision occurs to determine which cranial nerves are affected. During the examination, all six cardinal positions of gaze should be tested, not only for muscle palsies but also to see if diplopia is elicited. The examiner may use a light source to see if the light falls on the same spot on both corneas in each position of gaze, which determines which cranial nerves are affected. The most common palsy is a sixth nerve palsy, followed by third nerve and fourth nerve palsies. Involvement of multiple cranial nerves is the least common presentation [17,18].

In this section, we divide the causes of binocular diplopia by each cranial nerve, and then neuroanatomically for each cranial nerve. When presented with diplopia, the emergency physician should determine which cranial nerves are affected. This determination may help in formulating a differential diagnosis and the urgency of such a presentation.

Cranial nerve III

The oculomotor nerve innervates the medial, superior, and inferior rectus, the inferior oblique, the levator palpebrae, and the parasympathetic pupillary constrictors. There is ptosis, pupillary dilation, and lateral deviation from unopposed action of the lateral rectus in a complete CN III lesion (see Fig. 6). The patient reports diplopia in all directions of gaze except on lateral gaze to the affected side. This discussion focuses on lesions according to their location: brainstem (nuclear and fascicular), subarachnoid, cavernous sinus, orbital apex, and neuromuscular lesions. Despite the wide differential, urgent evaluation is generally warranted for a patient presenting with new third nerve palsy, because this may herald serious diseases, such as brainstem infarction, aneurysm, and neoplasm. Vascular causes are the most common

known causes of oculomotor nerve palsy, whereas aneurysms are the second most common. Usually, the cause is never determined (Table 2) [17].

Brain stem lesions. Brainstem oculomotor lesions classically present with bilateral ptosis and contralateral superior rectus and ipsilateral oculomotor paresis. This presentation occurs because the levator palpebrae are innervated by an unpaired central nucleus and the superior recti are innervated by contralateral subnuclei. The most common cause is ischemia [19]. The patient should thus undergo a stroke evaluation with appropriate accompanying management. Besides mass lesions, compression, and inflammation, other causes for higher-order third nerve palsies are Wernicke encephalopathy and progressive supranuclear palsy. In Wernicke encephalopathy, the third nerve ophthalmoplegia is usually bilateral and is associated with a history of chronic alcohol use or malnutrition, ataxia, nystagmus, and altered mentation. There may be ophthalmoplegia because of involvement of CN

Table 2
Lesions of the oculomotor nerve

Anatomic location	Cause	Associated symptoms
Nuclear	Infarction, mass, infection, inflammation, compression	Bilateral ptosis and paresis of the contralateral superior rectus; lid function may be spared
	Wernicke-Korsakoff syndrome	Ataxia, abducens palsy, nystagmus, altered mentation
Fascicular	Infarction, mass, infection, inflammation, compression	Contralateral hemiparesis or tremor; pupil may be spared
	Demyelination	
Subarachnoid space	Aneurysm	Headache, stiff neck, pupil-involved
	Vasculopathic	Pupil generally spared
	Meningitis	Headache, CN involvement, meningismus, fever
	Miller-Fisher syndrome	Areflexia, ataxia, previous viral illness
	Migraine	Headache, family history
	Uncal herniation	Early pupil involvement, altered mentation, ipsilateral hemiparesis
Cavernous sinus	Neoplasm	Cavernous sinus syndrome, pain, sensory changes, ± sympathetic involvement
	Fistula	Exophthalmos, bruit, chemosis
	Thrombosis	Previous infection/trauma, pain, exophthalmos, chemosis
Superior orbital fissure	Neoplasm	Superior division involvement
Neuromuscular junction	Myasthenia gravis	No pupil involvement, frequent fluctuation, ptosis, ophthalmoparesis, orbicularis oculi weakness, dysarthria

Data from Bennett JL, Pelak VS. Palsies of the third, fourth, and sixth cranial nerves. Ophthalmol Clin North Am 2001;14(1):173.

IV and VI also. Progressive supranuclear palsy is an idiopathic degenerative disease that mainly affects the subcortical gray matter regions of the brain in older men. The ocular manifestations are ophthalmoplegia in all directions, although initially more severe with voluntary vertical gaze. This disease is also associated with dementia, decreased facial expression, pseudobulbar palsy, and axial dystonia. These patients should have routine follow-up with a neurologist. Although prognosis is poor, quality of life may be improved with multidisciplinary symptom management [20].

Subarachnoid lesions. The subarachnoid segment of CN III is that section after the nerve leaves the midbrain and before it enters the cavernous sinus (Fig. 18). Lesions generally present as unilateral ptosis and third nerve paresis, with or without pupillary dilation. A search for associated signs and symptoms is helpful because there are many causes of lesions of this portion of the oculomotor nerve, including meningitis, migraines, Miller-Fisher variant of Guillian-Barre, vasculopathy, uncal herniation, and aneurysm. The nerve travels near the junction of the internal carotid and posterior communicating artery and between the posterior cerebral and the superior cerebellar arteries, and is thus susceptible to compression from aneurysms. In fact, about 30% of oculomotor palsies are from aneurysms, most

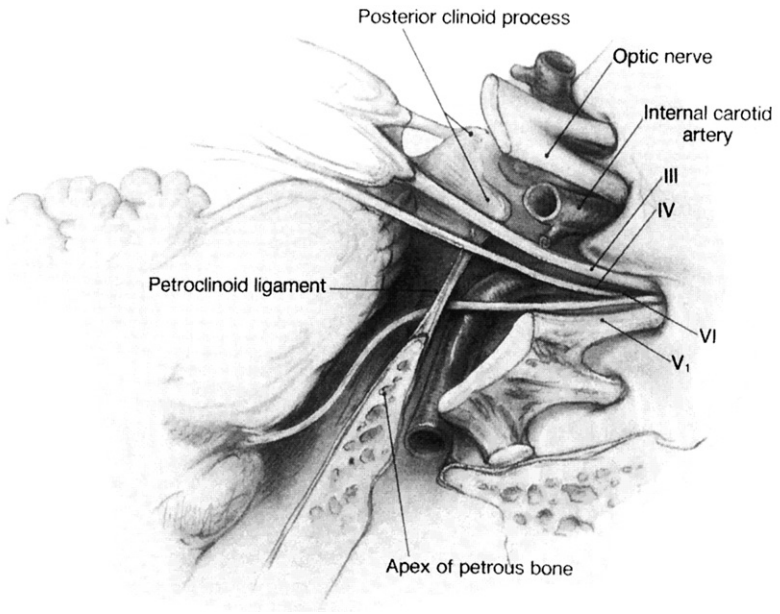


Fig. 18. Subarachnoid and intracavernous courses of the third, fourth, and sixth cranial nerves. (*From* Porter JD, Baker RS. Anatomy and embryology of the ocular motor system. In: Miller NR, Newman NJ, editors. Walsh and Hoyt's clinical neuro-ophthalmology. 5th edition. Baltimore (MD): Williams & Wilkins; 1998. p. 1066; with permission.)

commonly from the posterior communicating artery [21]. A third nerve palsy may also result from aneurysms of the basilar, superior cerebellar, and posterior cerebral arteries. The aneurysm causes oculomotor paresis by compression of the nerve. Parasympathetic fibers travel in the periphery of the subarachnoid portion of the nerve, with the motor fibers centrally located. Oculomotor involvement from an aneurysm commonly causes pupillary dilation. Aneurysm is extremely unusual if there is not pupillary involvement in the presence of a complete palsy [21]. CT angiography is the study of choice for noninvasive diagnosis of unruptured aneurysms, with sensitivities ranging from 85% to 90% for aneurysms larger than 5 mm and 79% for aneurysms smaller than 5 mm [22]. MR angiography is an alternative, able to detect aneurysms as small as 3 mm. It is not as sensitive, however, especially for aneurysms smaller than 5 mm [19,21,22]. CT scan with or without lumbar puncture should be undertaken if aneurysmal rupture with subarachnoid bleed is suspected. Definitive treatment includes surgical clipping or endovascular coil placement.

Migraine headache variants, such as cranial neuralgias and ophthalmoplegic migraine, present with ocular and pupillary dysfunction. This diagnosis usually requires the exclusion of other, more serious disease processes. Presentations supportive of a migraine diagnosis are a previous history of migraines, especially with childhood onset, aura, typical positive and negative visual phenomena (scotoma, transient visual distortions), and migrainelike headache. The International Headache Society requires at least two attacks of a migrainelike headache accompanied or followed by oculomotor paresis within 4 hours, not attributed to other disorders, for diagnosis of ophthalmoplegic migraine [23]. This condition is rare and usually presents in the pediatric population [24]. The ophthalmoplegia is usually transient but rarely may become permanent. Consultation with a neurologist is important because acute treatment with corticosteroids has been shown to provide relief and may prevent a permanent deficit [23,25].

Cavernous sinus lesions. Diplopia may be the presenting symptom of a cavernous sinus fistula, seen in about 60% to 70% of cases [21]. These fistulas are abnormal communications between the cavernous sinus and the carotid artery, usually the result of trauma, but also occur as a complication of surgery or after rupture of a cavernous carotid artery aneurysm. They typically present days to weeks after traumatic head injury with conjunctival chemosis, proptosis, and a cranial bruit, either subjective or objective. Conjunctival chemosis occurs from the arterialization of the conjunctival veins. Proptosis occurs from the arterialization of the orbital veins and edema of the orbital tissue. Pulsating exophthalmos may be visually or palpably appreciated on examination, and occurs in about 95% of cases [21]. Diplopia occurs through compression or ischemia of the ocular nerves by the fistula itself. Most commonly CN VI is involved, although ophthalmoplegia may be attributable to any combination of ocular nerve involvement. Definitive diagnosis

requires arteriography with selective injection of the internal and external carotid arteries, although CT and MR imaging may be suggestive of a fistula and can help exclude other disease processes. Visual loss may be delayed or immediate and is the main morbidity associated with this condition, occurring in up to 90% of cases. Other complications include intracranial or subarachnoid hemorrhage, venous infarction, and epistaxis, although life-threatening sequelae are rare [21]. Addressing these high-flow carotid-cavernous fistulas usually requires urgent treatment.

Superior orbital fissure lesions. The most common cause of a third nerve palsy from a superior orbital fissure lesion is a neoplasm. When vision is affected, the lesion is almost always in the orbital apex [19]. Other associated signs include conjunctival injection and chemosis, proptosis, and lid swelling. CN IV, CN VI, and also CN V_1 may be involved because of their proximity to one another. MR imaging is the modality of choice, keeping in mind that the most common cause is a neoplasm. CT may have a role, but early in the growth of a tumor the neoplasm may be isodense with normal brain tissue.

Neuromuscular disease. Neuromuscular disease, such as myasthenic syndromes, may mimic isolated nerve palsies. There is a separate discussion later in this article.

Cranial nerve IV

Trochlear nerve palsy presents with paresis of the superior oblique muscle. The function of this muscle is tested in isolation with downward gaze with the eye adducted, which is the position of gaze that elicits the most pronounced diplopia. The involved eye is elevated in neutral position and the degree of elevation is increased with adduction and decreased with abduction (see Fig. 8).

A lesion causing a fourth nerve palsy can also occur anywhere along the path of the nerve, from the nucleus to the superior oblique muscle. Determining where the lesion lies may be difficult, requiring a search for associated, or absent, symptoms and signs along with neurologic consultation and imaging. For instance, association with an oculomotor palsy strongly suggests a cavernous sinus lesion. Most fourth nerve palsies have no known cause, but of the known causes, most are attributable to head trauma. Vasculopathies are the next most common cause (Table 3) [17,26].

Brain stem lesions. Nuclear and fascicular lesions of the fourth cranial nerve present as a contralateral superior oblique palsy because of the crossing of the fascicles in the brainstem. They may be caused by ischemia, trauma, inflammation, a mass, or in the case of a fascicular lesion, MS. There are usually other associated neurologic findings attributable to involvement of nearby structures. The periaqueductal gray matter carries sympathetic

Table 3
Lesions of the trochlear nerve

Anatomic location	Cause	Associated symptoms
Nuclear	Infarction	Internuclear ophthalmoplegia, Horner syndrome, relative afferent pupillary defect
	Trauma, tumor, infection, inflammation	As above
Fascicular	Infarction	As above
	Trauma, tumor, infection, inflammation	As above
	Demyelination	Isolated or with midbrain signs above
Subarachnoid space	Trauma, hydrocephalus	May be bilateral
	Vasculopathic	Usually isolated
	Mass lesion	Contralateral hemiparesis or ipsilateral ataxia
Cavernous sinus	As with third nerve palsy	Cavernous sinus syndrome
	Herpes zoster ophthalmic	Rash, trigeminal sensory loss V1 or V2 distribution
Orbit	Inflammation, trauma, tumor	Oculomotor, abducens, optic nerve dysfunction, proptosis

Data from Bennett JL, Pelak VS. Palsies of the third, fourth, and sixth cranial nerves. Ophthalmol Clin North Am 2001;14(1):180.

fibers. There may thus be a preganglionic Horner syndrome. The medial longitudinal fasciculus is just anterior to the nucleus and a lesion affecting this causes an internuclear ophthalmoplegia. Evaluation for a nuclear trochlear nerve lesion should include MR imaging and a stroke workup [5].

Subarachnoid lesions. The trochlear nerve has a relatively long subarachnoid course after it leaves the brainstem posteriorly, which makes it susceptible to trauma, the most common cause of a fourth nerve palsy [17,26]. The trauma may cause unilateral or bilateral isolated trochlear nerve palsy. Other causes of fourth nerve palsies in the subarachnoid space are meningitis, aneurysm of the superior cerebellar artery, schwannoma, and small vessel infarction [17,19,26]. Work-up includes MR imaging to rule out a mass lesion, detect the extent of trauma, and direct any possible neurosurgical intervention.

Distal nerve lesions. Just as with third nerve palsies, orbital fissure lesions and neuromuscular lesions may produce a fourth nerve palsy. A nonneurologic entity that may mimic isolated trochlear nerve palsy is Brown superior oblique tendon syndrome, likely caused by a tenosynovitis or scarring of the superior oblique tendon. The superior oblique tendon is prohibited from free movement through the trochlear pulley. There is inhibition with a forced duction test where the entrapped muscles resist forced movement, indicating mechanical trapping of the superior oblique muscle. Referral to an ophthalmologist is required because surgery may be the best option for the patient.

Cranial nerve VI

Of the three cranial nerves involved in extraocular movement, the abducens nerve is the most commonly affected [17]. A unilateral sixth nerve lesion results in diplopia on lateral gaze, attributable to paresis of the lateral rectus muscle. In neutral position, the affected eye is adducted and fails to abduct with examination (see Fig. 10). Similar to the third and fourth cranial nerve, lesions of the sixth cranial nerve can be subdivided anatomically with some distinguishing features associated with each lesion. The most commonly determined cause for a sixth nerve palsy is a neoplasm, most often metastatic disease or a meningioma, followed by head trauma and vascular disease (Table 4) [17].

Brainstem lesion. A nuclear sixth nerve lesion produces conjugate, horizontal gaze palsy toward the side of the lesion. Nuclear lesions of the abducens nucleus rarely present with an isolated ophthalmoplegia, however. These lesions are associated with damage to the surrounding brainstem structures, such as the facial nerve nucleus, the pontine lateral gaze centers, and the reticular activating system. There may thus be facial weakness, impaired conjugate gaze, and depressed level of consciousness, respectively. The sixth cranial nerve has two projections, one to the ipsilateral lateral rectus and the other to the contralateral CN III nucleus by way of the MLF (see Fig. 12). A pontine lesion involving the adjacent MLF and the pontine lateral gaze centers produces a one-and-a-half syndrome, seen as a complete gaze palsy

Table 4
Lesions of the abducens nerve

Anatomic location	Cause	Associated symptoms
Nuclear	Infarction	Ipsilateral facial paralysis, INO
	Infiltration, trauma, inflammation	
	Wernicke-Korsakoff	Ataxia, nystagmus, altered mentation
Fascicular	Infarction, tumor, inflammation, MS	Ipsilateral facial nerve paralysis and contralateral hemiplegia
	Anterior inferior cerebellar artery infarction	Ipsilateral facial paralysis, loss of taste, ipsilateral Horner, ipsilateral trigeminal dysfunction, and ipsilateral deafness
Subarachnoid	Mass	Contralateral hemiparesis
	Ischemia	Usually isolated
	Trauma	Papilledema, headache
	Intracranial hypertension or hypotension	Headache
Petrous apex	Mastoiditis, skull fracture, lateral sinus thrombosis, neoplasms, tumor	Ipsilateral facial paralysis, severe facial pain
Cavernous sinus	As with third nerve palsy	Cavernous sinus syndrome

Data from Bennett JL, Pelak VS. Palsies of the third, fourth, and sixth cranial nerves. Ophthalmol Clin North Am 2001;14(1):180.

in one direction and a unilateral (half) gaze palsy in the other direction. The lesion to the MLF causes an internuclear ophthalmoplegia and the lesion to the pontine lateral gaze center causes a conjugate gaze palsy to the side of the lesion. Attempted gaze away from the lesion activates the unaffected contralateral lateral gaze center and abducens nucleus but with paresis of ipsilateral adduction. On gaze toward the lesion, neither eye can effectively move laterally, because the pontine lateral gaze center cannot be activated. The most common causes of a one-and-a-half syndrome include pontine infarct, pontine hemorrhage, and multiple sclerosis. Wernicke encephalopathy may present with a nuclear sixth nerve palsy. If a nuclear abducens nerve lesion is suspected, the patient should undergo MR imaging and a stroke workup, because infarction may be the cause of such a lesion.

Subarachnoid lesions. The sixth cranial nerve has a unique course in the subarachnoid space. It emerges from the brainstem just between the pons and the medulla and courses just lateral to the basilar artery and just posterior to the clivus in the prepontine cistern before entering the cavernous sinus. This course makes it susceptible to injury from trauma and changes in intracranial pressure (ICP). The nerve may be compressed between the pons and the basilar artery or the clivus. In addition to MR imaging, the patient may require evaluation for elevated or diminished ICP.

Aneurysms of the basilar artery, and less commonly of the anterior and posterior inferior cerebellar arteries, and the vertebral arteries can produce a sixth nerve palsy. Sixth nerve palsy from an aneurysm is less common than a third nerve palsy [21]. Diagnosis and management have been mentioned previously.

Cavernous sinus lesions. Ophthalmoplegia may be the presenting symptom of a cavernous sinus thrombosis, usually affecting all the extraocular muscles. These occur from trauma, but more commonly from infection. CN VI is usually affected first, however, because it lies freely within the sinus and not within the lateral walls of the sinus as CN III and CN IV do [19,27]. Besides headache, which is present in about 90% of cases, the most common accompanying signs are fever, ptosis, proptosis, and chemosis, occurring in 80% to 100% of infectious cases [19,27,28]. Periorbital swelling and papilledema only occur in 50% to 80% of cases [27]. MRI with MR angiography is the most sensitive noninvasive modality, approaching 100% sensitivity for all types of sinus thromboses in small studies [28,29]. Another promising diagnostic option is CT venography, but more study is required [27]. The gold standard is angiography, although its diagnostic use has dramatically declined. Therapeutically, cavernous sinus thromboses may be treated with anticoagulation and antibiotics, in addition to supportive measures and management of elevated intracranial pressures. There are no rigorous, large trials on the use of anticoagulation in venous sinus thrombosis. A recent prospective observational study showed that more than 80% of the

624 patients received anticoagulation with a good safety profile [30]. The outcomes were fairly encouraging in this subgroup, with only 5% rated as severely handicapped and 8% having died. In cases of septic cavernous sinus thrombosis, broad-spectrum antibiotics should be given. The most common offending organism is *Staphylococcus aureus*, and less commonly streptococcus, gram-negative bacilli, and anaerobes [27]. Surgical drainage of the sinus thrombosis is rarely performed, although decompression of a hemorrhagic infarction may be indicated.

Nystagmus

Nystagmus is rhythmic oscillation of the eyes. To detect nystagmus, the eyes should be observed in primary position and each of the six positions of gaze. Nystagmus is described by the position in which it occurs, precipitating factors, such as head position, and the direction of the fast phase. It is useful to classify nystagmus as physiologic or pathologic, and subdivide the pathologic causes as peripheral or central.

Physiologic nystagmus occurs normally at the extremes of gaze. In this instance a clear image is preserved as reflexes reset the position of the eyes and prevent the image from slipping on the retina [31]. These reflexes are collectively known as the slow eye movement system. Their function is to maintain clear vision with a quick corrective saccade, resulting in nystagmus. Pathologic nystagmus is usually accompanied by vertigo, oscillopsia, nausea, gait disturbance, and other symptoms depending on the cause. The patient may complain of oscillopsia, a sensation of oscillation of the environment in the direction of the fast phase.

Peripheral nystagmus

In general, pathologic peripheral vestibular causes of nystagmus and vertigo are less worrisome and less emergent than central causes. The nystagmus from vestibular causes usually has a combined horizontal and torsional component, which can be inhibited by visual fixation onto an object. The horizontal component does not change direction with gaze (unidirectional). Nausea, vomiting, auditory symptoms, and vertigo are significant components of the presentation. Vertical nystagmus may be present in addition to horizontal nystagmus, but is far less common in peripheral causes. Vertical nystagmus has been shown to be about 80% sensitive for central causes of vertigo in a small prospective trial (Table 5) [32].

A common emergency department presentation of horizontal nystagmus is benign paroxysmal positional vertigo (BPPV). BPPV presents with a combined horizontal and torsional nystagmus and vertigo on provocation with the Dix-Hallpike maneuver. The nystagmus lasts for less than 1 minute, and fatigues on repeated testing. It has a positive predictive value of 83% and negative predictive value of 52% for BPPV. If the induced nystagmus is vertical, and not preceded by a latency, or does not fatigue with repeated

Table 5
Peripheral versus central nystagmus

Feature	Peripheral	Central
Direction of nystagmus	Horizontal/torsional	Pure vertical, pure torsional, or mixed
Visual fixation	Inhibits nystagmus	No inhibition
Severity of vertigo symptoms	May be severe	Usually mild
Associated eye movements	None	May have pursuit or saccadic defects
Other findings	Hearing loss	May have other CN or long tract signs

Data from Moster, ML. Nystagmus. Ophthalmol Clin North Am 2001;14(1):205.

provocation, then a central cause cannot be excluded [33]. If BPPV is diagnosed, the treatment of choice is canalith repositioning, such as the Epley maneuver. In a meta-analysis of nine studies, canalith repositioning was 4.6 times more likely to have symptom resolution at the time of first follow-up, compared with those who did not have repositioning [34]. Although commonly used, vestibular suppressant (anticholinergic and benzodiazepine) pharmacotherapy has not been well studied or shown to improve symptoms in those who have BPPV. Its use is discouraged because it does not seem to reduce the frequency of attacks and may even worsen a patient's imbalance [35].

Drug intoxication from alcohol, anticonvulsants, and sedative-hypnotics is the most common cause of nystagmus. The nystagmus is usually in the horizontal plane, but can occasionally appear in the vertical plane. Antiepileptic medications, including the newer agents, may cause a gaze-evoked nystagmus and even diplopia. Other types of nystagmus are rare with anticonvulsants, so other causes for the nystagmus should be sought if they are not gaze-evoked [36]. Other peripheral causes of nystagmus and vertigo include BPPV, Ménière disease, labyrinthitis, perilymphatic fistula, and Ramsey-Hunt syndrome.

Central nystagmus

In contrast to peripheral causes of nystagmus, central causes (from the brainstem or cerebellum) generally produce a purely vertical, horizontal, or torsional nystagmus that is not inhibited by visual fixation, and the fast phase may change direction with gaze (bidirectional). Vertical nystagmus should not be considered as arising from a vestibular cause. Downbeat nystagmus, which is always of central origin, is characteristic of lesions in the medullary–cervical region, Chiari malformation, and demyelinative plaques. Upbeat nystagmus has less localizing value [31]. Rarely are there auditory symptoms with central nystagmus [37]. Instead, there are other neurologic symptoms, including dysarthria, weakness, and diplopia. These differences between peripheral and central nystagmus are only guidelines and not absolute rules. Brainstem and cerebellar lesions causing central nystagmus include cerebellopontine angle tumors, cerebellar disease, cerebrovascular disease, seizures, migraine, and MS.

Cerebellopontine angle tumors, including vestibular schwannomas, ependymomas, brainstem gliomas, medulloblastomas, and neurofibromatosis

can cause vertigo and nystagmus. The nystagmus is usually coarse and bidirectional. Hearing loss of insidious onset is usually the initial symptom, and then gait ataxia, facial pain, tinnitus, a sensation of fullness in the ear, or facial weakness may ensue.

Cerebellar mass lesions or ischemia may cause nystagmus that is gaze-evoked, bidirectional, downbeat, or even pendular [38]. Pendular nystagmus is nystagmus with no fast component. Rather, the eyes move back and forth with slow velocity; this is also seen in MS. Cerebellar lesions usually have associated dysfunction in coordination, equilibrium, and gait.

Arnold-Chiari malformations are congenital abnormalities at the base of the brain that cause extensions of a tongue of cerebellar tissue into the cervical canal with displacement of the medulla into the cervical canal, along with the inferior part of the fourth ventricle. The herniated tissue blocks the circulation of cerebrospinal fluid in the brain and can lead to the formation of a cavity (syrinx) within the spinal cord. Without the meningomyelocele, it is classified as a type I malformation, and with a meningomyelocele, a type II malformation. The nystagmus is generally downbeating. Other associated symptoms are occipital headache (from increased intracranial pressure), ataxia, quadriparesis, and sensory loss (from cervical syringomyelia) [37].

MS may cause various types of nystagmus [13,39]. The most common is the nystagmus exhibited by INO, discussed in more detail later. The nystagmus in INO is seen during abduction of the unaffected eye, and the affected eye is unable to adduct. Demyelinating lesions of the cerebellum may cause a downbeat nystagmus, whereas bilateral internuclear ophthalmoplegia can cause an upbeat nystagmus. Multiple sclerosis is the most common cause of pendular nystagmus, in any direction [13,31].

The extraocular movement disorders of Alzheimer disease and Parkinson disease are usually delays of saccades and impairment of smooth pursuit, but not nystagmus [40].

Myasthenia gravis

Half of all patients who have myasthenia gravis (MG) present with pure ocular findings. Of these, 70% eventually develop generalized myasthenia [41]. Ptosis and diplopia are the presenting complaint in 75% of patients and develop eventually in 90% of patients who have MG [41–43].

The clinical hallmarks of myasthenia gravis are variable muscular weakness and fatigability, with amelioration after rest. Normally, there are more than enough acetylcholine receptors to ensure a muscle action potential after repeated ligand and receptor interactions. In MG, however, the number of available receptors quickly diminishes with each muscle contraction, resulting in variability and fatigability. Variability is caused by the decreased probability that acetylcholine will trigger an action potential given the reduced number of acetylcholine receptors. Fatigability results from depletion of acetylcholine after repeated action potentials.

Propensity for the muscles of extraocular movement is not well understood [41]. Ptosis is a common manifestation, which may be unilateral or asymmetric, and is exacerbated with prolonged upward gaze. Diplopia results from weakness of one or more of the extraocular muscles. There may be strabismus evident on examination, or loss of conjugate gaze on prolonged eccentric gaze. There are no sensory changes, loss of muscle bulk, or reflex changes. In general, the pupils are not affected, although there is disagreement if this is universal [41,42]. On examination there may be weakness of the orbicularis oculi muscles. The examiner may find weakness in forced eyelid closure, whereas normally it is very difficult to retract the eyelids against forced eye closure.

The differential may be fairly limited in more advanced disease or with generalized myasthenia, but can be broader in the earlier stages because there are fewer stigmata of MG. MG can mimic a single nerve palsy and other peripheral or central neuropathic diseases described previously. There are also other neuromuscular junction diseases, although they are less common. Lambert-Eaton myasthenic syndrome, like MG, is an autoimmune disease affecting the neuromuscular junction. It affects the presynaptic nerve terminal, however. With repeated stimulation, the nerve terminal eventually releases adequate acetylcholine. This process is clinically evident with improvement of power as a contraction is maintained, most prominently affecting the proximal muscles. Lambert-Eaton rarely affects the extraocular muscles [4,41]. Treatment of Lambert-Eaton syndrome is similar to treatment of MG as described later. Botulism may cause a myasthenic-like syndrome. The *Clostridium botulinum* toxin prevents the release of acetylcholine at the neuromuscular junction and autonomic synapses. Weakness begins 2 to 36 hours after toxin ingestion and fulminating weakness begins 12 to 72 hours after ingestion with a distinctive pattern of development [4,44]. There is descending flaccid paralysis, with virtually all cases starting with cranial nerve palsies, including extraocular nerve palsies. Unlike MG, there are also autonomic symptoms in botulism, such as dry mouth, ileus, postural hypotension, and blurring of vision. There may be similar symptoms in clusters of people, strongly indicating botulism. It is also important to consider botulism in intravenous drug users who have cranial nerve palsies, including diplopia. Treatment includes hospitalization because respiratory compromise may develop quickly. Elective intubation should be considered because there seems to be a mortality benefit over those who suffer a respiratory arrest before intubation [44]. Antitoxin should be administered, although this only binds circulating toxins and does not reverse established paralysis. All cases are public health emergencies and must be reported to public health officials. Organophosphate poisoning may also present with a combination of neuromuscular and autonomic symptoms and signs, classically as a cholinergic crisis. Treatment is supportive, along with atropine or pralidoxime. Finally, medications may produce myasthenic syndromes or exacerbate the symptoms of those who have MG (Table 6).

Table 6
Drugs that exacerbate myasthenia gravis

Antibiotics	Aminoglycosides
	Polymyxin
	Clindamycin
	Lincomycin
	Tetracycline
	Ciprofloxacin
	Chloroquine
	Pyrantel
Antiarrhythmics	Quinidine
	Procainamide
	Lidocaine
	Propafenone
Beta blockers	
Calcium channel blockers	
Anticonvulsants	Phenytoin
	Trimethadione
Psychiatric drugs	Lithium
	Chlorpromazine
	Phenelzine
Other	Cocaine
	Steroids
	Magnesium
	Iodinated contrast

Data from Barton JJS, Fouladvand M. Ocular aspects of myasthenia gravis. Semin Neurol 2000;20(1):17.

Diagnosis of MG and differentiation from other neuromuscular disorders is generally confirmed with clinical response to acetylcholinesterase inhibitors, EMG, and antibody/toxin assays. Treatment of ocular MG is generally not emergent, but timely referral or consultation with a neurologist is important. These patients may be offered symptomatic treatment, immunosuppressive therapies, and thymectomy if there is a demonstrated thymoma. Those in a myasthenic crisis (ie, weakness of respiration requiring mechanical ventilation) temporarily benefit from plasmapheresis or intravenous immunoglobulins [4,43].

Multiple sclerosis

In addition to optic neuropathy, MS may cause ocular motility dysfunction, mimicking cranial nerve lesions at any neuroanatomic level. It is clinically defined by neurologic disturbances separated by time and space. In other words, deficits involve different areas of the central nervous system at different times. After the initial symptoms resolve in days to weeks, there may be an interval of months to years before other neurologic deficits appear.

The most common oculomotor nerve palsy in multiple sclerosis is CN VI palsy, which may be the initial presentation of MS [39]. After trauma and

mass lesions, it is one of the most common causes of an abducens palsy. Trochlear nerve palsies are rare in MS because of the limited myelination of the trochlear nerve [39].

INO is a distinctive feature of MS, caused by a demyelinating lesion of the MLF (see Fig. 12). The MLF carries ascending projections from the CN VI nucleus to the contralateral CN III nucleus to coordinate horizontal gaze. It is characterized by lost or limited adduction of one eye and a horizontal nystagmus, during abduction, of the contralateral eye. Many cases of INO are subtle because the deficit is partial and no diplopia with lateral gaze is reported [39]. It is present in 17% to 41% of patients who have MS [13]. Other common causes of INO include vascular disease and infection, whereas less common causes include trauma, tumor, hemorrhage, and vasculitis [13]. Isolated INO without other accompanying symptoms or signs is uncommon, but work-up should still include neurologic consultation and MRI.

Stroke syndromes and gaze palsies

Stroke syndromes and the visual system

Stroke should be considered in any evaluation of visual or ocular disturbance. Visual field defects are a common consequence of a large vessel cerebrovascular accident (CVA). The type of visual field defect depends on the location of the lesion, which can range anywhere from the retina to the occipital lobe (Fig. 19). These lesions lead to predictable patterns of visual field deficits. The simplest and most appropriate emergency method of testing visual fields is the confrontation technique described previously. Oculomotor dysfunction in the setting of CVA is more indicative of brainstem and posterior circulation ischemia. Ischemia of the brain has been mentioned in virtually all sections thus far, but we dedicate a section to the effects of stroke on the visual and oculomotor system, organized by the affected artery. A full discussion of stroke and its diagnosis and management is outside the scope of this article.

Anterior cerebral artery

The anterior cerebral artery supplies the parasagittal cerebral cortex. A CVA involving the anterior cerebral artery does not typically result in a visual or oculomotor defect.

Internal carotid artery

The internal carotid artery (ICA) feeds into the circle of Willis, and because of collateral circulation, no part of the brain is completely dependent on it. In fact, 30% to 40% of occlusions are asymptomatic [37]. The ICA gives rise to two branches of interest to the visual system: the ophthalmic artery and the anterior choroidal artery. A lesion of these branches may cause monocular blindness and homonymous hemianopia, respectively. An

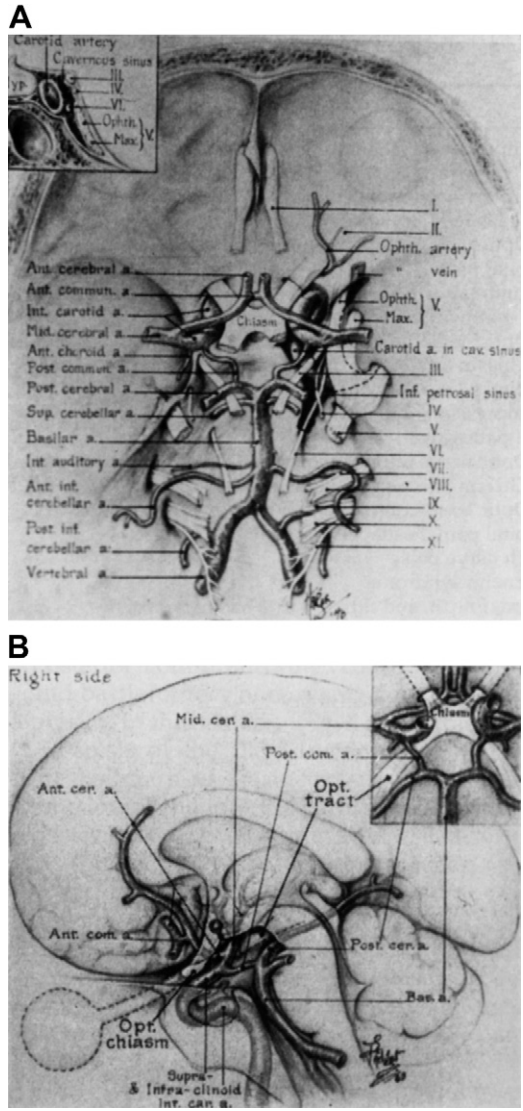


Fig. 19. (*A*) The regional anatomy of the base of the skull, cranial nerves, and circle of Willis. (*B*) The section through the brain showing the relationship between arteries of the circle of Willis and adjacent component parts of the visual pathways. (*From* Walsh FB. Visual field defects due to aneurysms at the circle of Willis. Arch Ophthalmol 1964:71:49; with permission.)

ICA lesion must be considered in these presentations. Vascular studies of the carotid system should be performed as part of the stroke work-up to determine if carotid endarterectomy is indicated.

The ophthalmic artery supplies the retina. Ischemia from ICA occlusion may initially manifest as transient monocular blindness attributable to retinal

artery ischemia, whereas infarction leads to more persistent monocular blindness. Because the ICA is connected to the middle and anterior cerebral arteries by the circle of Willis, other symptoms, such as hemiplegia and hemisensory deficits, may accompany the ocular blindness.

The anterior choroidal artery comes off the ICA near the posterior communicating artery. It supplies parts of the globus pallidus, internal capsule, and various contiguous structures, including the optic tract. In addition to the motor and sensory deficits in an anterior choroidal artery infarct, there is also a homonymous hemianopia contralateral to the side of the lesion. In general, there is preservation of language and cognition. Anterior choroidal artery strokes have not been well studied or documented and there is debate as to whether there is a distinct syndrome [37].

Middle cerebral artery

The middle cerebral artery (MCA) supplies the lateral convexity of the cerebral hemisphere, including the frontal eye field, the lateral geniculate nucleus, and the optic radiations, the region of the cortex related to macular vision. Deep branches supply the basal ganglia and the internal capsule. It is the most commonly involved vessel in strokes. MCA strokes are anatomically separated into a superior division and an inferior division depending on which branch is affected after the MCA bifurcates, although a more proximal lesion can occur that includes the superior and inferior divisions.

The superior division of the MCA does not supply the optic tract or the radiations, but it does supply the frontal eye field and the cortical region responsible for voluntary lateral conjugate gaze. Superior division strokes thus do not result in a visual field defect, but may cause a conjugate gaze deviation [4,37]. This phenomenon is discussed further in the section on gaze palsies. Inferior division strokes may cause a homonymous quadrantanopia or hemianopia depending on how extensively the optic radiation is affected.

Posterior cerebral artery

The posterior cerebral artery (PCA) supplies the occipital visual cerebral cortex, the medial temporal lobes, thalamus, and rostral midbrain. Ischemia in the PCA distribution is most commonly attributable to embolic PCA infarcts that affect the visual cortex causing a homonymous hemianopia because of unilateral ischemia of the occipital lobe. There may be macular sparing (central visual field) because of the collateral blood supply to the section of cortex involved in macular vision from the MCA.

Involvement of the extraocular muscles occurs through ischemia of cranial nerve nuclei, resulting in nerve palsies, vertical gaze palsies, and internuclear ophthalmoplegia. When deep branches of the posterior cerebral artery in the midbrain are affected, there can be involvement of the third cranial nerve nucleus, causing an oculomotor palsy. These arterial branches

also supply other nearby structures and, in addition to the third nerve palsy, can cause an accompanying contralateral hemiplegia (Weber syndrome) if the corticospinal tracts are involved, or a contralateral ataxia and tremor (Claude syndrome), if the red nucleus is involved [37].

Cortical blindness may result from bilateral occlusion of the PCA, which is a rare event, and more commonly cortical blindness is the result of trauma to the occipital lobe, or global ischemia, such as in cardiac arrest. The hallmark of cortical blindness or cortical visual impairment is normally functioning pupils and a normal funduscopic examination with no perceptible vision. The occipital lobe is particularly vulnerable to insult from global ischemia because of its location in the border zone between the middle and posterior cerebral arteries. Cortical blindness from global ischemia is usually transient, but may be permanent [4].

Basilar artery

The basilar artery supplies deep structures of the cerebrum and the entire brainstem and cerebellum. Occlusion of the basilar artery is usually incompatible with life [4]. If the proximal basilar artery is affected there may be unilateral or bilateral abducens nerve palsy, usually with associated neurologic findings, such as paresis.

''Top of the basilar'' syndrome occurs when there is an embolism small enough to lodge at the basilar artery bifurcation into the posterior cerebral arteries. Unilateral or bilateral third nerve palsies are characteristic in this syndrome. The basilar artery supplies a large number of structures and is associated with numerous other defects, however. There is generally coma because of involvement of the reticular activating system and multiple motor-sensory deficits.

Vertebal arteries

The vertebral arteries supply the medulla and their branches supply the cerebellum. Occlusion of the vertebral artery and its branch, the posterior inferior cerebellar artery, may cause lateral medullary (Wallenberg) syndrome because of infarction of a lateral wedge of the medulla. This is the most common ischemic lesion involving the vertebral arteries. The complete syndrome involves the vestibular nuclei (vertigo, nystagmus, vomiting); spinothalamic tract (impairment of pain and thermal sense over half the body); descending sympathetic tract (ipsilateral Horner syndrome); the ninth and tenth cranial nerves (hoarseness, dysphagia, diminished gag reflex); otolithic nucleus (vertical diplopia and illusion of tilting of vision); olivocerebellar or spinocerebellar tracts (ipsilateral ataxia of limbs, falling or toppling to the ipsilateral side, or lateropulsion); the fifth cranial nerve (pain, burning, and impaired sensation over half of the face); and nucleus and tractus solitarius (loss of taste) [37]. The most common findings are vertigo, nystagmus, lateropulsion, and limb ataxia. This syndrome does not characteristically involve the motor system.

Gaze palsies/conjugate gaze deviation

The decision to move one's eyes laterally begins in the cerebral hemisphere. Cortical fibers then travel down to the CN VI nucleus and the contralateral CN III nucleus through the MLF as described previously for conjugate horizontal gaze (see Fig. 12). A gaze palsy, or impairment of conjugate eye movement, mainly results from lesions above the level of the cranial nerve nuclei. In this case, an impairment of one hemisphere results in an imbalance in neural tone between the two hemispheres. The result is a conjugate gaze deviation. In this section we discuss gaze palsies and their causes by their location in the cerebral cortex, midbrain, or pons.

Hemispheric lesions

The most common cause of gaze palsy is a hemispheric lesion. In destructive lesions of the frontal eye field (Brodmann area 8) of the cerebral cortex, there is gaze palsy toward the side of the lesion in the area of the anterior circulation. Hemispheric ischemia or infarction can result in a conjugate gaze deviation. Seizure activity to the frontal eye field causes a gaze deviation away from the affected hemisphere because of uninhibited neural stimulation.

The incidence of gaze palsy in stroke has been documented to be approximately 20% to 32% and its presence has been associated with poorer functional outcomes [45]. In an acute stroke or transient ischemic attack, the eye is deviated away from the side of the hemiparesis and toward the side of the lesion. At times this physical examination finding is subtle if the patient's gaze is fixated during examination. The eyes are still yoked, so there is usually no diplopia. Visualization of the conjugate eye deviation on CT scanning has been offered as a sign supporting acute stroke. Patients usually close their eyes, removing gaze fixation and revealing underlying tonic eye deviation [46,47]. This phenomenon has not been prospectively studied, however.

Midbrain lesions

The dorsal midbrain has centers responsible for voluntary upward gaze. This area may be damaged by trauma, hydrocephalus, compressive masses such as pineal tumors, demyelinating disorders, infection, ischemia, or hemorrhage, resulting in features of Parinaud syndrome [46,48]. The syndrome is characterized by up-gaze paresis. There is preservation of vertical eye movements with the doll's eye maneuver and with voluntary downward gaze, and nystagmus mainly on downward gaze, eyelid retraction, midposition pupils, and loss of accommodation. These patients require MRI for further delineation of the cause and confirmation of a midbrain lesion. Although most case reports describe clinically stable patients [46,48], patients who are suspected to have Parinaud syndrome should have prompt neurologic consultation and admission given the potentially life-threatening causes and location of the lesion.

Pontine lesions

The paramedian pontine reticular formation, mentioned previously, is involved in conjugate horizontal gaze. Unlike lesions of the cerebral hemisphere, the gaze deviation is away from the side of the lesion and toward the side of the hemiparesis, as in the case of unilateral ischemia to the pons, because of the level of the lesion in relation to the decussation of the motor pathways. Also in contrast to hemispheric or midbrain lesions, gaze paresis from pontine lesions is more resistant to attempts to move by doll's eye maneuver or caloric stimulation [4]. It is rare to have isolated gaze palsy from a pontine lesion, except in MS. Evaluation is similar to other gaze palsies and usually requires neurologic consultation, neuroimaging, and treatment of the underlying cause.

Summary

Neuro-ophthalmology is a complex, broad-ranging area of ophthalmology. Appropriate work-ups, correct diagnosis, treatment, and referral all depend on a thorough understanding of the neuroanatomy and neuro-ophthalmologic examination. Recognizing subtle physical findings, such as cranial nerve abnormalities or visual field cuts, may be the key to finding significant pathology in emergency department patients.

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