6 - Eye Disorders

Chapter 60. Approach to the Ophthalmologic Patient

Introduction

The eye can be examined with routine equipment, including a standard ophthalmoscope; thorough examination requires special equipment and evaluation by an ophthalmologist. (See Fig. 60-1 for a cross-section of the eye.)

History

History includes location, speed of onset, and duration of current symptoms and history of previous ocular symptoms; the presence and nature of pain, discharge, or redness; and changes in visual acuity. Worrisome symptoms besides vision loss and eye pain include flashing lights, showers of floaters (both of which may be symptoms of retinal detachment), diplopia, and loss of peripheral vision.

Physical Examination

Visual acuity: The first step is to record visual acuity. Many patients do not give a full effort. Providing adequate time and coaxing patients tend to yield more accurate results. Visual acuity is measured with and without the patient's own glasses. If patients do not have their glasses, a pinhole refractor is used. If a commercial pinhole refractor is unavailable, one can be made at the bedside by poking holes through a piece of cardboard using an 18-gauge needle and varying the diameter of each hole slightly. Patients choose the hole that corrects vision the most. If acuity corrects with pinhole refraction, the problem is a refractive error. Pinhole refraction is a rapid, efficient way to diagnose refractive errors, which are the most common cause of blurred vision. However, with pinhole refraction, best correction is usually to only about 20/30, not 20/20.

[**Fig. 60-1.** Cross-section of the eye.]

Visual acuity in each eye is tested as the opposite eye is covered with a solid object (not the patient's fingers, which may separate during testing). Patients look at an eye chart 20 ft (6 m) away. If this test cannot be done, acuity can be measured using a chart held about 36 cm (14 in) from the eye. Normal and abnormal vision is quantified by Snellen notation. A Snellen notation of 20/40 (6/12) indicates that the smallest letter that can be read by someone with normal vision at 40 ft (12 m) has to be brought to 20 ft (6 m) before it is recognized by the patient. Vision is recorded as the smallest letter patients read correctly, even if patients feel that the letter is blurry or they have to guess. If the patient cannot read the top line of the Snellen chart at 20 ft (6 m), acuity is tested at 10 ft (3 m). If nothing can be read from a chart even at the closest distance, the examiner holds up different numbers of fingers to see whether the patient can accurately count them. If not, the examiner tests whether the patient can perceive hand motion. If not, a light is shined into the eye to see whether light is perceived.

Near vision is checked by asking patients to read a standard near card or newsprint at 14 in (35 cm); patients > 40 yr who require corrective lenses (reading glasses) should wear them during near vision testing.

Refractive error can be estimated roughly with a handheld ophthalmoscope by noting the lens necessary for the examiner to focus on the retina; this procedure requires examiners to use their own corrective lenses and is never a substitute for a comprehensive assessment of refraction. More commonly, refractive error is measured with a standard phoropter or an automated refractor (a device that measures changes in light projected and reflected by the patient's eye). These devices also measure astigmatism (see p. 571).

Eyelid and conjunctival examination: Eyelid margins and periocular cutaneous tissues are examined under a focal light and magnification (eg, provided by loupe, slit lamp, or ophthalmoscope focused at the examiner's working distance). In cases of suspected dacryocystitis or canaliculitis, the lacrimal sacs are palpated and an attempt is made to express any contents through the canaliculi and puncta. After eyelid

eversion, the palpebral and bulbar conjunctivae and the fornices can be inspected for foreign bodies, signs of inflammation (eg, follicular hypertrophy, exudate, hyperemia, edema), or other abnormalities.

Corneal examination: Indistinct or blurred edges of the corneal light reflex (reflection of light from the cornea when illuminated) suggest the corneal surface is not intact or is roughened, as occurs with a corneal abrasion or keratitis. Fluorescein staining reveals abrasions and ulcers. Before staining, a drop of topical anesthetic (eg, proparacaine 0.5%, tetracaine 0.5%) may be added to facilitate examination if the patient is in pain or if it is necessary to touch the cornea or conjunctiva (eg, to remove a foreign body or measure intraocular pressure). A sterile, individually packaged fluorescein strip is moistened with 1 drop of sterile saline or topical anesthetic and, with the patient's eye turned upward, is touched momentarily to the inside of the lower eyelid. The patient blinks several times to spread the dye into the tear film, and then the eye is examined under magnification and cobalt blue illumination. Areas where corneal or conjunctival epithelium is absent (abraded or ulcerated) fluoresce green.

Pupil examination: The size and shape of the pupils are noted, and pupillary reaction to light is tested in each eye, one at a time, while the patient looks in the distance. Then the swinging flashlight test is done with a penlight to compare direct and consensual pupillary response. There are 3 steps:

1. One pupil is maximally constricted by being exposed to light from the penlight for 1 to 3 sec.

2. The penlight is rapidly moved to the other eye for 1 to 3 sec.

3. The light is moved back to the first eye.

Normally, a pupil constricts similarly when light is shone on it (direct response) and when light is shone on the other eye (consensual response). However, if one eye has less light perception than the other, as caused by dysfunction of the afferent limb (from the optic nerve to the optic chiasm) or extensive retinal disease, then the *consensual* response in the affected eye is stronger than the *direct* response. Thus, on step 3 of the swinging light test, when the light is shined back on the affected eye, it paradoxically appears to dilate. This finding indicates a relative afferent pupillary defect (RAPD, or Marcus Gunn pupil).

Extraocular muscles: The examiner guides the patient to look in 8 directions (up, up and right, right, down and right, down, down and left, left, left and up) with a moving finger, penlight, or transillumination light, observing for gaze deviation, limitation of movement, disconjugate gaze, or a combination consistent with cranial nerve palsy, orbital disease, or other abnormalities that restrict movement.

Ophthalmoscopy: Ophthalmoscopy can be done directly by using a handheld ophthalmoscope or indirectly by using a head-mounted ophthalmoscope with a handheld lens. With handheld ophthalmoscopy, the examiner dials the ophthalmoscope to zero diopters, then increases or decreases the setting until the fundus comes into focus. The view of the retina is limited with a handheld ophthalmoscope, whereas indirect ophthalmoscopy gives a 3-dimensional view and is better for visualizing the peripheral retina, where retinal detachment most commonly occurs. The view of the fundus can be improved by dilating the pupils. Before dilation, the anterior chamber depth is estimated because mydriasis can precipitate an attack of acute angle-closure glaucoma if the anterior chamber is shallow. Depth can be estimated with a slit lamp (see below) or less accurately with a penlight held at the temporal limbus parallel to the plane of the iris and pointed toward the nose. If the medial iris is in shadow, the chamber is shallow and dilation should be avoided. Other contraindications to dilation include head trauma, suspicion of a ruptured globe, a narrow angle, and angle-closure glaucoma.

Pupils can be dilated using 1 drop of tropicamide 1%, phenylephrine 2.5%, or both (repeated in 5 to 10 min if necessary); for longer action, a larger dilated pupil, or both, cyclopentolate 1% can be substituted for tropicamide.

Ophthalmoscopy can detect lens or vitreous opacities, assess the optic cup-to-disk ratio, and identify retinal and vascular changes. The optic cup is the central depression, and the optic disk is the entire area of the optic nerve head. The normal ratio of the cup-to-nerve diameters is 0 to 0.4. A ratio of ≥ 0.5 may signify loss of ganglion cells and may be a sign of glaucoma. Retinal changes include hemorrhage, manifested as small or large areas of blood, and drusen (small subretinal yellow-white spots that may

signify dry age-related macular degeneration). Vascular changes include arteriovenous nicking, a sign of chronic hypertension in which retinal veins are compressed by arteries where the two cross; copper wiring, a sign of arteriosclerosis in which thickened arteriolar walls increase the thickness of the light reflex; silver wiring, a sign of hypertension in which thin, fibrotic arteriolar walls decrease the thickness of the light reflex; and loss of venous pulsations, a sign of increased intracranial pressure in patients known to have had pulsations.

Slit-lamp examination: A slit lamp focuses the height and width of a beam of light for a precise stereoscopic view of the eyelids, conjunctiva, cornea, anterior chamber, iris, lens, and anterior vitreous. It is especially useful for the following:

- Identifying corneal foreign bodies and abrasions
- Measuring depth of the anterior chamber
- Detecting cells (RBCs or WBCs) and flare (evidence of protein) in the anterior chamber
- Identifying ciliary flush (dilation of blood vessels localized to the limbal region overlying the ciliary body), which occurs with uveitis
- Identifying scleral edema, which is seen as a bowing forward of the slit beam when it is focused beneath the conjunctiva and which is usually a sign of scleritis

Tonometry (see p. 540) and gonioscopy, which quantifies the iridocorneal angle and requires the use of a special lens, may be done.

Visual field testing: Visual fields may be impaired by lesions anywhere in the neural visual pathways from the optic nerves to the occipital lobes (see Table 60-1 and Fig. 69-1 on p. 620). Glaucoma causes loss of peripheral vision. Fields can be assessed grossly by direct confrontation testing or by more precise, detailed testing.

In **direct confrontation**, patients maintain a fixed gaze at the examiner's eye or nose. The examiner brings a small target (eg, a match or a finger) from the patients' visual periphery into each of the 4 visual quadrants and asks patients to indicate when they first see the object. Wiggling the small target helps patients separate and define it. Another method of direct confrontation visual field testing is to hold a number of fingers in each quadrant and ask patients how many they see. For both methods, each eye is tested separately. Abnormalities in target detection should prompt detailed testing with more precise instruments.

More detailed methods include use of a tangent screen, Goldmann perimeter, or computerized automated perimetry (in which the visual field is mapped out in detail based on patient response to a series of flashing lights in different locations controlled by a standardized computer program). The Amsler grid is used to test central vision. Distortion of the grid (metamorphopsia) or a missing area (central scotoma) may indicate disease of the macula (eg, choroidal neovascularization), as occurs in age-related macular degeneration.

Color vision testing: Twelve to 24 Ishihara color plates, which have colored numbers or symbols hidden in a field of colored dots, are commonly used to test color vision. Colorblind patients or patients with acquired color deficiency (eg, in optic nerve diseases) cannot see some or all of the hidden numbers. Most

[**Table 60-1.** Types of Field Defects]

congenital color blindness is red-green; most acquired (eg, caused by glaucoma or optic nerve disease) is blue-yellow.

Testing

Tonometry: Tonometry measures intraocular pressure by determining the amount of force needed to indent the cornea. Handheld pen-type tonometers are used for screening. This test requires topical anesthesia (eg, proparacaine 0.5%). Office-based screening with noncontact air-puff tonometry also can be used; it requires less training because it makes no direct corneal contact. Goldmann applanation tonometry is the most accurate method but requires more training and typically is used only by ophthalmologists. Measurement of intraocular pressure alone is not adequate screening for glaucoma; the optic nerve also should be examined.

Fluorescein angiography: After IV injection of fluorescein solution, the retinal, choroidal, optic disk, or iris vasculature is photographed in rapid sequence. Fluorescein angiography is used to investigate underperfusion and neovascularization in conditions such as diabetes, age-related macular degeneration, retinal vascular occlusion, and ocular histoplasmosis. It is also useful in preoperative assessment for retinal laser procedures.

Electroretinography: Electrodes are placed on each cornea and on the surrounding skin, and electrical activity in the retina is recorded. This technique evaluates retinal function in patients with retinal degeneration. It does not evaluate vision.

Ultrasonography: B-mode ultrasonography provides 2-dimensional structural information even in the presence of opacities of the cornea and lens. Examples of ophthalmologic applications include assessment of retinal tumors, detachments, and vitreous hemorrhages; location of foreign bodies; detection of posterior scleral edema characteristic of posterior scleritis; and distinction of choroidal melanoma from metastatic carcinoma and subretinal hemorrhage.

A-mode ultrasonography is 1-dimensional ultrasonography used to determine the axial length of the eye, a measurement needed to calculate the power of an intraocular lens for implantation as a part of cataract surgery.

Ultrasonic pachymetry is use of ultrasonography to measure the thickness of the cornea before refractive surgery (eg, LASIK) and in patients with corneal dystrophies.

CT and MRI: These imaging techniques most often are used for evaluation of ocular trauma, particularly if an intraocular foreign body is suspected, and in the evaluation of orbital tumors, optic neuritis, and optic nerve tumors. MRI should not be done when there is suspicion of a metallic intraocular foreign body.

Electronystagmography: See p. 414.

Acute Vision Loss

Loss of vision is usually considered acute if it develops within a few minutes to a couple of days. It may affect one or both eyes and all or part of a visual field. Patients with small visual field defects (eg, caused by a small retinal detachment) may describe their symptoms as blurred vision.

Pathophysiology

Acute loss of vision has 3 general causes:

- Opacification of normally transparent structures through which light rays pass to reach the retina (eg, cornea, vitreous)
- Retinal abnormalities
- Abnormalities affecting the optic nerve or visual pathways

Etiology

The most common causes of acute loss of vision are

• Vascular occlusions of the retina (central retinal artery occlusion, central retinal vein occlusion)

• Ischemic optic neuropathy (often in patients with temporal arteritis)

• Vitreous hemorrhage (caused by diabetic retinopathy or trauma)

• Trauma

In addition, sudden recognition of loss of vision (pseudo-sudden loss of vision) may manifest initially as sudden onset. For example, a patient with long-standing reduced vision in one eye (possibly caused by a dense cataract) suddenly is aware of the reduced vision in the affected eye when covering the unaffected eye.

Presence or absence of pain helps categorize loss of vision (see Table 60-2).

Most disorders that cause total loss of vision when they affect the entire eye may affect only part of the eye and cause only a visual field defect (eg, branch occlusion of the retinal artery or retinal vein, focal retinal detachment).

Less common causes of acute loss of vision include

• Anterior uveitis (a common disorder, but one that usually causes eye pain severe enough to trigger evaluation before vision is lost)

• Highly aggressive retinitis

• Certain drugs (eg, methanol, salicylates, ergot alkaloids, quinine)

Evaluation

History: History of present illness should describe loss of vision in terms of onset, duration, progression, and location (whether it is monocular or binocular and whether it involves the entire visual field or a specific part and which part). Important associated visual symptoms include floaters, flashing lights, halos around lights, distorted color vision,

[**Table 60-2.** Some Disorders that Cause Acute Vision Loss]

and jagged or mosaic patterns (scintillating scotomata). The patient should be asked about eye pain and whether it is constant or occurs only with eye movement.

Review of systems should seek extraocular symptoms of possible causes, including jaw or tongue claudication, temporal headache, proximal muscle pain, and stiffness (giant cell arteritis); and headaches (ocular migraine).

Past medical history should seek known risk factors for eye disorders (eg, contact lens use, severe myopia, recent eye surgery or injury), risk factors for vascular disease (eg, diabetes, hypertension), and hematologic disorders (eg, sickle cell anemia or disorders such as Waldenstrom's macroglobulinemia or multiple myeloma that could cause a hyperviscosity syndrome).

Family history should note any family history of migraine headaches.

Physical examination: Vital signs, including temperature, are measured.

If the diagnosis of a transient ischemic attack is under consideration, a complete neurologic examination is done. The facial skin is inspected for vesicles or ulcers in the V_1 distribution (ophthalmic division of the trigeminal nerve), and the temples are palpated for pulses, tenderness, or nodularity over the course of

the temporal artery. However, most of the examination focuses on the eye.

Eye examination includes the following:

• Visual acuity is measured.

• Peripheral visual fields are assessed by confrontation.

• Central visual fields are assessed by Amsler grid.

• Direct and consensual pupillary light reflexes are examined using the swinging flashlight test.

• Ocular motility is assessed.

• Color vision is tested with color plates.

• The eyelids, sclera, and conjunctiva are examined using a slit lamp if possible.

• The cornea is examined with fluorescein staining.

• The anterior chamber is examined for cells and flare in patients who have eye pain or conjunctival injection.

• The lens is checked for cataracts using a direct ophthalmoscope, slit lamp, or both.

• Intraocular pressure is measured.

• Ophthalmoscopy is done, preferably after dilating the pupil with a drop of a sympathomimetic (eg, 2.5% phenylephrine), cycloplegic (eg, 1% cyclopentolate or 1% tropicamide), or both; dilation is nearly full after about 20 min. The entire fundus, including the retina, macula, fovea, vessels, and optic disk and its margins, is examined.

• If pupillary light responses are normal and functional loss of vision is suspected (rarely),

[
Fig. 60-2. Evaluation of acute vision loss.]

optokinetic nystagmus is checked. If an optokinetic drum is unavailable, a mirror can be held near the patient's eye and slowly moved. If the patient can see, the eyes usually track movement of the mirror.

Red flags: Acute loss of vision is itself a red flag; most causes are serious.

Interpretation of findings: Diagnosis can be begun systematically. Fig. 60-2 describes a simplified, general approach. Specific patterns of visual field deficit help suggest a cause (see Table 60-1). Other clinical findings also help suggest a cause (see Table 60-2):

• Difficulty seeing the red reflex during ophthalmoscopy suggests opacification of transparent structures (eg, caused by corneal ulcer, vitreous hemorrhage, or severe endophthalmitis).

• Retinal abnormalities that are severe enough to cause acute loss of vision are detectable during ophthalmoscopy, particularly if the pupils are dilated. Retinal detachment may show retinal folds; retinal vein occlusion may show marked retinal hemorrhages; and retinal artery occlusion may show a pale retina with cherry-red fovea.

• An afferent pupillary defect (absence of a direct pupillary light response but a normal consensual response) with an otherwise normal examination (except sometimes an abnormal optic disk) suggests an abnormality of the optic nerve or retina (ie, anterior to the chiasm).

In addition, the following facts may help:

- Monocular symptoms suggest a lesion anterior to the optic chiasm.
- Bilateral, symmetric visual field defects suggest a lesion posterior to the chiasm.
- Constant eye pain suggests a corneal lesion (ulcer or abrasion), anterior chamber inflammation, or increased intraocular pressure, whereas eye pain with movement suggests optic neuritis.
- Temporal headaches suggest giant cell arteritis or migraine.

Testing: ESR is done for all patients with symptoms (eg, temporal headaches, jaw claudication, proximal myalgias, stiffness) or signs (eg, temporal artery tenderness or induration, pale retina, papilledema) suggesting optic nerve or retinal ischemia to exclude giant cell arteritis.

Other testing is listed in Table 60-2. The following are of particular importance:

- Ultrasonography is done to view the retina if the retina is not clearly visible with pupillary dilation and indirect ophthalmoscopy done by an ophthalmologist.
- Gadolinium-enhanced MRI is done for patients who have eye pain with movement or afferent pupillary defect, particularly with optic nerve swelling on ophthalmoscopy, to diagnose multiple sclerosis.

Treatment

Causative disorders are treated. Treatment should usually commence immediately if the cause is treatable. In many cases (eg, vascular disorders), treatment is unlikely to salvage the affected eye but can decrease the risk of the same process occurring in the contralateral eye.

Key Points

- Diagnosis and treatment should occur as rapidly as possible.
- Acute monocular loss of vision with an afferent pupillary defect indicates a lesion of the eye or of the optic nerve anterior to the optic chiasm.
- Optic nerve lesion, particularly ischemia, is considered in patients with acute monocular loss of vision or afferent pupillary defect and in those with or without optic nerve abnormalities on ophthalmoscopy but no other abnormalities on eye examination.
- Corneal ulcer, acute angle-closure glaucoma, endophthalmitis, or severe anterior uveitis is considered in patients with acute monocular loss of vision, afferent pupillary defect, eye pain, and conjunctival injection.

Anisocoria

(Unequal Pupils)

Anisocoria is unequal pupil sizes. Anisocoria itself does not cause symptoms.

Etiology

The most common cause of anisocoria is

- Physiologic (present in about 20% of people)

See Table 60-3 for other causes of anisocoria.

Many disorders are accompanied by anisocoria due to iris or neurologic dysfunction but usually manifest with other, more bothersome symptoms (eg, uveitis, optic neuritis, stroke, subarachnoid hemorrhage, acute angle-closure glaucoma).

Evaluation

The goal of evaluation is to elucidate the physiologic mechanism of anisocoria. By identifying certain mechanisms (eg, Horner's syndrome, 3rd cranial nerve palsy), clinicians can diagnose the occasional serious occult disorder (eg, tumor, aneurysm) manifesting with anisocoria.

History: History of present illness includes the presence, nature, and duration of symptoms. Any history of head or ocular trauma is noted.

Review of systems seeks symptoms that may suggest a cause, such as birth defects or chromosomal abnormalities (congenital defects); droopy eyelid, cough, chest pain, or dyspnea (Horner's syndrome); genital lesions, adenopathy, rashes, or fever (syphilis); and headaches or other neurologic symptoms (Horner's syndrome or 3rd cranial nerve palsy).

Past medical history includes known ocular disorders and surgeries and exposure to drugs.

[Table 60-3. Some Common Causes of Anisocoria]

Physical examination: Pupillary size and light responses should be examined in lighted and dark rooms. Accommodation and extraocular movements should be tested. Ocular structures are inspected by using a slit lamp or other magnification to identify structural abnormalities and ptosis. Other ocular symptoms are evaluated by eye examination as clinically indicated. An old photograph of the patient or the patient's driver's license should be examined (under magnification if possible) to see whether anisocoria was present previously.

Testing: Testing is usually unnecessary but is indicated for clinically suspected disorders. Patients with Horner's syndrome or 3rd cranial nerve palsy usually require brain MRI or CT.

Red flags: The following findings are of particular concern:

• Ptosis

• Anhidrosis

• Pupils that respond more to accommodation than light

• Impaired extraocular movements

Interpretation of findings: If the difference in size is greater in the dark, the smaller pupil is abnormal. Common causes include Horner's syndrome and physiologic anisocoria. An ophthalmologist can differentiate them because the small pupil in Horner's syndrome does not dilate after instillation of an ocular dilating drop (eg, 10% cocaine).

If the difference in pupillary sizes is greater in light, the larger pupil is abnormal. If extraocular movements are impaired, particularly with ptosis, 3rd cranial nerve palsy is likely. If extraocular movements are intact, an ophthalmologist can further differentiate among causes by instilling a drop of a pupillary constrictor (eg, 0.1% pilocarpine). If the large pupil constricts, the cause is probably Adie's tonic pupil; if the large pupil does not constrict, the cause is probably drugs or structural (eg, traumatic, surgical) damage to the iris.

Treatment

Treatment of anisocoria is unnecessary.

Key Points

• Physiologic anisocoria is very common and causes < 1 mm of difference between the pupils in size.

• Examining the pupils in light and dark and inspecting an old photograph or the driver's license of the patient provide a great deal of diagnostic information.

• Serious disorders should be considered in patients with Horner's syndrome or 3rd cranial nerve palsy.

Blurred Vision

Blurred vision is the most common visual symptom. It usually refers to decreased visual acuity of gradual onset. For sudden, complete loss of vision in one or both eyes (blindness), see p. 541. Patients with small visual field defects (eg, caused by a small retinal detachment) may describe their symptoms as blurring.

Etiology

The most common causes of blurred vision (see Table 60-4) include

• Refractive errors (the most common cause overall)

• Age-related macular degeneration

• Cataracts

• Diabetic retinopathy

• Glaucoma

Blurred vision has 4 general mechanisms:

• Opacification of normally transparent ocular structures (cornea, lens, vitreous) through which light rays must pass to reach the retina

• Disorders affecting the retina

• Disorders affecting the optic nerve or its connections

• Refractive errors

Certain disorders can have more than one mechanism. For example, refraction can be impaired by early cataracts or the reversible lens swelling caused by poorly controlled diabetes.

Patients with certain disorders that cause blurred vision (eg, acute corneal lesions [such as abrasions], ulcers, herpes simplex keratitis, herpes zoster ophthalmicus, acute angle-closure glaucoma) are more likely to present with other symptoms such as eye pain and red eye.

Rare disorders that can cause blurred vision include hereditary optic neuropathies (eg, dominant optic atrophy, Leber's hereditary optic neuropathy) and corneal scarring due to vitamin A deficiency or amiodarone toxicity.

Evaluation

History: History of present illness should ascertain the onset, duration, and progression of symptoms, as well as whether they are bilateral or unilateral. The symptom should be defined as precisely as possible by asking an open-ended question or request (eg, "Please describe what you mean by blurred

vision"). For example, loss of detail is not the same as loss of contrast. Also, visual field defects may not be recognized as such by patients, who may instead describe symptoms such as missing steps or the inability to see words when reading. Important associated symptoms include eye redness, photophobia, floaters, sensation of lightning-like flashes of light (photopsias), and pain at rest or with eye movement. The effects of darkness (night vision), bright lights (ie, causing blur, star bursts, halos, photophobia), distance from an object, and corrective lenses and whether central or peripheral vision seems to be more affected should be ascertained.

Review of systems includes questions about symptoms of possible causes, such as increased thirst and polyuria (diabetes).

Past medical history should note previous eye injury or other diagnosed eye disorders and ask about disorders known to be risk factors for eye disorders (eg, hypertension, diabetes, HIV/AIDS, SLE, sickle cell anemia, disorders that could cause hyperviscosity syndrome such as multiple myeloma or Waldenstrom's macroglobulinemia). Drug history should include questions about use of drugs that could affect vision (eg, amiodarone, corticosteroids) and treatments for disorders affecting vision (eg, diabetic retinopathy).

Physical examination: Nonvisual symptoms are evaluated as needed; however, examination of the eyes may be all that is necessary.

Testing **visual acuity** is key. Many patients do not give a full effort. Providing adequate time and coaxing patients tend to yield more accurate results.

Acuity ideally is measured while the patient stands 6 m (about 20 ft) from a Snellen chart posted on a wall. If this test cannot be done, acuity can be measured using a chart held about 36 cm (14 in) from the eye. Measurement of near vision should be done with reading correction in place for patients > age 40. Each eye is measured separately while the other eye is covered with a solid object (not the patient's fingers, which may separate during testing). If the patient cannot read the top line of the Snellen chart at 6 m, acuity is tested at 3 m. If nothing can be read from a chart even at the closest distance, the examiner holds up different numbers of fingers to see whether the patient can accurately count them. If not, the examiner tests whether the patient can perceive hand motion. If not, a light is shined into the eye to see whether light is perceived.

Visual acuity is measured with and without the patients' own glasses. If acuity is corrected

[Table 60-4. Some Causes of Blurred Vision]

with glasses, the problem is a refractive error. If patients do not have their glasses, a pinhole refractor is used. If a commercial pinhole refractor is unavailable, one can be made at the bedside by poking holes through a piece of cardboard using an 18-gauge needle and varying the diameter of each hole slightly. Patients choose the hole that corrects vision the most. If acuity corrects with pinhole refraction, the problem is a refractive error. Pinhole refraction is a rapid, efficient way to diagnose refractive errors, which are the most common cause of blurred vision. However, with pinhole refraction, best correction is usually to only about 20/30, not 20/20.

Eye examination is also important. Direct and consensual pupillary light responses are examined using the swinging flashlight test. Visual fields are checked using confrontation and an Amsler grid.

The cornea is examined for opacification, ideally using a slit lamp. The anterior chamber is examined for cells and flare using a slit lamp if possible, although results of this examination are unlikely to explain visual blurring in patients without eye pain or redness.

The lens is examined for opacities using an ophthalmoscope, slit lamp, or both.

Ophthalmoscopy is done using a direct ophthalmoscope. More detail is visible if the eyes are dilated for ophthalmoscopy with a drop of a sympathomimetic (eg, 2.5% phenylephrine), cycloplegic (eg, 1% tropicamide or 1% cyclopentolate), or both; dilation is nearly full after about 20 min. As much of the fundus

as is visible, including the retina, macula, fovea, vessels, and optic disk and its margins, is examined. To see the entire fundus (ie, to see a peripheral retinal detachment), the examiner, usually an ophthalmologist, must use an indirect ophthalmoscope.

Intraocular pressure is measured.

Red flags: The following findings are of particular concern:

- Sudden change in vision
- Eye pain (with or without eye movement)
- Visual field defect (by history or examination)
- Visible abnormality of the retina or optic disk
- HIV/AIDS or other immunosuppressive disorder
- A systemic disorder that could cause retinopathy (eg, sickle cell anemia, possible hyperviscosity syndrome, diabetes, hypertension)

Interpretation of findings: Symptoms and signs help suggest a cause (see Table 60-4).

If visual acuity is corrected with glasses or a pinhole refractor, simple refractive error is the cause of blurring. Loss of contrast or glare may still be caused by cataract, which should be considered.

However, red flag findings suggest a more serious ophthalmologic disorder (see Table 60-5) and need for a complete examination, including slit-lamp examination, tonometry, ophthalmoscopic examination with pupillary dilation, and, depending on findings, possibly immediate or urgent ophthalmologic referral.

Specific retinal findings help suggest a cause (see Table 60-6).

[**Table 60-5.** Interpretation of Some Red Flag Findings]

[**Table 60-6.** Interpretation of Retinal Findings]

Testing: If acuity corrects appropriately with refraction, patients are referred to an optometrist or ophthalmologist for routine formal refraction. If visual acuity is not corrected with refraction but there are no red flag findings, patients are referred to an ophthalmologist for routine evaluation. With certain red flag findings, patients are referred for immediate or urgent ophthalmologic evaluation.

Patients with symptoms or signs of systemic disorders should have appropriate testing:

- Diabetes: Fingerstick or random glucose measurement
- Poorly controlled hypertension and acute hypertensive retinopathy (hemorrhages, exudates, or papilledema): Urinalysis, renal function testing, BP monitoring, and possibly ECG
- HIV/AIDS and retinal abnormalities: HIV serology and CD4+ count
- SLE and retinal abnormality: Antinuclear antibodies, ESR, and CBC
- Waldenstrom's macroglobulinemia, multiple myeloma, or sickle cell anemia: CBC with differential count and other testing (eg, serum protein electrophoresis) as clinically indicated

Treatment

Underlying disorders are treated. Corrective lenses may be used to improve visual acuity, even when the disorder causing blurring is not purely a refractive error (eg, early cataract).

Geriatrics Essentials

Although some decrease in visual acuity normally occurs with aging, acuity normally is correctable to 20/20 with refraction, even in very elderly patients.

Key Points

- If visual acuity is corrected with pinhole refraction, refractive error is the problem.
- Because glaucoma is common, intraocular pressure should be measured.
- If pinhole refraction does not correct acuity and there is no obvious cataract or corneal abnormality, ophthalmoscopy should be done after pupillary dilation.
- Many abnormalities on ophthalmoscopy, particularly if symptoms are recently worsening, require urgent or immediate ophthalmologic referral.

Diplopia

(Double Vision)

Diplopia is the perception of 2 images of a single object. Diplopia may be monocular or binocular. Monocular diplopia is present when only one eye is open. Binocular diplopia disappears when either eye is closed.

Etiology

Monocular diplopia can occur when something distorts light transmission through the eye to the retina. There may be > 2 images. One of the images is of normal quality (eg, brightness, contrast, clarity); the rest are of inferior quality. The most common causes of monocular diplopia are

- Cataract
- Corneal shape problems, such as keratoconus or surface irregularity
- Uncorrected refractive error, usually astigmatism

Other causes include corneal scarring and dislocated lens. Complaints also may represent malingering.

Binocular diplopia suggests disconjugate alignment of the eyes. There are only 2 images, and they are of equal quality. There are many possible causes of binocular diplopia (see Table 60-7). The most common are

- Cranial nerve (3rd, 4th, or 6th) palsy
- Myasthenia gravis
- Orbital infiltration (eg, thyroid infiltrative ophthalmopathy, orbital pseudotumor)

Most commonly, the eyes are misaligned because of a disorder affecting the cranial nerves innervating the extraocular muscles (3rd, 4th, or 6th cranial nerves). These palsies may be isolated and idiopathic or the result of various disorders involving the cranial nerve nuclei or the infranuclear nerve or nerves. Other causes involve mechanical interference with ocular motion or a generalized disorder of neuromuscular transmission.

Evaluation

History: History of present illness should determine whether diplopia involves one or both eyes, whether diplopia is intermittent or constant, and whether the images are separated vertically, horizontally, or both. Any associated pain is noted, as well as whether it occurs with or without eye movement.

Review of systems should seek symptoms of other cranial nerve dysfunction, such as vision abnormalities (2nd cranial nerve); numbness of forehead and cheek (5th cranial nerve); facial weakness (7th cranial nerve); dizziness, hearing loss, or gait difficulties (8th cranial nerve); and swallowing or speech difficulties (9th and 12th cranial nerves). Other neurologic symptoms, such as weakness and sensory abnormalities, should be sought noting whether these are intermittent or constant. Nonneurologic symptoms of potential causes are ascertained; they include nausea, vomiting, and diarrhea (botulism); palpitations, heat sensitivity, and weight loss (Graves' disease); and difficulty with bladder control (multiple sclerosis).

Past medical history should seek presence of known hypertension, diabetes, or both; atherosclerosis, particularly including cerebrovascular disease; and alcohol abuse.

Physical examination: Examination begins with a review of vital signs for fever and general appearance for signs of toxicity (eg, prostration, confusion).

Eye examination begins with measuring visual acuity (with correction) in each eye and both together, which also helps determine whether diplopia is monocular or binocular. Eye examination should note presence of bulging of one or both eyes, eyelid droop, pupillary abnormalities, and disconjugate eye movement and nystagmus during ocular motility testing. Ophthalmoscopy should be done, particularly noting any abnormalities of the lens (eg, cataract, displacement) and retina (eg, detachment).

Ocular motility is tested by having the patient hold the head steady and track the examiner's finger, which is moved to extreme gaze to the right, left, upward, downward, diagonally to either side, and finally inward toward the patient's nose (convergence). However, mild paresis of ocular motility sufficient to cause diplopia may escape detection by such examination.

If diplopia occurs in one direction of gaze, the eye that produces each image can be determined by repeating the examination with a red glass placed over one of the patient's eyes. The image that is more peripheral originates in the paretic eye; ie, if the more peripheral image is red, the red glass is covering the paretic eye. If a red glass is not available, the paretic eye can sometimes be identified by having the patient close each eye. The paretic eye is the eye that when closed eliminates the more peripheral image.

The other cranial nerves are tested, and the remainder of the neurologic examination, including strength, sensation, reflexes, cerebellar function, and observation of gait, is completed.

Relevant nonneurophthalmologic components of the examination include palpation of the neck for goiter and inspection of the shins for pretibial myxedema (Graves' disease).

Red flags: The following findings are of particular concern:

- More than one cranial nerve deficit
- Pupillary involvement of any degree
- Any neurologic symptoms or signs besides diplopia
- Pain
- Proptosis

Interpretation of findings: Findings sometimes suggest which nerve is involved.

• Nerve III: Eyelid droop, eye deviated laterally and down, sometimes pupillary dilation

[**Table 60-7.** Some Causes of Binocular Diplopia]

• Nerve IV: Vertical diplopia worse on downward gaze (patient tilts head to improve vision)

• Nerve VI: Eye deviated medially, diplopia worse on lateral gaze (patient turns head to improve vision)

Other findings help suggest a cause (see Table 60-7).

Intermittent diplopia suggests a waxing and waning neurologic disorder, such as myasthenia gravis or multiple sclerosis, or unmasking of a latent phoria (eye deviation). Patients with latent phoria do not have any other neurologic manifestations.

Internuclear ophthalmoplegia (INO) results from a brain stem lesion in the medial longitudinal fasciculus (MLF). INO manifests on horizontal gaze testing with diplopia, weak adduction on the affected side (usually cannot adduct eye past midline), and nystagmus of the contralateral eye. However, the affected eye adducts normally on convergence testing (which does not require an intact MLF).

Pain suggests a compressive lesion or inflammatory disorder.

Testing: Patients with monocular diplopia are referred to an ophthalmologist to evaluate for ocular pathology; no other tests are required beforehand.

For binocular diplopia, patients with a unilateral, single cranial nerve palsy, a normal pupillary light response, and no other symptoms or signs can usually be observed without testing for a few weeks. Many cases resolve spontaneously. Ophthalmologic evaluation may be done to monitor the patient and help further delineate the deficit.

Most other patients require neuroimaging with MRI to detect orbital, cranial, or CNS abnormalities. CT may be substituted if there is concern about a metallic intraocular foreign body or if MRI is otherwise contraindicated or unavailable. Imaging should be done immediately if findings suggest infection, aneurysm, or acute (< 3 h) stroke.

Patients with manifestations of Graves' disease should have thyroid tests (serum thyroxine [T_4] and thyroid-stimulating hormone [TSH] levels). Testing for myasthenia gravis and multiple sclerosis should be strongly considered for those with intermittent diplopia.

Treatment

Treatment is management of the underlying disorder.

Key Points

• Isolated, pupil-sparing nerve palsy in patients with no other symptoms may resolve spontaneously.

• Imaging is required for those with red flag findings.

• Focal weakness (in any muscle) may indicate a disorder of neuromuscular transmission.

Eyelid Swelling

Eyelid swelling can be unilateral or bilateral. It may be asymptomatic or accompanied by itching or pain.

Etiology

Eyelid swelling has many causes (see

Table 60-8). It usually results from an eyelid disorder but may result from disorders in and around the orbit or from systemic disorders that cause generalized edema.

The most common causes are allergic, including

• Local allergy (contact sensitivity)

• Systemic allergy (eg, angioedema, systemic allergy accompanying allergic rhinitis)

Focal swelling of one eyelid is most often caused by a chalazion.

The most immediately dangerous causes are orbital cellulitis and cavernous sinus thrombosis (rare).

[**Table 60-8.** Some Causes of Eyelid Swelling]

In addition to the disorders listed in Table 60-8, eyelid swelling may result from the following:

• Disorders that may involve the eyelid but do not cause swelling unless very advanced (eg, eyelid tumors, including squamous cell carcinomas and melanoma)

• Disorders (eg, dacryocystitis, canaliculitis) that cause swelling that begins and is usually most severe in structures near, but not part of, the eyelids

• Disorders in which swelling occurs but is not the presenting symptom (eg, basilar skull fracture, burns, trauma, postsurgery)

Evaluation

History: History of present illness should ascertain how long swelling has been present, whether it is unilateral or bilateral, and whether it has been preceded by any trauma (including insect bites). Important accompanying symptoms to identify include itching, pain, headache, change in vision, fever, and eye discharge.

Review of systems should seek symptoms of possible causes, including runny nose, itching, rash, and wheezing (systemic allergic reaction); headache, nasal congestion, and purulent nasal discharge (sinusitis); toothache (dental infection); dyspnea, orthopnea, and paroxysmal nocturnal dyspnea (heart failure); cold intolerance and changes in skin texture (hypothyroidism); and heat intolerance, anxiety, and weight loss (hyperthyroidism).

Past medical history should include recent eye injury or surgery; known heart, liver, renal, or thyroid disease; and allergies and exposure to possible allergens. Drug history should specifically include use of ACE inhibitors.

Physical examination: Vital signs should be assessed for fever and tachycardia.

Eye inspection should assess the location and color of swelling (erythematous or pale), including whether it is present on one eyelid, both eyelids, or both eyes and whether it is tender, warm, or both. The examiner should observe whether the finding represents edema of the eyelids, protrusion of the globe (proptosis), or both. Eye examination should particularly note visual acuity and range of extraocular motion (full or limited). This examination can be difficult when swelling is marked but is important because deficits suggest an orbital or retro-orbital disorder rather than an eyelid disorder; an assistant may be required to hold the eyelids open. Conjunctivae are examined for injection and discharge. Any eyelid or eye lesions are evaluated using a slit lamp.

General examination should assess signs of toxicity, suggesting a serious infection, and signs of a causative disorder. Facial skin is inspected for dryness and scales (which may suggest hypothyroidism) and greasy scales or other signs of seborrheic dermatitis. Extremities and the presacral area are examined for edema, which suggests a systemic cause. If a systemic cause is suspected, see p. 2031 for

further discussion of the evaluation.

Red flags: The following findings are of particular concern:

• Fever

• Loss of visual acuity

• Impaired extraocular movements

• Proptosis

Interpretation of findings: Some findings help distinguish among categories of disorders. The first important distinction is between inflammation or infection and allergy or fluid overload. Pain, redness, warmth, and tenderness suggest inflammation or infection. Painless, pale swelling suggests angioedema. Itching suggests allergic reaction, and absence of itching suggests cardiac or renal dysfunction.

Swelling localized to one eyelid in the absence of other signs is rarely caused by a dangerous disorder. Massive swelling of the eyelids of one or both eyes should raise suspicion of a serious problem. Signs of inflammation, proptosis, loss of vision, and impaired extraocular movements suggest an orbital disorder (eg, orbital cellulitis, cavernous sinus thrombosis) that may be pushing the globe forward or affecting the nerves or muscles. Other suggestive and specific findings are listed in Table 60-8.

Testing: In most cases, diagnosis can be established clinically and no testing is necessary. If orbital cellulitis or cavernous sinus thrombosis is suspected, diagnosis and treatment should proceed as rapidly as possible. Immediate imaging with CT or MRI should be done. If cardiac, liver, renal, or thyroid dysfunction is suspected, organ function is evaluated with laboratory tests and imaging as appropriate for that system.

Treatment

Treatment is directed at the underlying disorder. There is no specific treatment for the swelling.

Key Points

• Proptosis with impaired vision or extraocular movements suggests orbital cellulitis or cavernous sinus thrombosis, and diagnosis and treatment should proceed as rapidly as possible.

• Eyelid disorders should be differentiated from orbital and systemic causes of swelling.

Eye Pain

Eye pain may be described as sharp, aching, or throbbing and should be distinguished from superficial irritation or a foreign body sensation. In some disorders, pain is worsened by bright light. Eye pain may be caused by a serious disorder and requires prompt evaluation. Many causes of eye pain also cause a red eye.

Pathophysiology

The cornea is richly innervated and highly sensitive to pain. Many disorders that affect the cornea or anterior chamber (eg, uveitis) also cause pain via ciliary muscle spasm; when such spasm is present, bright light causes muscle contraction, worsening pain.

Etiology

Disorders that cause eye pain can be divided into those that affect primarily the cornea, other ocular disorders, and disorders that cause pain referred to the eye (see Table 60-9).

The most common causes overall are

• Corneal abrasion

• Foreign bodies

However, most corneal disorders can cause eye pain.

A feeling of scratchiness or of a foreign body may be caused by either a conjunctival or a corneal disorder.

Evaluation

History: History of present illness should address the onset, quality, and severity of pain and any history of prior episodes (eg, daily episodes in clusters). Important associated symptoms include true photophobia (shining a light into the unaffected eye causes pain in the affected eye when the affected eye is shut), decreased visual acuity, foreign body sensation and pain when blinking, and pain when moving the eye.

Review of systems should seek symptoms suggesting a cause, including presence of an aura (migraine); fever and chills (infection); and pain when moving the head, purulent rhinorrhea, productive or nocturnal cough, and halitosis (sinusitis).

Past medical history should include known disorders that are risk factors for eye pain, including autoimmune disorders, multiple sclerosis, migraine, and sinus infections. Additional risk factors to assess include use (and overuse) of contact lenses (contact lens keratitis), exposure to excessive sunlight or to welding (UV keratitis), hammering or drilling metal (foreign body), and recent eye injury or surgery (endophthalmitis).

Physical examination: Vital signs are checked for the presence of fever. The nose is inspected for purulent rhinorrhea, and the face is palpated for tenderness. If the eye is red, the preauricular region is checked for adenopathy. Hygiene during examination must be scrupulous when examining patients who have chemosis, preauricular adenopathy, punctate corneal staining, or a combination; these findings suggest epidemic keratoconjunctivitis, which is highly contagious.

Eye examination should be as complete as possible for patients with eye pain. Best corrected visual acuity is checked. Visual fields are typically tested by confrontation in patients with eye pain, but this test can be insensitive (particularly for small defects) and unreliable because of poor patient cooperation. A light is moved from one eye to the other to check for pupillary size and direct and consensual pupillary light responses. In patients who have unilateral eye pain, a light is shined in the unaffected eye while the affected eye is shut; pain in the affected eye represents true photophobia. Extraocular movements are checked. The orbital and periorbital structures are inspected. Conjunctival injection that seems most intense and confluent around the cornea and limbus is called ciliary flush.

Slit-lamp examination is done if possible. The cornea is stained with fluorescein and examined under magnification with cobalt blue light. If a slit lamp is unavailable, the cornea can be examined after fluorescein staining with a Wood's light using magnification. Ophthalmoscopy is done, and ocular pressures are measured (tonometry). In patients with a foreign body sensation or unexplained corneal abrasions, the eyelids are everted and examined for foreign bodies.

Red flags: The following findings are of particular concern:

• Vomiting, halos around lights, or corneal edema

• Signs of systemic infection (eg, fever, chills)

• Decreased visual acuity

• Proptosis

• Impaired extraocular motility

Interpretation of findings: Suggestive findings are listed in Table 60-9. Some findings suggest categories of disorders.

Scratchiness or a foreign body sensation is most often caused by disorders of the eyelids, conjunctivae, or superficial cornea. Photosensitivity is possible.

Surface pain with photophobia is often accompanied by a foreign body sensation and pain when blinking; it suggests a corneal lesion, most often a foreign body or abrasion.

Deeper pain—often described as aching or throbbing—usually indicates a serious disorder such as glaucoma, uveitis, scleritis, endophthalmitis, orbital cellulitis, or orbital pseudotumor. Within this group, eyelid swelling, proptosis, or both and impaired extraocular movements or visual acuity suggest orbital pseudotumor, orbital cellulitis, or possibly severe endophthalmitis. Fever, chills, and tenderness suggest infection (eg, orbital cellulitis, sinusitis).

A red eye suggests that the disorder causing pain is ocular rather than referred.

If pain develops in the affected eye in response to shining light in the unaffected eye when the affected eye is shut (true photophobia), the cause is most often a corneal lesion or uveitis.

If topical anesthetic drops (eg, proparacaine) abolish pain in a red eye, the cause is probably a corneal disorder.

Some findings are more suggestive of particular disorders. Pain and photophobia days after blunt eye trauma suggest uveitis. Hammering or drilling metal is a risk factor for occult metal intraocular foreign body. Pain with movement of extraocular muscles and loss of pupillary light response that is disproportionate to loss of visual acuity suggest optic neuritis.

Testing: Testing is not usually necessary, with some exceptions (see Table 60-9). Gonioscopy is done if glaucoma is suspected based on increased intraocular pressure. Imaging, usually with CT or MRI, is done if orbital pseudotumor or orbital cellulitis is suspected or if sinusitis is suspected but the diagnosis is not clinically clear. MRI is often done when optic neuritis is suspected, looking for demyelinating lesions in the brain suggesting multiple sclerosis.

Intraocular fluids (vitreous and aqueous humor) may be cultured for suspected endophthalmitis. Viral cultures can be used to confirm herpes zoster ophthalmicus or herpes

[**Table 60-9.** Some Causes of Eye Pain]

simplex keratitis if the diagnosis is not clear clinically.

Treatment

The cause of pain is treated. Pain itself is also treated. Systemic analgesics are used as needed. Pain caused by uveitis and many corneal lesions is also relieved with cycloplegic eye drops (eg, homatropine 5% qid).

Key Points

• Most diagnoses can be made by clinical evaluation.

• Infection precautions should be maintained when examining patients with bilateral red eyes.

- Important danger signs are vomiting, halos around lights, fever, decreased visual acuity, proptosis, and impaired extraocular motility.

- Pain in the affected eye in response to shining light in the unaffected eye when the affected eye is shut (true photophobia) suggests a corneal lesion or uveitis.

- If a topical anesthetic (eg, proparacaine) relieves pain, the cause of pain is a corneal lesion.

- Hammering or drilling on metal is a risk factor for occult intraocular foreign body.

Proptosis

(Exophthalmos)

Proptosis is protrusion of the eyeball. Exophthalmos means the same thing, and this term is usually used when describing proptosis due to Grave's disease. Disorders that may cause changes in the appearance of the face and eyes that resemble proptosis but are not include hyperthyroidism without infiltrative eye disease, Cushing's disease, and severe obesity.

Etiology

The **most common cause** is Graves' disease (see Table 60-10), which causes edema and lymphoid infiltration of the orbital tissues.

Evaluation

Rate of onset may provide a clue to diagnosis. Sudden unilateral onset suggests intraorbital hemorrhage (which can occur after surgery, retrobulbar injection, or trauma) or inflammation of the orbit or paranasal sinuses. A 2- to 3-wk onset suggests chronic inflammation or orbital inflammatory pseudotumor (non-neoplastic cellular infiltration and proliferation); slower onset suggests an orbital tumor.

Ocular examination findings typical of hyperthyroidism but unrelated to infiltrative eye disease include eyelid retraction, eyelid lag, temporal flare of the upper eyelid, and staring. Other signs include eyelid erythema and conjunctival hyperemia. Prolonged exposure of larger-than-usual areas of the eyeball to air causes corneal drying and can lead to infection and ulceration.

Testing: Proptosis can be confirmed with exophthalmometry, which measures the distance between the lateral angle of the bony orbit and the cornea; normal values are < 20 mm in whites and < 22 mm in blacks. CT or MRI is often useful to confirm the diagnosis and to identify structural causes of unilateral proptosis. Thyroid function testing is indicated when Graves' disease is suspected.

[**Table 60-10.** Some Causes of Proptosis]

Treatment

Lubrication to protect the cornea is required in severe cases. When lubrication is not sufficient, surgery to provide better coverage of the eye surface or to reduce proptosis may be required. Systemic corticosteroids (eg, prednisone 1 mg/kg po once/day for 1 wk, tapered over ≥ 1 mo) are often helpful in controlling edema and orbital congestion due to thyroid eye disease or inflammatory orbital pseudotumor. Other interventions vary by etiology. Graves' exophthalmos is not affected by treatment of the thyroid condition but may lessen over time. Tumors must be surgically removed. Selective embolization or, rarely, trapping procedures may be effective in cases of arteriovenous fistulas involving the cavernous sinus.

Floaters

Floaters are opacities that move across the visual field and do not correspond to external visual objects.

Pathophysiology

With aging, the vitreous humor can contract and separate from the retina. The age at which this change occurs varies but most often is between 50 and 75 yr. During this separation, the vitreous can intermittently tug on the retina. The mechanical traction stimulates the retina, which sends a signal that is perceived by the brain and interpreted as light. Complete separation of the vitreous leads to an increase in floaters, which may last for years.

However, traction on the retina may create a hole (retinal tear), and if fluid leaks behind the tear, the retina may detach. Retinal detachment may also be caused by other factors (eg, trauma, primary retinal disorders). Lightning-like flashes, common in retinal detachment, are called **photopsias**. Photopsias can also occur when rubbing the eyes or when looking around after awakening.

Etiology

The most common cause of vitreous floaters is

• Contraction of the vitreous humor that occurs for unknown reasons (idiopathic)

Less common causes are listed in
Table 60-11.

Rare causes of floaters include intraocular tumors (eg, lymphoma). Intraocular foreign bodies can cause floaters but usually manifest with other symptoms, such as loss of vision, eye pain, or redness.

Evaluation

The most important goal is to identify serious vitreous and retinal disorders. If these disorders cannot be ruled out, patients should be examined by an ophthalmologist using an indirect ophthalmoscope after pupillary dilation. Recognizing ocular migraine is also helpful.

History: History of present illness should ascertain onset and duration of symptoms and the shape and volume of floaters, as well as whether they are unilateral or bilateral and whether they have been preceded by trauma. The patient should try to distinguish floaters from lightning-like flashes of light (as in photopsias) or jagged lines across the visual field (as in migraine). Important associated symptoms include loss of vision (and its distribution in the visual field) and eye pain.

Review of systems should seek symptoms of possible causes, such as headaches (ocular migraine) and eye redness (vitreous inflammation).

Past medical history should note diabetes (including diabetic retinopathy), migraine headaches, eye surgery, severe myopia, and any disorders that could affect the immune system (eg, AIDS).

Physical examination: Eye examination should be reasonably complete. Best corrected visual acuity is measured. The eyes are inspected for redness. Visual fields are assessed in all patients. However, recognition of visual field defects by bedside examination is very insensitive, so inability to show such a defect is not evidence that the patient has full visual fields. Extraocular movements and pupillary light responses are assessed. If patients have a red eye or eye pain, the corneas are examined under magnification after fluorescein staining, and slit-lamp examination is done if possible. Ocular pressure is measured (tonometry).

Ophthalmoscopy is the most important part of the examination. It is done using a direct ophthalmoscope and after dilating the pupils. To dilate the pupils, the physician first makes sure to record pupillary size and light responses, then instills drops, usually 1 drop each of a short-acting α-adrenergic agonist (eg, 2.5% phenylephrine) and a cycloplegic (eg, 1% tropicamide or 1% cyclopentolate). The pupils are fully dilated about 20 min after these drops are instilled.

Red flags: The following findings are of particular concern:

[Table 60-11. Some Causes of Floaters]

- Sudden increase in floaters
- Lightning-like flashes (photopsias)
- Loss of vision, diffuse or focal (visual field defect)
- Recent eye surgery or eye trauma
- Eye pain
- Loss of red reflex
- Abnormal retinal findings

Interpretation of findings: Retinal detachment is suggested by sudden increases in floaters, photopsias, or any of its other, more specific characteristics (eg, visual field defects, retinal abnormalities). Bilateral synchronous symptoms suggest ocular migraine, although patients often have difficulty deciphering the laterality of their symptoms (eg, they often interpret scintillating scotoma of the left field of both eyes as left-eyed). Loss of red reflex suggests opacification of the vitreous (eg, vitreous hemorrhage or inflammation), but it also can be caused by advanced cataracts. Loss of vision suggests a serious disorder causing dysfunction of the vitreous or retina.

Testing: Patients who require evaluation by an ophthalmologist may need testing. However, tests can be selected by or in conjunction with the ophthalmologist. For example, patients suspected of having chorioretinitis may require microbiologic testing.

Treatment

Idiopathic vitreous floaters require no treatment. Other disorders causing symptoms are treated.

Key Points

- Floaters by themselves rarely indicate a serious disorder.
- Patients with any abnormal findings on examination require ophthalmologic referral.
- If floaters are accompanied by any other symptoms (eg, persistent flashing lights, visual deficit, sensation of a moving curtain of vision loss), patients require ophthalmologic referral, regardless of examination findings.

Red Eye

(Pink Eye)

Red eye refers to a red appearance of the opened eye, reflecting dilation of the superficial ocular vessels.

Pathophysiology

Dilation of superficial ocular vessels can result from

- Infection
- Allergy
- Inflammation (noninfectious)

• Elevated intraocular pressure

Several ocular components may be involved, most commonly the conjunctiva, but also the uveal tract, episclera, and sclera.

Etiology

The most common causes of red eye include

• Infectious conjunctivitis

• Allergic conjunctivitis

Corneal abrasions and foreign bodies are common causes (see Table 60-12). Although the eye is red, patients usually present with a complaint of injury, eye pain, or both. However, in young children and infants, this information may be unavailable.

Evaluation

Most disorders can be diagnosed by a general health care practitioner.

History: History of present illness should note the onset and duration of redness and presence of any change in vision, itching, scratchy sensation, pain, or discharge. Nature and severity of pain, including whether pain is worsened by light (photophobia), are noted. The clinician should determine whether discharge is watery or purulent. Other questions assess history of injury, including exposure to irritants and use of contact lenses (eg, possible overuse, such as wearing them while sleeping). Prior episodes of eye pain or redness and their time patterns are elicited.

Review of systems should seek symptoms suggesting possible causes, including headache, nausea, vomiting, and halos around lights (acute angle-closure glaucoma); runny nose and sneezing (allergies, URI); and cough, sore throat, and malaise (URI).

Past medical history includes questions about known allergies and autoimmune disorders. Drug history should specifically ask about recent use of topical ophthalmic drugs (including OTC drugs), which might be sensitizing.

Physical examination: General examination should include head and neck examination for signs of associated disorders (eg, URI, allergic rhinitis, zoster rash).

Eye examination involves a formal measure of visual acuity and usually requires a penlight, fluorescein stain, and slit lamp.

Best corrected visual acuity is measured. Pupillary size and reactivity to light are assessed. True photophobia (sometimes called

[**Table 60-12.** Some Causes of Red Eye]

consensual photophobia) is present if shining light into an unaffected eye causes pain in the affected eye when the affected eye is shut. Extraocular movements are assessed, and the eye and periorbital tissues are inspected for lesions and swelling. The tarsal surface is inspected for follicles. The corneas are stained with fluorescein and examined with magnification. If a corneal abrasion is found, the eyelid is everted and examined for hidden foreign bodies. Inspection of the ocular structures and cornea is best done using a slit lamp. A slit lamp is also used to examine the anterior chamber for cells, flare, and pus (hypopyon). Ocular pressure is measured using tonometry, although it may be permissible to omit this test if there are no symptoms or signs suggesting a disorder other than conjunctivitis.

Red flags: The following findings are of particular concern:

• Sudden, severe pain and vomiting

• Zoster skin rash

• Decreased visual acuity

• Corneal crater

• Branching, dendritic corneal lesion

• Ocular pressure > 40 mm Hg

• Failure to blanch with phenylephrine eye drop

Interpretation of findings: Conjunctival disorders and **episcleritis** are differentiated from other causes of red eye by the absence of pain, photophobia, and corneal staining. Among these disorders, episcleritis is differentiated by its focality, and subconjunctival hemorrhage is usually differentiated by the absence of lacrimation, itching, and photosensitivity. Clinical criteria do not accurately differentiate viral from bacterial conjunctivitis.

Corneal disorders are differentiated from other causes of red eye (and usually from each other) by fluorescein staining. These disorders also tend to be characterized by pain and photophobia. If instillation of an ocular anesthetic drop (eg, proparacaine 0.5%), which is done before tonometry and ideally before fluorescein instillation, completely relieves pain, the cause is probably limited to the cornea. If pain is present and is not relieved by an ocular anesthetic, the cause may be anterior uveitis, glaucoma, or scleritis. Because patients may have anterior uveitis secondary to corneal lesions, persistence of pain after instillation of the anesthetic does not exclude a corneal lesion.

Anterior uveitis, glaucoma, acute angle-closure glaucoma, and **scleritis** can usually be differentiated from other causes of red eye by the presence of pain and the absence of corneal staining. Anterior uveitis is likely in patients with pain, true photophobia, absence of corneal fluorescein staining, and normal intraocular pressure; it is definitively diagnosed based on the presence of cells and flare in the anterior chamber. However, these findings may be difficult for general health care practitioners to discern. Acute angle-closure glaucoma can usually be recognized by the sudden onset of its severe and characteristic symptoms, but tonometry is definitive.

Instillation of phenylephrine 2.5% causes blanching in a red eye unless the cause is scleritis. Phenylephrine is instilled to dilate the pupil in patients needing a thorough retinal examination. However, it should not be used in patients who have the following:

• Suspected acute angle-closure glaucoma

• A history of angle-closure glaucoma

• A narrow anterior chamber

Testing: Testing is usually unnecessary. Viral cultures may help if herpes simplex or herpes zoster is suspected and the diagnosis is not clear clinically. Corneal ulcers are cultured by an ophthalmologist. Gonioscopy is done in patients with glaucoma. Testing for autoimmune disorders may be worthwhile in patients with uveitis and no obvious cause (eg, trauma). Patients with scleritis undergo further testing as directed by an ophthalmologist.

Treatment

The cause is treated. Red eye itself does not require treatment. Topical vasoconstrictors are not recommended.

Key Points

• Most cases are caused by conjunctivitis.

• Pain and true photophobia suggest other, more serious diagnoses.

• In patients with pain, slit-lamp examination with fluorescein staining and tonometry are key.

• Persistence of pain despite an ocular anesthetic in a patient with a normal fluorescein examination suggests anterior uveitis, scleritis, or acute angle-closure glaucoma. These diagnoses should not be missed.

Tearing

(Epiphora)

Excess tearing may cause a sensation of watery eyes or result in tears falling down the cheek (epiphora).

Pathophysiology

Tears are produced in the lacrimal gland and drain through the upper and lower puncta into the canaliculi and then into the lacrimal sac and nasolacrimal duct (see Fig. 60-3). Obstruction of tear drainage can lead to stasis and infection. Recurrent infection of the lacrimal sac (dacryocystitis) can sometimes spread, potentially leading to orbital cellulitis.

Etiology

Overall, the most common causes of tearing are

• URI

• Allergic rhinitis

Tearing can be caused by increased tear production or decreased nasolacrimal drainage.

Increased tear production: The most common causes are

• URI

• Allergic rhinitis

• Allergic conjunctivitis

• Dry eyes (reflex tearing produced in response to dryness of the ocular surface)

• Trichiasis

Any disorder causing conjunctival or corneal irritation can increase tear production (see Table 60-13). However, most patients with corneal disorders that cause excess tearing (eg, corneal abrasion, corneal ulcer, corneal foreign body, keratitis) or with primary angle-closure glaucoma or anterior uveitis present with eye symptoms other than tearing (eg, eye pain, redness). Most people who have been crying do not present for evaluation of tearing.

Decreased nasolacrimal drainage: The most common causes are

• Idiopathic age-related nasolacrimal duct stenosis

• Dacryocystitis

• Ectropion

[Fig. 60-3. Anatomy of the lacrimal system.]

Nasolacrimal drainage system obstruction may be caused by strictures, tumors, or foreign bodies (eg, stones, often associated with subclinical infection by *Actinomyces*). Obstruction can also be a congenital malformation. Many disorders and drugs can cause stricture or obstruction of nasolacrimal drainage.

Other causes of nasolacrimal drainage stricture or obstruction include

• Burns

• Chemotherapy drugs

• Eye drops (particularly echothiophate iodide, epinephrine, and pilocarpine)

• Infection, including canaliculitis (eg, caused by *Staphylococcus aureus*, *Actinomyces*, *Streptococcus*, *Pseudomonas*, herpes zoster virus, herpes simplex conjunctivitis, infectious mononucleosis, human papillomavirus, *Ascaris*, leprosy, TB)

• Inflammatory disorders (sarcoidosis, Wegener's granulomatosis)

• Injuries (eg, nasoethmoid fractures; nasal, orbital, or endoscopic sinus surgery)

• Obstruction of nasal outlet despite an intact nasolacrimal system (eg, URI, allergic rhinitis, sinusitis)

• Radiation therapy

• Stevens-Johnson syndrome

• Tumors (eg, primary lacrimal sac tumors, benign papillomas, squamous and basal cell carcinoma, transitional cell carcinoma, fibrous histiocytomas, midline granuloma, lymphoma)

Evaluation

History: History of present illness addresses the duration, onset, and severity of symptoms, including whether tears drip down the cheek (true epiphora). The effects of weather, environmental humidity, and cigarette smoke are ascertained.

Review of symptoms should seek symptoms of possible causes, including itching, rhinorrhea, or sneezing, particularly when occurring perennially or after exposure to specific potential allergens (allergic reaction); eye irritation or pain (blepharitis, corneal abrasion, irritant chemicals); and pain near the medial canthus (dacryocystitis). Other symptoms are of lower yield but should be sought; they include positional headache, purulent rhinorrhea, nocturnal cough, and fever (sinusitis, Wegener's granulomatosis); rash (Stevens-Johnson syndrome); cough, dyspnea, and chest pain (sarcoidosis); and epistaxis, hemoptysis, polyarthralgias, and myalgias (Wegener's granulomatosis).

Past medical history asks about known disorders that can cause tearing, including Wegener's granulomatosis, sarcoidosis, and

[Table 60-13. Some Causes of Tearing]

cancer treated with chemotherapy drugs; disorders that cause dry eyes (eg, RA, sarcoidosis, Sjogren's syndrome); and drugs, such as echothiophate, epinephrine, and pilocarpine. Previous ocular and nasal history, including infections, injuries, surgical procedures, and radiation exposure, is ascertained.

Physical examination: Examination focuses on the eye and surrounding structures.

The face is inspected; asymmetry suggests congenital or acquired obstruction of nasolacrimal duct drainage. When available, a slit lamp should be used to examine the eyes. The conjunctivae and corneas are inspected for lesions, including punctate spots, and redness. The cornea is stained with fluorescein and examined. The lids are everted to detect hidden foreign bodies. The eyelids, including the lacrimal puncta, are closely inspected for foreign bodies, blepharitis, hordeola, ectropion, entropion, and trichiasis. The lacrimal sac (near the medial canthus) is palpated for warmth, tenderness, and swelling. Any swellings are palpated for consistency and to see whether pus is expressed.

The nose is examined for congestion, purulence, and bleeding.

Red flags: The following findings are of particular concern:

• Repeated, unexplained episodes of tearing

• Hard mass in or near the nasolacrimal drainage structures

Interpretation of findings: Findings that suggest obstruction of nasolacrimal drainage include

• Tears running down the cheek (true epiphora)

• Absence of signs of a specific cause

A cause is often evident from the clinical evaluation (see Table 60-14).

[**Table 60-14.** Findings that Suggest the Cause of Nasolacrimal Obstruction]

Testing: Testing is often unnecessary because the cause is usually evident from the examination.

Schirmer's test with a large amount of wetting (eg, > 25 mm) suggests an evaporative dry eye as the etiology of tearing. Schirmer's test with very little wetting (< 5.5 mm) suggests an aqueous teardeficient dry eye. Usually, Schirmer's test is done by an ophthalmologist to ensure it is done and interpreted correctly.

Probing and saline irrigation of the lacrimal drainage system can help detect anatomic obstruction of drainage, as well as stenosis due to complete obstruction of the nasolacrimal drainage system. Irrigation is done with and without fluorescein dye. Reflux through the opposite punctum or canaliculus signals fixed obstruction; reflux and nasal drainage signify stenosis. This test is considered adjunctive and is done by ophthalmologists.

Imaging tests and procedures (dacryocystography, CT, nasal endoscopy) are sometimes useful to delineate abnormal anatomy when surgery is being considered or occasionally to detect an abscess.

Treatment

Underlying disorders (eg, allergies, foreign bodies, conjunctivitis) are treated.

The use of artificial tears lessens tearing when dry eyes or corneal epithelial defects are the cause.

Congenital nasolacrimal duct obstruction often resolves spontaneously. In patients < 1 yr, manual compression of the lacrimal sac 4 or 5 times/day may relieve the distal obstruction. After 1 yr, the nasolacrimal duct may need probing with the patient under general anesthesia. If obstruction is recurrent, a temporary drainage tube may be inserted.

In acquired nasolacrimal duct obstruction, irrigation of the nasolacrimal duct may be therapeutic when underlying disorders do not respond to treatment. As a last resort, a passage between the lacrimal sac and the nasal cavity can be created surgically (dacryocystorhinostomy).

In cases of punctal or canalicular stenosis, dilation is usually curative. If canalicular stenosis is severe and bothersome, a surgical procedure that places a glass tube leading from the caruncle into the nasal cavity can be considered.

Geriatrics Essentials

Idiopathic age-related nasolacrimal duct stenosis is the most common cause of unexplained epiphora in elderly patients; however, tumors should also be considered.

Key Points

• If tears do not run down the cheek, dry eyes is often the cause.

• If tears run down the cheek, obstruction of nasolacrimal drainage is likely.

• Testing is often unnecessary but is needed in cases of recurrent infectious dacryocystitis, which can progress to more serious conditions such as orbital cellulitis.

Other Eye Symptoms

Dry eyes are discussed under Keratoconjunctivitis sicca (see p. 592) The disorder is most often idiopathic or associated with older age but can also be caused by connective tissue diseases (eg, Sjogren's syndrome, RA, SLE).

Eye discharge: Discharge is often accompanied by a red eye (see p. 563) and commonly is caused by allergic or infectious conjunctivitis, blepharitis, and, in infants, ophthalmia neonatorum (neonatal conjunctivitis). Infectious discharge may be purulent in bacterial infection, such as staphylococcal conjunctivitis or gonorrhea. Less common causes include dacryocystitis and canaliculitis.

Diagnosis is usually made clinically. Allergic conjunctivitis can often be distinguished from infectious by predominance of itching, clear discharge, and presence of other allergic symptoms (eg, runny nose, sneezing). Clinical differentiation between viral and bacterial conjunctivitis is difficult. Cultures are not usually done, but are indicated for patients with the following:

• Clinically suspected gonococcal or chlamydial conjunctivitis

• Severe symptoms

• Immunocompromise

• A vulnerable eye (eg, after a corneal transplant, in exophthalmos due to Graves' disease)

• Ineffective initial therapy

Halos: Halos around light may result from cataracts; conditions that result in corneal edema, such as acute angle-closure glaucoma or disorders that cause bullous keratopathy; corneal haziness; mucus on the cornea; or drugs, such as digoxin or chloroquine.

Blue hues: Certain conditions may cause a blue tint to the visual field (cyanopsia). Cyanopsia may occur for a few days after cataract removal or as an adverse effect of sildenafil and possibly other phosphodiesterase-5 (PDE5) inhibitors.

Scotomata: Scotomata are visual field deficits and are divided into

• Negative scotomata (blind spots)

• Positive scotomata (light spots or scintillating flashes)

Negative scotomata may not be noticed by patients unless they involve central vision and interfere significantly with visual acuity; the complaint is most often decreased visual acuity (see p. 541). Negative scotomata have multiple causes that can sometimes be distinguished by the specific type of field deficit (see Table 60-1) as identified by use of a tangent screen, Goldmann perimeter, or computerized automated perimetry (in which the visual field is mapped out in detail based on patient response to a series of flashing lights in different locations controlled by a standardized computer program).

Positive scotomata represent a response to abnormal stimulation of some portion of the visual system, as occurs in migraines.

Chapter 61. Refractive Error

Introduction

In the emmetropic (normally refracted) eye, entering light rays are focused on the retina by the cornea and the lens, creating a sharp image that is transmitted to the brain. The lens is elastic, more so in younger people. During accommodation, the ciliary muscles adjust lens shape to properly focus images. Refractive errors are failure of the eye to focus images sharply on the retina, causing blurred vision (see Fig. 61-1).

In **myopia** (nearsightedness), the point of focus is in front of the retina because the cornea is too steeply curved, the axial length of the eye is too long, or both. Distant objects are blurred, but near objects can be seen clearly. To correct myopia, a concave (minus) lens is used. Myopic refractive errors in children frequently increase until the child stops growing.

In **hyperopia** (farsightedness), the point of focus is behind the retina because the cornea is too flatly curved, the axial length is too short, or both. In adults, both near and distant objects are blurred. Children and young adults with mild hyperopia may be able to see clearly because of their ability to accommodate. To correct hyperopia, a convex (plus) lens is used.

[**Fig. 61-1.** Errors of refraction.]

In **astigmatism,** nonspherical (variable) curvature of the cornea or lens causes light rays of different orientations (eg, vertical, oblique, horizontal) to focus at different points. To correct astigmatism, a cylindric lens (a segment cut from a cylinder) is used. Cylindric lenses have no refractive power along one axis and are concave or convex along the other axis.

Presbyopia is loss of the lens' ability to change shape to focus on near objects due to aging. Typically, presbyopia becomes noticeable by the time a person reaches the early or mid 40s. A convex (plus) lens is used for correction when viewing near objects. These lenses may be supplied as separate glasses or built into a lens as bifocals or variable focus lenses.

Anisometropia is a significant difference between the refractive errors of the 2 eyes (usually > 3 diopters). When corrected with eyeglasses, a difference in image size (aniseikonia) is produced; it can lead to difficulties with fusion of the 2 differently sized images and even to suppression of one of the images.

Symptoms and Signs

The primary symptom of refractive errors is blurred vision for distant objects, near objects, or both. Sometimes the excessive ciliary muscle tone can cause headaches. Occasionally, excessive staring can lead to ocular surface desiccation, causing eye irritation, itching, visual fatigue, foreign body sensation, and redness. Frowning when reading and excessive blinking or rubbing of the eyes are symptoms in children.

Diagnosis

Refraction should be checked every 1 or 2 yr. Screening children helps detect refractive errors before they interfere with learning. A comprehensive eye examination (see p. 537) should accompany refraction testing, whether done by an ophthalmologist or an optometrist.

Contact Lenses

Contact lenses often provide better visual acuity and peripheral vision than do eyeglasses and can be prescribed to correct myopia, hyperopia, astigmatism, anisometropia, aniseikonia, aphakia (absence of the lens) after cataract removal, and keratoconus (a conical-shaped cornea). Either soft or rigid lenses are used to correct myopia and hyperopia. Toric soft contact lenses (which have different curvatures molded onto the front lens surface) or rigid lenses are used to correct significant astigmatism; they are

satisfactory in many cases but require expert fitting.

Presbyopia can also be corrected with contact lenses. In one approach, termed monovision, the nondominant eye is corrected for reading and the dominant eye is corrected for distant vision. Rigid and soft bifocal and multifocal contact lenses can also be successful, but the fitting procedure is time-consuming because precise alignment is essential.

Neither rigid nor soft contact lenses offer the eyes the protection against blunt or sharp injury that eyeglasses do.

Care and Complications

Instructions for hygiene and handling lenses must be strictly observed. Poor contact lens hygiene may lead to persistent inflammation or infection of the cornea.

Contact lenses occasionally cause painless superficial corneal changes. Contact lenses can be painful when

- The corneal epithelium is abraded (see p. 3236); the cornea becomes red and inflamed and stains with fluorescein.
- The lenses fit poorly (eg, too tight, too loose, poorly centered).
- There is too little moisture to keep the lens floating above the cornea.
- The lenses are worn in a nonideal environment (eg, O_2-poor, smoky, windy).
- A lens is improperly inserted or removed.
- A small foreign particle (eg, soot, dust) becomes trapped between the lens and the cornea.
- The lenses are worn for a long time (overwear syndrome).

In overwear syndrome, spontaneous healing may occur in a day or so if lenses are not worn. In some cases, active treatment is required—eg, topical antibiotic eyedrops or ointments and dilation of the pupil with a mydriatic to ease photophobia. (Mydriatics work by paralyzing the muscles of the iris and ciliary body [movement of the inflamed muscles causes pain].) Recovery is usually rapid, complete, and without vision impairment. An ophthalmologist should be consulted before lenses are worn again.

Risk factors for contact lens-related corneal infection (keratitis) include the following:

- Poor lens hygiene
- Overnight or extended wear
- Use of tap water in the cleaning regimen
- Eyes with a compromised ocular surface (eg, dryness, poor corneal sensation)

Infections require rapid management by an ophthalmologist.

Corneal ulcer: A corneal ulcer, which is a potentially vision-threatening infection of the cornea, is suspected when a contact lens wearer experiences intense eye pain (both foreign body sensation and ache), redness, photophobia, and tearing (see also p. 588).

Diagnosis is by slit-lamp examination and fluorescein staining. A corneal infiltrate (collection of WBCs in the corneal stroma) is present. At times, the corneal infiltrate is large and dense enough to be seen with handheld magnification or even with the naked eye as a white spot on the cornea. Microbiologic analysis

of cultures and smears of the corneal infiltrate, contact lens, and contact lens case is indicated.

Treatment includes cessation of contact lens wear and antibiotic drops. Initial therapy includes broad-spectrum antibiotic coverage using a fluoroquinolone antibiotic drop q 15 to 60 min around the clock for 24 to 72 h, then at gradually longer intervals. Drops of an additional antibiotic, such as cefazolin, vancomycin, or concentrated tobramycin, are used if the ulcer is large, deep, or close to the visual axis. The antibiotic may be changed later based on culture results. Neglected cases may respond poorly or not at all to treatment, and severe vision loss may result.

Rigid Corneal Contact Lenses

Older polymethyl methacrylate rigid contact lenses have been replaced by gas-permeable contact lenses (GPCLs) made of fluorocarbon and polymethyl methacrylate admixtures. GPCLs are 6.5 to 10 mm in diameter and cover part of the cornea, floating on the tear layer overlying it.

Rigid contact lenses can improve vision for people with myopia, hyperopia, and astigmatism. If the corneal surface is irregular, rigid lenses often provide a smooth refracting surface and thus improve visual acuity noticeably more than soft contact lenses or eyeglasses.

For complete wearing comfort, rigid contact lenses require an adaptation period, sometimes as long as 1 wk. During this time, the wearer gradually increases the number of hours the lenses are worn each day. Importantly, no pain should occur at any time. Pain is a sign of an ill-fitting contact lens or corneal irritation. Wearers usually experience temporary (< 2 h) blurred vision (spectacle blur) when wearing eyeglasses after removing rigid contact lenses.

Soft Hydrophilic Contact Lenses

Soft contact lenses are made of poly-2-hydroxyethyl methacrylate and other flexible plastics and are 30 to 79% water. They are 13 to 15 mm in diameter and cover the entire cornea. Soft contact lenses can improve vision for people with myopia and hyperopia. Because soft contact lenses mold to the existing corneal curvature, anything greater than minimal astigmatism cannot be treated unless a special toric lens, which has different curvatures molded onto the front lens surface, is used. Weighting the lower aspect of the lens maintains its orientation.

Soft contact lenses are also prescribed for treatment of recurrent corneal erosions and other corneal disorders (called bandage or therapeutic contact lenses). Prophylactic antibiotic eyedrops (eg, fluoroquinolone qid) may be advisable with a bandage lens. Extended wearing of contact lenses, especially in aphakia after cataract surgery, is practical, but an ophthalmologist should examine the patient at least 4 times/yr. The patient should clean the lenses once/wk.

Because of their larger size, soft contact lenses are easier to handle, are not as likely as rigid lenses to eject spontaneously, and are less likely to allow foreign bodies to lodge beneath them. Immediate wearing comfort allows for a brief adaptation period.

Soft contact lenses have a higher incidence of corneal infections, which increases for every night a person wears them during sleep. When dry, soft contact lenses are brittle and break easily. They absorb a certain amount of moisture (based on the water content) from the tear film to retain adequate shape and pliability. Therefore, patients with dry eye are usually more comfortable wearing lenses that have a low water content.

Refractive Surgery

Corneal refractive surgery alters the curvature of the cornea to focus light more precisely on the retina. The goal of refractive surgery is to decrease dependence on eyeglasses or contact lenses. Most people who undergo refractive surgery achieve this goal; about 95% do not need corrective lenses for distance vision. Ideal candidates for refractive surgery are people with healthy eyes who are not satisfied wearing eyeglasses or contact lenses. Preoperative examination excludes people with active ocular diseases, including severe dry eye. Candidates should not have a history of autoimmune or connective tissue

disease because of potential problems with wound healing. Latent herpes simplex virus may be reactivated after surgery; patients should be advised accordingly. Refraction should be stable for at least 1 yr, and candidates should be > 18 yr. Another contraindication is use of isotretinoin or amiodarone.

Adverse effects of refractive surgery include temporary foreign body sensation, glare, halos, and dryness; occasionally, these symptoms persist. Potential complications include overcorrection and undercorrection, infection, and irregular astigmatism. In excimer laser procedures performed on the superficial corneal stroma, haze formation is possible. If infection, irregular astigmatism, or haze formation causes permanent changes in the central cornea, best-corrected acuity could be lost. The overall complication rate is low; chance of vision loss is < 1% if the patient is considered a good candidate for refractive surgery preoperatively.

Laser In Situ Keratomileusis

In laser in situ keratomileusis (LASIK), a flap of corneal tissue is created with a laser or mechanical microkeratome and turned back, the underlying stromal bed is sculpted (photo-ablated) with the excimer laser, and the flap is replaced without suturing. Because surface epithelium is not disrupted centrally, vision returns rapidly. Most people notice a significant improvement the next day. LASIK can be used to treat myopia, astigmatism, and hyperopia.

Advantages of LASIK over photorefractive keratectomy (PRK) include the desirable lack of healing response (the central corneal epithelium is not removed, thereby decreasing the risk of central haze formation that occurs during healing), the shorter visual rehabilitation period, and minimal postoperative pain. Disadvantages include possible intraoperative and postoperative flap-related complications, such as irregular flap formation, flap dislocation, and the need for adequate corneal thickness to prevent long-term corneal ectasia. Ectasia occurs when the cornea has become so thin that intraocular pressure causes instability and bulging of the thinned and weakened corneal stroma. Blurring, increasing myopia, and irregular astigmatism can result.

Photorefractive Keratectomy

In PRK, the excimer laser is used to sculpt (photoablate) the anterior curvature of the corneal stromal bed to treat myopia, hyperopia, and astigmatism. The corneal epithelium is removed before photoablation and generally takes 3 to 4 days to regenerate; during this time a bandage contact lens is worn. Unlike LASIK, no corneal flap is created.

PRK may be more suitable for patients with thin corneas or anterior basement membrane dystrophy.

Advantages of PRK include an overall thicker residual stromal bed (thereby reducing risk of ectasia) and lack of flap-related complications. Disadvantages include potential for corneal haze formation if a large amount of corneal tissue is ablated and the need for postoperative corticosteroid drops for 3 to 4 mo. More than 95% of patients see 20/40 or better without eyeglasses after surgery.

Intracorneal Ring Segments

Intracorneal ring segments (INTACS) are thin arc-shaped segments of biocompatible plastic that are inserted in pairs through a small radial corneal incision into the peripheral corneal stroma at two-thirds depth. After INTACS are inserted, the central corneal curvature is flattened, reducing myopia. INTACS are used for mild myopia (< 3 diopters) and minimal astigmatism (< 1 diopter). INTACS maintain a central, clear, optical zone because the 2 segments are placed in the corneal periphery. INTACS can be replaced or removed if desired.

Risks include induced astigmatism, undercorrection and overcorrection, infection, glare, halo, and incorrect depth placement. Vision results are very good; in US clinical studies, 97% of patients saw 20/40 or better and 74% of patients saw 20/20 or better.

Conductive Keratoplasty

Conductive keratoplasty (CK) is a thermal technique that can treat spherical hyperopia (ie, hyperopia without associated astigmatism) and presbyopia. CK uses radiofrequency energy applied with a fine probe in a ring pattern to the peripheral cornea to contract the periphery and steepen the center, thereby increasing the refractive power of the cornea. For presbyopic patients who wear only reading glasses, CK is typically done in the nondominant eye (monovision) to induce myopia in that eye and enable the patient to regain reading vision. As the presbyopia progresses, additional rings of treatment are added. Risks of CK include induced astigmatism and regression of effect.

Phakic Intraocular Lenses

Phakic intraocular lenses (IOLs) are lens implants that are used to treat severe myopia in patients who are not suitable candidates for laser vision correction. Unlike in cataract surgery, the patient's natural lens is not removed. The phakic IOL is inserted directly anterior or posterior to the iris through an incision in the eye. This procedure is intraocular surgery and must be done in an operating room.

Risks include cataract formation, glaucoma, infection, and loss of corneal endothelial cells.

Because phakic IOLs do not correct astigmatism, patients can undergo subsequent laser vision correction to refine refractive results in a technique known as bioptics. Because the bulk of the myopia is corrected with the phakic IOL, less corneal tissue is removed with LASIK, and the risk of ectasia is thus low.

Clear Lensectomy

Clear lensectomy can be considered in patients with high hyperopia who are already presbyopic. This procedure is identical to cataract surgery except the patient's lens is clear and not cataractous. A multifocal intraocular lens, which allows the patient to focus over a wide range of distances without external lens correction, can be inserted.

The main risks of clear lensectomy are infection and rupture of the posterior capsule of the lens, which would necessitate further surgery. Clear lensectomy should be done with great caution in young myopic patients because they have an increased risk of retinal detachment.

Radial and Astigmatic Keratotomy

Radial and astigmatic keratotomy procedures change the shape of the cornea by making deep corneal incisions using a diamond blade.

Radial keratotomy has been replaced by laser vision correction and is rarely used because it offers no clear advantages over laser vision correction, has a greater need for subsequent retreatment, leads to visual and refractive results that change through the day, and tends to cause hyperopia in the long term.

Astigmatic keratotomy is used to treat astigmatism at the time of cataract surgery or after corneal transplantation.

Chapter 62. Eyelid and Lacrimal Disorders

Introduction

Common eyelid and lacrimal disorders include blepharitis, blepharospasm, canaliculitis, chalazion and hordeolum, dacryocystitis, dacryostenosis, entropion and ectropion, trichiasis, and tumors.

Blepharitis

Blepharitis is inflammation of the eyelid margins that may be acute or chronic. Symptoms and signs include itching and burning of the eyelid margins with redness and edema. Diagnosis is by history and examination. Acute ulcerative blepharitis is usually treated with topical antibiotics or systemic antivirals. Acute nonulcerative blepharitis is occasionally treated with topical corticosteroids. Chronic disease is treated with tear supplements, warm compresses, and occasionally oral antibiotics (eg, a tetracycline) for meibomian gland dysfunction or with eyelid hygiene and tear supplements for seborrheic blepharitis.

Etiology

Blepharitis may be acute (ulcerative or nonulcerative) or chronic (meibomian gland dysfunction, seborrheic blepharitis).

Acute: Acute ulcerative blepharitis is usually caused by bacterial infection (usually staphylococcal) of the eyelid margin at the origins of the eyelashes; the lash follicles and meibomian glands are also involved. It may also be due to a virus (eg, herpes simplex, varicella zoster).

Acute nonulcerative blepharitis is usually caused by an allergic reaction involving the same area (eg, atopic blepharodermatitis and seasonal allergic blepharoconjunctivitis, which cause intense itching, rubbing, and a rash; contact sensitivity [dermatoblepharo-conjunctivitis]).

Chronic: Chronic blepharitis is noninfectious inflammation of unknown cause. Meibomian glands in the eyelid produce lipids (meibum) that reduce tear evaporation by forming a lipid layer on top of the aqueous tear layer. In meibomian gland dysfunction, the lipid composition is abnormal, and gland ducts and orifices become inspissated with hard, waxy plugs. Many patients have rosacea (see p. 654) and recurrent hordeola or chalazia.

Many patients with seborrheic blepharitis have seborrheic dermatitis of the face and scalp (see p. 671) or acne rosacea. Secondary bacterial colonization often occurs on the scales that develop on the eyelid margin. Meibomian glands can become obstructed.

Most patients with meibomian gland dysfunction or seborrheic blepharitis have increased tear evaporation and secondary keratoconjunctivitis sicca.

Symptoms and Signs

Symptoms common to all forms of blepharitis include itching and burning of the eyelid margins and conjunctival irritation with lacrimation, photosensitivity, and foreign body sensation.

Acute: In acute ulcerative blepharitis, small pustules may develop in eyelash follicles and eventually break down to form shallow marginal ulcers. Tenacious adherent crusts leave a bleeding surface when removed. During sleep, eyelids can become glued together by dried secretions. Recurrent ulcerative blepharitis can cause eyelid scars and loss of eyelashes.

In acute nonulcerative blepharitis, eyelid margins become edematous and erythematous; eyelashes may become crusted with dried serous fluid.

Chronic: In meibomian gland dysfunction, examination reveals dilated, inspissated gland orifices that, when pressed, exude a waxy, thick, yellowish secretion with pressure. In seborrheic blepharitis, greasy,

easily removable scales develop on eyelid margins. Most patients with seborrheic blepharitis and meibomian gland dysfunction have symptoms of keratoconjunctivitis sicca, such as foreign body sensation, grittiness, eye strain and fatigue, and blurring with prolonged visual effort.

Diagnosis

Diagnosis is usually by slit-lamp examination. Chronic blepharitis that does not respond to treatment may require biopsy to exclude eyelid tumors that can simulate the condition.

Prognosis

Acute blepharitis most often responds to treatment but may recur, develop into chronic blepharitis, or both. Chronic blepharitis is indolent, recurrent, and resistant to treatment. Exacerbations are inconvenient, uncomfortable, and cosmetically unappealing but do not usually result in corneal scarring or vision loss.

Treatment

Acute: Acute ulcerative blepharitis is treated with an antibiotic ointment (eg, bacitracin/polymyxin B, erythromycin, or gentamicin 0.3% qid for 7 to 10 days). Acute viral ulcerative blepharitis is treated with systemic antivirals (eg, for herpes simplex, acyclovir 400 mg po tid for 7 days; for varicella zoster, famciclovir 500 mg po tid or valacyclovir 1 g po tid for 7 days).

Treatment of acute nonulcerative blepharitis begins with avoiding the offending action (eg, rubbing) or substance (eg, new eye drops). Warm compresses over the closed eyelid may relieve symptoms and speed resolution. If swelling persists > 24 h, topical corticosteroids (eg, fluorometholone ophthalmic ointment 0.1% tid for 7 days) can be used.

Chronic: The initial treatment for both meibomian gland dysfunction and seborrheic blepharitis is directed toward the secondary keratoconjunctivitis sicca (see p. 592). Tear supplements, bland ointments at night, and, if necessary, punctal plugs (inserts that obstruct the puncta and thus decrease tear drainage) are effective in most patients.

If needed, additional treatment for meibomian gland dysfunction includes warm compresses to melt the waxy plugs and occasionally eyelid massage to extrude trapped secretions and coat the ocular surface. A tetracycline (eg, doxycycline 100 mg po bid tapered over 3 to 4 mo) may also be effective because it changes the composition of meibomian gland secretions.

If needed, additional treatment for seborrheic blepharitis includes gentle cleansing of the eyelid margin 2 times a day with a cotton swab dipped in a dilute solution of baby shampoo (2 to 3 drops in 1/2 cup of warm water). A topical antibiotic ointment (bacitracin/polymyxin B or sulfacetamide 10% bid for up to 3 mo) may be added to reduce bacterial counts on the eyelid margin when cases are unresponsive to weeks of eyelid hygiene.

Blepharospasm

Blepharospasm is spasm of muscles around the eye causing involuntary blinking and eye closing.

The cause of blepharospasm is most often unknown. It affects women more than men and tends to occur in families. Blepharospasm may be secondary to eye disorders, including those that cause ocular irritation (eg, trichiasis, corneal foreign body, keratoconjunctivitis sicca) and systemic neurologic diseases that cause spasm (eg, Parkinson's disease).

Symptoms are involuntary blinking and closing of the eyes; in severe cases, people cannot open their eyes. Spasms may be made worse by fatigue, bright light, and anxiety.

Treatment involves injecting botulinum toxin type A into the eyelid muscles; treatment must be repeated in

most instances. Anxiolytics may help. Surgery to cut the periorbital muscles is also effective but, because of potential complications, is considered only if botulinum toxin is ineffective. Sunglasses help decrease the light sensitivity that may cause or accompany blepharospasm.

Canaliculitis

Canaliculitis is inflammation of the canaliculus (see Fig. 60-3 on p. 567).

The most common cause is infection with *Actinomyces israelii*, a gram-positive bacillus with fine branching filaments, but other bacteria, fungi (eg, *Candida albicans*), and viruses (eg, herpes simplex) may be causative. Symptoms and signs are tearing, discharge, red eye (especially nasally), and mild tenderness over the involved side.

Diagnosis is suspected based on symptoms and signs, expression of turbid secretions with pressure over the lacrimal sac, and a gritty sensation caused by necrotic material that can be felt during probing of the lacrimal system. Canaliculitis can be differentiated from dacryocystitis. In canaliculitis, the punctum and canaliculus are red and swollen; in dacryocystitis, the punctum and canaliculus are normal, but a red, swollen, tender mass is located in or near the lacrimal sac.

Treatment is warm compresses, irrigation of the canaliculus with antibiotic solution (by an ophthalmologist), and removal of any concretions, which usually requires surgery. Antibiotic selection is usually empiric with a 1st-generation cephalosporin or penicillinase-resistant synthetic penicillin but may be guided by irrigation samples.

Chalazion and Hordeolum

Chalazia and hordeola are sudden-onset localized swellings of the eyelid. A chalazion is caused by noninfectious meibomian gland occlusion, whereas a hordeolum is caused by infection. Both conditions initially cause eyelid hyperemia and edema, swelling, and pain. With time, a chalazion becomes a small nontender nodule in the eyelid center, whereas a hordeolum remains painful and localizes to an eyelid margin. Diagnosis is clinical. Treatment is with hot compresses. Both conditions improve spontaneously, but incision or, for chalazia, intralesional corticosteroids may be used to hasten resolution.

Chalazion: A chalazion is noninfectious obstruction of a meibomian gland causing extravasation of irritating lipid material in the eyelid soft tissues with focal secondary granulomatous inflammation (see Plate 7). Disorders that cause abnormally thick meibomian gland secretions (eg, meibomian gland dysfunction, acne rosacea) increase the risk of meibomian gland obstruction.

Hordeolum: A hordeolum (stye) is an acute, localized, pyogenic (usually staphylococcal) infection or abscess of the eyelid that may be external or internal (see Plate 16). Most hordeola are external and result from obstruction and infection of an eyelash follicle and adjacent glands of Zeis or Moll's glands. Follicle obstruction may be associated with blepharitis. An internal hordeolum, which is very rare, results from infection of a meibomian gland. Sometimes cellulitis accompanies hordeola.

Symptoms and Signs

Chalazia and hordeola each cause eyelid redness, swelling, and pain.

Chalazion: After 1 or 2 days, a chalazion localizes to the body of the eyelid. Typically, a small nontender nodule or lump develops. A chalazion usually drains through the inner surface of the eyelid or is absorbed spontaneously over 2 to 8 wk; rarely, it persists longer. Vision may be slightly blurred.

Hordeolum: After 1 to 2 days, an external hordeolum localizes to the eyelid margin. There may be tearing, photophobia, and a foreign body sensation. Typically, a small yellowish pustule develops at the base of an eyelash, surrounded by hyperemia, induration, and diffuse edema. Within 2 to 4 days, the

lesion ruptures and discharges pus, thereby relieving pain and resolving the lesion.

Symptoms of an internal hordeolum are the same as those of a chalazion, with pain, redness, and edema localized to the posterior tarsal conjunctival surface. Inflammation may be severe, sometimes with fever or chills. Inspection of the tarsal conjunctivae shows a small elevation or yellow area at the site of the affected gland. Later, an abscess forms. Spontaneous rupture is rare; however, when it does occur, it usually occurs on the conjunctival side of the eyelid and sometimes erupts through the skin side. Recurrence is common.

Diagnosis

• Clinical assessment

Diagnosis of chalazion and both kinds of hordeola is clinical; however, during the first 2 days, they may be clinically indistinguishable. Because internal hordeola are so rare, they are not usually suspected unless inflammation is severe or fever or chills are present. If the chalazion or hordeolum lies near the inner canthus of the lower eyelid, it must be differentiated from dacryocystitis (see below), which can usually be excluded by noting the location of maximum induration and tenderness (eg, eyelid for a chalazion, under the medial canthus near the side of the nose for dacryocystitis). Chronic chalazia that do not respond to treatment require biopsy to exclude tumor of the eyelid.

Treatment

• Hot compresses

• Sometimes drainage or drug therapy

Hot compresses for 5 to 10 min 2 or 3 times a day can be used to hasten resolution of chalazia and external hordeola.

Chalazion: Incision and curettage or intrachalazion corticosteroid therapy (0.05 to 0.2 mL triamcinolone 25 mg/mL) may be indicated if chalazia are large, unsightly, and persist for more than several weeks despite conservative therapy.

Hordeolum: An external hordeolum that does not respond to hot compresses can be incised with a sharp, fine-tipped blade. Systemic antibiotics (eg, dicloxacillin or erythromycin 250 mg po qid) are indicated when cellulitis accompanies a hordeolum.

Treatment of internal hordeola is oral antibiotics and incision and drainage if needed. Topical antibiotics are usually ineffective.

Dacryocystitis

Dacryocystitis is infection of the lacrimal sac, usually with staphyloccocal or streptococcal species and usually as a consequence of nasolacrimal duct obstruction.

In acute dacryocystitis, the patient presents with pain, redness, and edema around the lacrimal sac. Diagnosis is suspected based on symptoms and signs and when pressure over the lacrimal sac causes reflux of mucoid material through the puncta. Initial treatment is with warm compresses and oral antibiotics for mild cases or IV antibiotics for more severe cases. The antibiotic is usually a 1st-generation cephalosporin or penicillinase-resistant synthetic penicillin. If the infection does not respond as expected, consideration should be given to methicillin-resistant *Staphylococcus aureus* (MRSA), and antibiotics changed accordingly. The abscess can be drained and the antibiotics can be changed based on culture results if the initial antibiotic proves ineffective.

Patients with chronic dacryocystitis usually present with a mass under the medial canthal tendon and chronic conjunctivitis. Definitive treatment for resolved acute dacryocystitis or chronic conjunctivitis is usually surgery that creates a passage between the lacrimal sac and the nasal cavity

(dacryocystorhinostomy).

Dacryostenosis

Dacryostenosis is obstruction or stenosis of the nasolacrimal duct, causing excess tearing.

Nasolacrimal obstruction may be congenital or acquired. One cause of congenital obstruction is inadequate development of any part of the nasolacrimal ducts. Typically, a membrane at the distal end of the nasolacrimal duct persists. There is tearing and purulent discharge; the condition may manifest as chronic conjunctivitis, usually beginning after the age of 2 wk (most often at age 3 to 12 wk).

Causes of acquired nasolacrimal duct obstruction are listed in Table 62-1. The cause is most often age-related stenosis of the nasolacrimal duct. Other causes include past nasal or facial bone fractures and sinus surgery, which disrupt the nasolacrimal duct; inflammatory diseases (eg, sarcoidosis, Wegener's granulomatosis); and dacryocystitis.

Causes of punctal or canalicular stenosis include chronic conjunctivitis (especially herpetic), certain types of chemotherapy, adverse reactions to eye drops (especially topical echothiophate iodide), and radiation.

Diagnosis

Diagnosis is usually based on clinical criteria. Sometimes ophthalmologists probe and irrigate the lacrimal drainage system with saline, with or without fluorescein dye. Reflux indicates stenosis.

Treatment

Congenital nasolacrimal duct obstruction often resolves spontaneously by about age 6 to 9 mo; before 1 yr, manual compression of the lacrimal sac 4 or 5 times/day may relieve the obstruction. After 1 yr, the nasolacrimal duct may need probing, usually under general anesthesia; if obstruction is recurrent, a temporary silastic tube may be inserted.

[**Table 62-1.** Causes of Acquired Nasolacrimal Duct Obstruction]

In acquired nasolacrimal duct obstruction, the underlying disorder is treated when possible. If treatment is not possible or is ineffective, a passage between the lacrimal sac and the nasal cavity can be created surgically (dacryocystorhinostomy).

In cases of punctal or canalicular stenosis, dilation is usually curative. If canalicular stenosis is severe and bothersome, a surgical procedure that places a glass tube (Jones tube) leading from the caruncle into the nasal cavity can be considered.

Entropion and Ectropion

Entropion is inversion of an eyelid. Ectropion is eversion of the lower eyelid.

Entropion: Entropion (inversion of an eyelid) is caused by age-related tissue relaxation, postinfectious or posttraumatic changes, or blepharospasm. Eyelashes rub against the eyeball and may lead to corneal ulceration and scarring. Symptoms can include foreign body sensation, tearing, and red eye. Diagnosis is clinical. Definitive treatment is surgery.

Ectropion: Ectropion (eversion of the lower eyelid—see Plate 12) is caused by age-related tissue relaxation, cranial nerve VII palsy, and posttraumatic or postsurgical changes. Symptoms are tearing (due to poor drainage of tears through the nasolacrimal system, which may no longer contact the eyeball) and symptoms of dry eyes (see p. 592), possibly due to inadequate blinking. Diagnosis is clinical. Symptomatic treatment can include tear supplements and, at night, ocular lubricants; definitive treatment is surgery.

Trichiasis

Trichiasis is an anatomic misalignment of eyelashes, which rub against the eyeball, in a patient with no entropion.

Trichiasis is most often idiopathic, but known causes include blepharitis, posttraumatic and postsurgical changes, conjunctival scarring (eg, secondary to cicatricial pemphigoid, atopic keratoconjunctivitis, Stevens-Johnson syndrome, or chemical injury), epiblepharon (an extra lower eyelid skinfold that directs lashes into a vertical position), and distichiasis (a congenital extra row of eyelashes). Corneal ulceration and scarring can occur in chronic cases. Symptoms are foreign body sensation, tearing, and red eye. Diagnosis is usually clinical. Trichiasis differs from entropion in that the eyelid position is normal. Evaluation includes fluorescein staining to exclude corneal abrasion or ulceration. Treatment is eyelash removal with forceps. If eyelashes grow back, electrolysis or cryosurgery is more effective at permanently preventing recurrence.

Tumors

The skin of the eyelids is a common site for growth of benign and malignant tumors.

Xanthelasma: Xanthelasma is a common, benign deposit of yellow-white flat plaques of lipid material that occur subcutaneously on the upper and lower eyelids. Although some people with xanthelasmas have dyslipidemias, most do not. Diagnosis is by appearance. No treatment is necessary, although xanthelasmas can be removed for cosmetic reasons, and underlying dyslipidemias should be treated.

Basal cell carcinoma: This skin cancer frequently occurs at the eyelid margins, at the inner canthus, and on the upper cheek (see also p. 749). Metastasis is rare. Biopsy establishes the diagnosis. Treatment is surgical excision using conventional techniques or by Mohs' surgery.

Other malignant tumors: These types of tumors are less common; they include squamous cell carcinoma, meibomian gland carcinoma, and melanomas. Eyelid tumors may simulate chronic blepharitis or chronic chalazion. Therefore, chronic blepharitis, chronic chalazion, or similar lesions should be biopsied if unresponsive to initial treatment.

Chapter 63. Conjunctival and Scleral Disorders

Introduction

The conjunctiva lines the back of the eyelids (palpebral or tarsal conjunctiva), crosses the space between the lid and the globe (forniceal conjunctiva), then folds back on itself as it spreads over the sclera to the cornea (bulbar conjunctiva). The conjunctiva helps maintain the tear film and protect the eye from foreign objects and infection.

The sclera is the thick white sphere of dense connective tissue that encloses the eye and maintains its shape. Anteriorly, the sclera fuses with the cornea, and posteriorly it blends with the meninges where the optic nerve penetrates the globe.

The episclera is a thin vascular membrane between the conjunctiva and the sclera.

The most common disorders are inflammatory (eg, conjunctivitis, episcleritis, scleritis). Conjunctivitis can be acute or chronic and is infectious, allergic, or irritant in origin. Scleritis usually results from immune-mediated disease and episcleritis often does as well. Episcleritis usually does not threaten vision, but scleritis can destroy vision and the eye. Major symptoms of conjunctivitides (eg, conjunctival hyperemia) are similar. Early, accurate diagnosis is important.

Select eye findings in conjunctival disorders: Edema of the bulbar conjunctiva results in a translucent, bluish, thickened conjunctiva. Gross edema with ballooning of the conjunctiva, often leading to prolapse of conjunctiva, is known as chemosis.

Edema of the tarsal conjunctiva (typical of allergic conjunctivitis) results in fine, minute projections (papillae), giving the conjunctiva a velvety appearance.

Hyperplasia of lymphoid follicles in the conjunctiva can occur in viral or chlamydial conjunctivitis. It appears as small bumps with pale centers, resembling cobblestones. It occurs most commonly in the inferior tarsal conjunctiva.

Cicatricial Pemphigoid

(Benign Mucous Membrane Pemphigoid; Mucous Membrane Pemphigoid; Ocular Cicatricial Pemphigoid)

Cicatricial pemphigoid is a chronic, bilateral, progressive scarring and shrinkage of the conjunctiva with opacification of the cornea. Early symptoms are hyperemia, discomfort, itching, and discharge; progression leads to eyelid and corneal damage and sometimes blindness. Diagnosis may be confirmed by biopsy, but biopsy is often not necessary. Treatment may require systemic immunosuppression.

Cicatricial pemphigoid is an autoimmune disease in which binding of anticonjunctival basement membrane antibodies results in conjunctival inflammation. It is unrelated to bullous pemphigoid.

Symptoms and Signs

Usually beginning as a chronic conjunctivitis, the condition progresses to symblepharon (adhesion between the tarsal and bulbar conjunctiva); trichiasis (in-turning eyelashes); keratoconjunctivitis sicca; corneal neovascularization, opacification, and keratinization; and conjunctival shrinkage and keratinization. Chronic corneal epithelial defects can lead to secondary bacterial ulceration, scarring, and blindness. Oral mucous membrane involvement with ulceration and scarring is common, but skin involvement, characterized by scarring bullae and erythematous plaques, is uncommon.

Diagnosis

• Unexplained symblepharon or biopsy findings

Diagnosis is suspected clinically in patients with conjunctival scarring plus corneal changes, symblepharon, or both. The differential diagnosis of progressive conjunctival scarring includes postradiation and atopic disease. Therefore, the clinical diagnosis of cicatricial pemphigoid is made when there is progression of symblepharon without a history of local radiation or severe perennial allergic conjunctivitis. Diagnosis can be confirmed by conjunctival biopsy showing antibody deposition on the basement membrane.

Treatment

• Epilation of in-turning lashes

• Sometimes systemic immunosuppression

Tear substitutes and epilation, cryoepilation, or electroepilation of the in-turning eyelashes may increase patient comfort and reduce the risk of ocular infection and secondary scarring. For progressive scarring or corneal opacification or for nonhealing corneal epithelial defects, systemic immunosuppression with dapsone or cyclophosphamide is indicated.

Conjunctivitis

Conjunctival inflammation typically results from infection, allergy, or irritation. Symptoms are conjunctival hyperemia and ocular discharge and, depending on the etiology, discomfort and itching. Diagnosis is clinical; sometimes cultures are indicated. Treatment depends on etiology and may include topical antibiotics, antihistamines, mast cell stabilizers, and corticosteroids.

Infectious conjunctivitis is most commonly viral or bacterial and is contagious. Rarely, mixed or unidentifiable pathogens are present. Numerous allergens can cause allergic conjunctivitis (see p. 584). Nonallergic conjunctival irritation can result from foreign bodies; wind, dust, smoke, fumes, chemical vapors, and other types of air pollution; and intense ultraviolet light of electric arcs, sunlamps, and reflection from snow.

Conjunctivitis is typically acute, but both infectious and allergic conditions can be chronic. Conditions that cause chronic conjunctivitis include ectropion, entropion, blepharitis, and chronic dacryocystitis.

Symptoms and Signs

Any source of inflammation causes lacrimation or discharge and diffuse conjunctival vascular dilation. Discharge may cause the eyes to crust overnight. Thick discharge may blur vision, but once discharge is cleared, visual acuity should be unaffected.

Itching and watery discharge predominate in allergic conjunctivitis. Chemosis and papillary hyperplasia also suggest allergic conjunctivitis. Irritation or foreign body sensation, photophobia, and discharge suggest infectious conjunctivitis; purulent discharge suggests a bacterial cause. Severe eye pain suggests scleritis (see p. 587).

Diagnosis

• Clinical evaluation

• Sometimes culture

Usually, diagnosis is made by history and examination (see also Table 63-1), usually including slit-lamp examination with fluorescein staining of the cornea and, if glaucoma is suspected, measurement of intraocular pressure.

Other disorders can cause a red eye (see p. 563). Deep pain in the affected eye when a light is shone in the unaffected eye (true photophobia) does not occur in uncomplicated conjunctivitis and suggests a disorder of the cornea or anterior uveal tract. Circumcorneal conjunctival hyperemia (sometimes

described as ciliary flush) is caused by dilated, fine, straight, deep vessels that radiate out 1 to 3 mm from the limbus, without significant hyperemia of the bulbar and tarsal conjunctivae. Ciliary flush occurs with uveitis, acute glaucoma, and some types of keratitis.

The cause of conjunctivitis is suggested by clinical findings. However, cultures are indicated for patients with severe symptoms, immunocompromise, a vulnerable eye (eg, after a corneal transplant, in exophthalmos due to Graves' disease), or ineffective initial therapy.

Clinical differentiation between viral and bacterial infectious conjunctivitis is not highly accurate. However, temporarily missing some cases of mild bacterial conjunctivitis is not likely to be harmful because the infection often resolves spontaneously and antibiotics can be prescribed if symptoms persist.

Treatment

• Prevention of spread

• Treatment of symptoms

Most infectious conjunctivitis is highly contagious and spreads by droplet, fomites, and hand-to-eye inoculation. To avoid transmitting infection, physicians must wash their hands thoroughly and disinfect equipment after examining patients. Patients should wash their hands thoroughly after touching their eyes or nasal secretions, avoid touching the noninfected eye after touching the infected eye, avoid sharing towels or pillows, and avoid swimming in pools. Eyes should be kept free of discharge and should not be patched. Small children with conjunctivitis should be kept home from school to avoid spread. Cool wash-cloths applied to the eyes may help relieve local burning and itching. Antimicrobials are used for certain infections.

Viral Conjunctivitis

Viral conjunctivitis is a highly contagious acute conjunctival infection usually caused by adenovirus. Symptoms include irritation, photophobia, and watery discharge. Diagnosis is clinical. Infection is self-limited, but severe cases sometimes require topical corticosteroids.

Etiology

Conjunctivitis may accompany the common cold and other systemic viral infections (especially measles, but also chickenpox, rubella, and mumps). Isolated viral conjunctivitis usually results from adenoviruses and sometimes enteroviruses.

Epidemic keratoconjunctivitis usually results from adenovirus serotypes Ad 5, 8, 11, 13, 19, and 37. Pharyngoconjunctival fever usually results from serotypes Ad 3, 4, and 7. Outbreaks of acute hemorrhagic conjunctivitis, a rare conjunctivitis associated with infection by enterovirus type 70, have occurred in Africa and Asia.

Symptoms and Signs

After an incubation period of about 5 to 12 days, conjunctival hyperemia, watery discharge, and ocular irritation usually begin in one eye and spread rapidly to the other. Follicles may be present on the palpebral conjunctiva. A preauricular lymph node is often enlarged and painful. Many patients have had contact with someone with conjunctivitis, a recent URI, or both.

[Table 63-1. Differentiating Features in Acute Conjunctivitis]

In severe adenoviral conjunctivitis, patients may have photophobia and foreign body sensation. Chemosis may be present. Pseudomembranes of fibrin and inflammatory cells on the tarsal conjunctiva, focal corneal inflammation, or both may blur vision. Even after conjunctivitis has resolved, residual corneal subepithelial opacities (multiple, coin-shaped, 0.5 to 1.0 mm in diameter) may be visible with a slit lamp for up to 2 yr. Corneal opacities occasionally result in decreased vision and significant glare.

Diagnosis

• Clinical evaluation

Diagnosis of conjunctivitis and differentiation between bacterial, viral, and noninfectious conjunctivitis are usually clinical; special tissue cultures are necessary for growth of the virus but are rarely indicated. Features that may help differentiate between viral and bacterial conjunctivitis can include purulence of eye discharge, presence of preauricular lymphadenopathy, and, in epidemic keratoconjunctivitis, chemosis. Patients with photophobia are stained with fluorescein and examined with a slit lamp. Epidemic keratoconjunctivitis may cause punctate corneal staining. Secondary bacterial infection of viral conjunctivitis is rare. However, if any signs suggest bacterial conjunctivitis (eg, purulent discharge), smears from the eye may be examined microscopically and cultured for bacteria.

Treatment

• Supportive measures

Viral conjunctivitis is highly contagious, and transmission precautions must be followed (as described previously). Children should generally be kept out of school until resolution.

Viral conjunctivitis is self-limiting, lasting 1 wk in mild cases to up to 3 wk in severe cases. It requires only warm or cool compresses for symptomatic relief. However, patients who have severe photophobia or whose vision is affected may benefit from topical corticosteroids (eg, 1% prednisolone acetate q 6 to 8 h). Corticosteroids, if prescribed, are usually prescribed by an ophthalmologist. Herpes simplex keratitis (see p. 589) must be ruled out first (by fluorescein staining and slit-lamp examination) because corticosteroids can exacerbate it.

Acute Bacterial Conjunctivitis

Acute conjunctivitis can be caused by numerous bacteria. Symptoms are hyperemia, lacrimation, irritation, and discharge. Diagnosis is clinical. Treatment is with topical antibiotics, augmented by systemic antibiotics in more serious cases.

Most bacterial conjunctivitis is acute; chronic bacterial conjunctivitis may be caused by *Chlamydia* and rarely *Moraxella*. Chlamydial conjunctivitis includes trachoma and adult or neonatal inclusion conjunctivitis.

Etiology

Bacterial conjunctivitis is usually caused by *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus* sp, or, less commonly, *Chlamydia trachomatis* (see p. 583). *Neisseria gonorrhoeae* causes gonococcal conjunctivitis, which usually results from sexual contact with a person who has a genital infection.

Ophthalmia neonatorum (see also p. 2824) is conjunctivitis that occurs in 20 to 40% of neonates delivered through an infected birth canal. It can be caused by maternal gonococcal or chlamydial infection.

Symptoms and Signs

Symptoms are typically unilateral but frequently spread to the opposite eye within a few days. Discharge is typically purulent.

The bulbar and tarsal conjunctivae are intensely hyperemic and edematous. Petechial subconjunctival hemorrhages, chemosis, photophobia, and an enlarged preauricular lymph node are typically absent. Eyelid edema is often moderate.

With adult gonococcal conjunctivitis, symptoms develop 12 to 48 h after exposure. Severe eyelid edema, chemosis, and a profuse purulent exudate are typical. Rare complications include corneal ulceration, abscess, perforation, panophthalmitis, and blindness.

Ophthalmia neonatorum caused by gonococcal infection appears 2 to 5 days after delivery. With ophthalmia neonatorum caused by a chlamydial infection, symptoms appear within 5 to 14 days. Symptoms of both are bilateral, intense papillary conjunctivitis with lid edema, chemosis, and mucopurulent discharge.

Diagnosis

• Clinical evaluation

Diagnosis of conjunctivitis and differentiation between bacterial, viral, and noninfectious conjunctivitis are usually clinical. Smears and bacterial cultures should be done in patients with severe symptoms, immunocompromise, ineffective initial therapy, or a vulnerable eye (eg, after a corneal transplant, in exophthalmos due to Graves' disease). Smears and conjunctival scrapings should be examined microscopically and stained with Gram stain to identify bacteria and stained with Giemsa stain to identify the characteristic epithelial cell basophilic cytoplasmic inclusion bodies of chlamydial conjunctivitis.

Treatment

• Antibiotics (topical for all causes except gonococcal)

Bacterial conjunctivitis is very contagious, and standard infection control measures (see p. 581) should be followed.

If neither gonococcal nor chlamydial infection is suspected, most clinicians treat presumptively with moxifloxacin 0.5% drops tid for 7 to 10 days or another fluoroquinolone or trimethoprim/polymyxin B qid. A poor clinical response after 2 or 3 days indicates that the cause is resistant bacteria, a virus, or an allergy. Culture and sensitivity studies determine subsequent treatment.

Adult gonococcal conjunctivitis requires a single dose of ceftriaxone 1 g IM. Fluoroquinolones are no longer recommended because resistance is now widespread. Bacitracin 500 U/g or gentamicin 0.3% ophthalmic ointment instilled into the affected eye q 2 h may be used in addition to systemic treatment. Sex partners should also be treated. Because chlamydial genital infection is often present in patients with gonorrhea, patients should also receive a single dose of azithromycin 1 g or doxycycline 100 mg po bid for 7 days.

Ophthalmia neonatorum is prevented by the routine use of silver nitrate eye drops or erythromycin ointment at birth. Infections that develop despite this treatment require systemic treatment. For gonococcal infection, ceftriaxone 25 to 50 mg/kg IV or IM is given once/day for 7 days. Chlamydial infection is treated with erythromycin 12.5 mg/kg po or IV qid for 14 days. The parents should also be treated.

Adult Inclusion Conjunctivitis

(Adult Chlamydial Conjunctivitis; Swimming Pool Conjunctivitis)

Adult inclusion conjunctivitis is caused by sexually transmitted *Chlamydia trachomatis*. Symptoms include chronic unilateral hyperemia and mucopurulent discharge. Diagnosis is clinical. Treatment is with systemic antibiotics.

Adult inclusion conjunctivitis is caused by *Chlamydia trachomatis* serotypes D through K. In most instances, adult inclusion conjunctivitis results from sexual contact with a person who has a genital infection. Usually, patients have acquired a new sex partner in the preceding 2 mo. Rarely, adult inclusion conjunctivitis is acquired from contaminated, incompletely chlorinated swimming pool water.

Symptoms and Signs

Adult inclusion conjunctivitis has an incubation period of 2 to 19 days. Most patients have a unilateral mucopurulent discharge. The tarsal conjunctiva is often more hyperemic than the bulbar conjunctiva. Characteristically, there is a marked tarsal follicular response. Occasionally, superior corneal opacities and vascularization occur. Preauricular lymph nodes may be swollen on the side of the involved eye. Often, symptoms have been present for many weeks or months and have not responded to topical antibiotics.

Diagnosis

• Clinical evaluation

• Laboratory testing

Chronicity, mucopurulent discharge, marked tarsal follicular response, and failure of topical antibiotics differentiate adult inclusion conjunctivitis from other bacterial conjunctivitides. Smears, bacterial cultures, and chlamydial studies should be done. Immunofluorescent staining techniques, PCR, and special cultures are used to detect *C. trachomatis*. Smears and conjunctival scrapings should be examined microscopically and stained with Gram stain to identify bacteria and stained with Giemsa stain to identify the characteristic epithelial cell basophilic cytoplasmic inclusion bodies of chlamydial conjunctivitis.

Treatment

• Antibiotics

Azithromycin 1 g po once only or either doxycycline 100 mg po bid or erythromycin 500 mg po qid for 1 wk cures the conjunctivitis and concomitant genital infection. Sex partners also require treatment.

Trachoma

(Egyptian Ophthalmia; Granular Conjunctivitis)

Trachoma is a chronic conjunctivitis caused by *Chlamydia trachomatis* and is characterized by progressive exacerbations and remissions. It is the leading cause of preventable blindness worldwide. Initial symptoms are conjunctival hyperemia, eyelid edema, photophobia, and lacrimation. Later, corneal neovascularization and scarring of the conjunctiva, cornea, and eyelids occur. Diagnosis is usually clinical. Treatment is with topical or systemic antibiotics.

Trachoma is endemic in poverty-stricken parts of North Africa, the Middle East, the Indian subcontinent, Australia, and Southeast Asia. The causative organism is *Chlamydia trachomatis* (serotypes A, B, Ba, and C). In the US, trachoma is rare, occurring occasionally among Native Americans and immigrants. The disease occurs mainly in children, particularly those between the ages of 3 and 6. Older children and adults are much less susceptible because of increased immunity and better personal hygiene. Trachoma is highly contagious in its early stages and is transmitted by eye-to-eye contact, hand-to-eye contact, eye-seeking flies, or the sharing of contaminated articles (eg, towels, handkerchiefs, eye makeup).

Symptoms and Signs

Trachoma usually affects both eyes. After an incubation period of about 7 days, conjunctival hyperemia, eyelid edema, photophobia, and lacrimation gradually appear, usually bilaterally. Small follicles develop in the upper tarsal conjunctiva 7 to 10 days later and gradually increase in size and number for 3 or 4 wk (see
Plate 20). Inflammatory papillae appear on the upper tarsal conjunctiva, and corneal neovascularization begins during this stage, with invasion of the upper half of the cornea by loops of vessels from the limbus (called pannus). The stage of follicular/papillary hypertrophy and corneal neovascularization may last from several months to > 1 yr, depending on response to therapy. The entire cornea may ultimately be involved, reducing vision.

Without treatment, a cicatricial (scarring) stage follows. The follicles and papillae gradually shrink and are replaced by scar tissue that often causes entropion and lacrimal duct obstruction. Entropion leads to further corneal scarring and neovascularization. Secondary bacterial infection is common, contributing to scarring and disease progression. The corneal epithelium becomes dull and thickened, and lacrimation is decreased. Small corneal ulcers may appear at the site of peripheral corneal infiltrates, stimulating further neovascularization.

With treatment and healing, the conjunctiva becomes smooth and grayish white. Rarely, corneal neovascularization regresses completely without treatment, and corneal transparency is restored. Impaired vision or blindness occurs in about 5% of people with trachoma.

Diagnosis

• Clinical findings (eg, tarsal lymphoid follicles, linear conjunctival scars, corneal pannus)

Diagnosis is usually clinical because testing is rarely available in endemic areas. Lymphoid follicles on the tarsal plate or along the corneal limbus, linear conjunctival scarring, and corneal pannus are considered diagnostic in the appropriate clinical setting. If diagnosis is uncertain, *C. trachomatis* can be isolated in culture or identified by PCR and immunofluorescence techniques. In the early stage, minute basophilic cytoplasmic inclusion bodies within conjunctival epithelial cells in Giemsa-stained conjunctival scrapings differentiate trachoma from nonchlamydial conjunctivitis. Inclusion bodies are also found in adult inclusion conjunctivitis (see p. 583), but the setting and developing clinical picture distinguish it from trachoma. Palpebral vernal conjunctivitis appears similar to trachoma in its follicular hypertrophic stage, but symptoms are different, milky flat-topped papillae are present, and eosinophils (not basophilic inclusion bodies) are found in the scrapings.

Treatment

• Oral azithromycin

For individual or sporadic cases, azithromycin 20 mg/kg (maximum 1 g) po as a single dose is 78% effective. Alternatives are doxycycline 100 mg bid or tetracycline 250 mg qid for 4 wk. In hyperendemic areas, tetracycline or erythromycin ophthalmic ointment applied bid for 5 consecutive days each month for 6 mo has been effective as treatment and prophylaxis. Endemic trachoma has been dramatically reduced by using community-wide oral azithromycin in a single dose or in repeated doses. Reinfection due to re-exposure is common among endemic areas. Better personal hygiene and environmental measures (eg, access to potable water) can reduce reinfection.

Eyelid deformities (eg, entropion) should be treated surgically.

Allergic Conjunctivitis

(Atopic Conjunctivitis; Atopic Keratoconjunctivitis; Hay Fever Conjunctivitis; Perennial Allergic Conjunctivitis; Seasonal Allergic Conjunctivitis; Vernal Keratoconjunctivitis)

Allergic conjunctivitis is an acute, intermittent, or chronic conjunctival inflammation usually caused by airborne allergens. Symptoms include itching, lacrimation, discharge, and conjunctival hyperemia. Diagnosis is clinical. Treatment is with topical antihistamines and mast cell stabilizers.

Etiology

Allergic conjunctivitis is due to a type I hypersensitivity reaction to a specific antigen.

Seasonal allergic conjunctivitis (hay fever conjunctivitis) is caused by airborne pollen of trees, grasses, or weeds. It tends to peak during the spring, late summer, or early fall and disappear during the winter months—corresponding to the life cycle of the causative plant.

Perennial allergic conjunctivitis (atopic conjunctivitis, atopic keratoconjunctivitis) is caused by dust mites, animal dander, and other nonseasonal allergens. These allergens, particularly those in the home, tend to cause symptoms year-round.

Vernal keratoconjunctivitis is a more severe type of conjunctivitis most likely allergic in origin. It is most common among males aged 5 to 20 who also have eczema, asthma, or seasonal allergies. Vernal conjunctivitis typically reappears each spring and subsides in the fall and winter. Many children outgrow the condition by early adulthood.

Symptoms and Signs

General: Patients report bilateral mild to intense ocular itching, conjunctival hyperemia, photosensitivity (photophobia in severe cases), eyelid edema, and watery or stringy discharge. Concomitant rhinitis is common. Many patients have other atopic diseases, such as eczema, allergic rhinitis, or asthma.

Findings characteristically include conjunctival edema and hyperemia and a discharge. The bulbar conjunctiva may appear translucent, bluish, and thickened. Chemosis and a characteristic boggy blepharedema of the lower eyelid are common. Chronic itching can lead to chronic eyelid rubbing, periocular hyperpigmentation, and dermatitis.

Seasonal and perennial conjunctivitis: Fine papillae on the upper tarsal conjunctiva give it a velvety appearance. In more severe forms, larger tarsal conjunctival papillae, conjunctival scarring, corneal neovascularization, and corneal scarring with variable loss of visual acuity can occur.

Vernal keratoconjunctivitis: Usually, the palpebral conjunctiva of the upper eyelid is involved, but the bulbar conjunctiva is sometimes affected. In the palpebral form, square, hard, flattened, closely packed, pale pink to grayish cobblestone papillae are present, chiefly in the upper tarsal conjunctiva (see Plate 8). The uninvolved tarsal conjunctiva is milky white. In the bulbar (limbal) form, the circumcorneal conjunctiva becomes hypertrophied and grayish. Discharge may be tenacious and mucoid, containing numerous eosinophils.

Occasionally, a small, circumscribed loss of corneal epithelium occurs, causing pain and increased photophobia. Other corneal changes (eg, central plaques) and white limbal deposits of eosinophils (Trantas' dots) may be seen.

Diagnosis

The diagnosis is usually clinical. Eosinophils are present in conjunctival scrapings, which may be taken from the lower or upper tarsal conjunctiva; however, such testing is rarely indicated.

Treatment

• Symptomatic measures

• Topical antihistamines, vasoconstrictors, NSAIDs, mast cell stabilizers, or a combination

• Topical corticosteroids or cyclosporine for recalcitrant cases

Avoidance of known allergens and use of tear supplements can reduce symptoms; antigen desensitization is occasionally helpful. Topical OTC antihistamine/vasoconstrictors (eg, naphazoline/pheniramine) are useful for mild cases. If these drugs are insufficient, topical prescription antihistamines (eg, olopatadine, ketotifen), NSAIDs (eg, ketorolac), or mast cell stabilizers (eg, pemirolast, nedocromil, azelastine) can be used separately or in combination. Topical corticosteroids (eg, loteprednol, fluorometholone 0.1%, prednisolone acetate 0.12% to 1% drops tid) can be useful in recalcitrant cases. Because topical corticosteroids can exacerbate ocular herpes simplex virus infections, possibly leading to corneal ulceration and perforation and, with long-term use, to glaucoma and possibly cataracts, their use should be initiated and monitored by an ophthalmologist. Topical cyclosporine may be indicated when

corticosteroids are needed but cannot be used.

Seasonal allergic conjunctivitis is less likely to require multiple drugs or intermittent topical corticosteroids.

Other Conjunctival Disorders

Pinguecula and pterygium: These lesions are benign growths of the conjunctiva that can result from chronic actinic irritation. Both typically appear adjacent to the cornea at the 3-o'clock position, the 9-o'clock position, or both (see Fig. 63-1).

A **pinguecula** is a raised yellowish white mass on the bulbar conjunctiva, adjacent to the cornea. It does not tend to grow onto the cornea. However, it may cause irritation or cosmetic blemish and, although rarely necessary, can easily be removed.

A **pterygium** is a fleshy triangular growth of bulbar conjunctiva that may spread across and distort the cornea, induce astigmatism, and change the refractive power of the eye. Symptoms may include decreased vision and foreign body sensation. It is more common in hot, dry climates. Removal is often indicated for cosmesis, to reduce irritation, and to improve or preserve vision.

Subconjunctival hemorrhages: These extravasations of blood beneath the conjunctiva usually result from minor trauma, straining, sneezing, or coughing; rarely, they occur spontaneously. The extent and location of hyperemia can help determine etiology. Diffuse hyperemia of the bulbar and tarsal conjunctivae is typical of conjunctivitis. Subconjunctival hemorrhages alarm the patient but are of no pathologic significance except when associated with blood dyscrasia, which is rare, or other facial or ocular injuries. They are absorbed spontaneously, usually within 2 wk. Topical corticosteroids, antibiotics, vasoconstrictors, and compresses do not speed reabsorption; reassurance is adequate therapy.

Episcleritis

Episcleritis is self-limiting, recurring, idiopathic inflammation of the episcleral tissue that does not threaten vision. Symptoms are a localized area of hyperemia of the globe, irritation, and lacrimation. Diagnosis is clinical. Treatment is symptomatic.

Episcleritis occurs in young adults, more commonly among women. It is usually idiopathic; it can be associated with connective tissue diseases and rarely with serious systemic diseases.

Mild irritation occurs. Additionally, a bright red patch is present just under the bulbar conjunctiva (simple episcleritis). A hyperemic, edematous, raised nodule (nodular episcleritis) may also be present. The palpebral conjunctiva is normal.

Episcleritis is distinguished from conjunctivitis because hyperemia is localized to a limited area of the globe and lacrimation is much less. It is distinguished from scleritis by lack of photophobia and lack of severe pain.

The condition is self-limited, and a diagnostic assessment for systemic disorders is not routinely warranted. A topical corticosteroid (eg, prednisolone acetate, 1% drops qid for 5 days, gradually reduced over 3 wk) or an oral NSAID usually shortens the attack; corticosteroids are usually prescribed by an ophthalmologist. Topical vasoconstrictors (eg, tetrahydrozoline) to improve appearance are optional.

[**Fig. 63-1.** Pinguecula and pterygium.]

Scleritis

Scleritis is a severe, destructive, vision-threatening inflammation involving the deep episclera and sclera. Symptoms are moderate to marked pain, hyperemia of the globe, lacrimation, and photophobia. Diagnosis is clinical. Treatment is with systemic corticosteroids and possibly immunosuppressants.

Scleritis is most common among women aged 30 to 50 yr, and many have connective tissue diseases, such as RA, SLE, polyarteritis nodosa, Wegener's granulomatosis, or relapsing polychondritis. A few cases are infectious in origin. About half of the cases of scleritis have no known cause. Scleritis most commonly involves the anterior segment and occurs in 3 types—diffuse, nodular, and necrotizing (scleromalacia perforans).

Symptoms and Signs

Pain (often characterized as a deep, boring ache) is severe enough to interfere with sleep and appetite. Photophobia and lacrimation may occur. Hyperemic patches develop deep beneath the bulbar conjunctiva and are more violaceous than those of episcleritis or conjunctivitis. The palpebral conjunctiva is normal. The involved area may be focal (usually one quadrant of the globe) or involve the entire globe and may contain a hyperemic, edematous, raised nodule (nodular scleritis) or an avascular area (necrotizing scleritis). Posterior scleritis is less common and is less likely to cause red eye but more likely to cause blurred or decreased vision.

In severe cases of necrotizing scleritis, perforation of the globe and loss of the eye may result. Connective tissue disease occurs in 20% of patients with diffuse or nodular scleritis and in 50% of patients with necrotizing scleritis. Necrotizing scleritis in patients with connective tissue disease signals underlying systemic vasculitis.

Diagnosis

Diagnosis is made clinically and by slit-lamp examination. Smears or rarely biopsies are necessary to confirm infectious scleritis. CT or ultrasonography may be needed for posterior scleritis.

Prognosis

Of patients with scleritis, 14% lose significant visual acuity within 1 yr, and 30% lose significant visual acuity within 3 yr. Patients with necrotizing scleritis and underlying systemic vasculitis have a mortality rate of up to 50% in 10 yr (mostly due to MI).

Treatment

• Systemic corticosteroids

Occasionally, NSAIDs are sufficient for mild cases. However, usually a systemic corticosteroid (eg, prednisone 1 mg/kg po once/day) is the initial therapy. If patients are unresponsive to or intolerant of systemic corticosteroids or have necrotizing scleritis and connective tissue disease, systemic immunosuppression with cyclophosphamide or azathioprine is indicated, but only in consultation with a rheumatologist. Scleral grafts may be indicated for threatened perforation.

Chapter 64. Corneal Disorders

Introduction

The cornea is subject to infection, noninfectious inflammation, ulceration, mechanical damage, and environmental injury. Infection (keratitis), frequently with secondary conjunctivitis, can be due to viruses, bacteria, *Acanthamoeba*, or fungi. Ulceration usually represents progression of keratitis. Symptoms that suggest corneal involvement rather than simple conjunctivitis include pain, particularly with exposure to light, and slight impairment of vision. Evaluation of the cornea requires slit-lamp examination and sometimes microbial studies.

Bullous Keratopathy

Bullous keratopathy is the presence of corneal epithelial bullae, resulting from corneal endothelial disease.

Bullous keratopathy is caused by edema of the cornea, resulting from failure of the corneal endothelium to maintain the normally dehydrated state of the cornea. Most frequently, it is due to Fuchs' corneal endothelial dystrophy or corneal endothelial trauma. Fuchs' dystrophy causes bilateral, progressive corneal endothelial cell loss, sometimes leading to symptomatic bullous keratopathy by age 50 to 60. Corneal endothelial trauma can occur during intraocular surgery (eg, cataract removal) or after placement of a poorly designed or malpositioned intraocular lens implant, leading to bullous keratopathy. Bullous keratopathy after cataract removal is called pseudophakic (if an intraocular lens implant is present) or aphakic (if no intraocular lens implant is present) bullous keratopathy.

Subepithelial fluid-filled bullae form on the corneal surface as the corneal stroma swells, leading to eye discomfort, decreased visual acuity, loss of contrast, glare, and photophobia. Sometimes bullae rupture, causing pain and foreign body sensation. Bacteria can invade a ruptured bulla, leading to a corneal ulcer.

The bullae and swelling of the corneal stroma can be seen on slit-lamp examination.

Treatment requires an ophthalmologist and includes topical dehydrating agents (eg, hypertonic saline), intraocular pressure-lowering agents, soft contact lenses for some mild to moderate cases, and treatment of any secondary microbial infection. Corneal transplantation is usually curative.

Corneal Ulcer

A corneal ulcer is a corneal epithelial defect with underlying inflammation (which soon results in necrosis of corneal tissue) due to invasion by bacteria, fungi, viruses, or *Acanthamoeba*. It can be initiated by mechanical trauma or nutritional deficiencies. Symptoms are progressive redness, foreign body sensation, ache, photophobia, and lacrimation. Diagnosis is by slit-lamp examination, fluorescein staining, and microbial studies. Treatment with topical antimicrobials and often dilating drops is urgent and requires an ophthalmologist.

Etiology

Corneal ulcers have many causes (see Table 64-1). Bacterial ulcers (most commonly due to contact lens wear) may complicate herpes simplex keratitis and be particularly refractory to treatment. Ulcers caused by *Acanthamoeba* (also most commonly due to contact lens wear) and fungi (most commonly due to trauma with vegetable material) are indolent but progressive; those caused by *Pseudomonas aeruginosa* (seen almost exclusively in contact lens wearers) develop rapidly, causing deep and extensive corneal necrosis. Wearing contact lenses while sleeping or wearing inadequately disinfected contact lenses can cause corneal ulcers (see p. 572).

Pathophysiology

Ulcers are characterized by corneal epithelial defects with underlying inflammation, and soon necrosis of

the corneal stroma develops. Corneal ulcers tend to heal with scar tissue, resulting in opacification of the cornea and decreased visual acuity. Uveitis, corneal perforation with iris prolapse, pus in the anterior chamber (hypopyon), panophthalmitis, and destruction of the eye may occur with or without treatment. More severe symptoms and complications tend to occur with deeper ulcers.

Symptoms and Signs

Conjunctival redness, eye ache, foreign body sensation, photophobia, and lacrimation may be minimal initially.

A corneal ulcer begins as a corneal epithelial defect that stains with fluorescein and an underlying dull, grayish, circumscribed superficial opacity. Subsequently, the ulcer suppurates and necroses to form an excavated ulcer. Considerable circumcorneal conjunctival hyperemia is usual (see Plate 9). In long-standing

[**Table 64-1.** Causes of Corneal Ulcers]

cases, blood vessels may grow in from the limbus (corneal neovascularization). The ulcer may spread to involve the width of the cornea, may penetrate deeply, or both. Hypopyon (layered WBCs in the anterior chamber) may occur.

Corneal ulcers due to *Acanthamoeba* are often intensely painful and may show transient corneal epithelial defects, multiple corneal stromal infiltrates, and, later, a large ringshaped infiltrate. Fungal ulcers, which are more chronic than bacterial ulcers, are densely infiltrated and show occasional discrete islands of infiltrate (satellite lesions) at the periphery.

Diagnosis

• Slit-lamp examination

Diagnosis is made by slit-lamp examination; a corneal infiltrate with an epithelial defect that stains with fluorescein is diagnostic. All but small ulcers should be cultured by scraping with a sterile platinum spatula (typically by an ophthalmologist). Microscopic examination of scrapings can identify *Acanthamoeba*.

Treatment

• Empiric topical broad-spectrum antibiotic therapy

• More specific antimicrobial therapy directed at the cause

Treatment for corneal ulcers, regardless of cause, begins with moxifloxacin 0.5% or gatifloxacin 0.3% for small ulcers and fortified (higher than stock concentration) antibiotic drops, such as tobramycin 15 mg/mL and cefazolin 50 mg/mL, for more significant ulcers, particularly those that are near the center of the cornea. Frequent dosing (eg, q 15 min for 4 doses, followed by q 1 h around the clock) is necessary initially. Patching is contraindicated because it creates a stagnant, warm environment that favors bacterial growth and prevents the administration of topical drugs.

Herpes simplex (see below) is treated with trifluridine 1% drops q 2 h while the patient is awake or acyclovir 400 mg po 5 times/day for about 14 days.

Fungal infections are treated with one of many topical antifungal drops (eg, natamycin 5%, amphotericin B 0.15%), initially q 1 h during the day and q 2 h overnight. Deep infections may require addition of oral ketoconazole, fluconazole, or itraconazole.

If *Acanthamoeba* is identified, traditional therapy is propamidine and neomycin supplemented with miconazole, clotrimazole, or oral ketoconazole. Additional treatments include polyhexamethylene biguanide 0.02% or chlorhexidine 0.02% q 1 to 2 h until clinical improvement is evident, then gradually reduced to 4 times/day and continued for a number of months until all inflammation has resolved.

Polyhexamethylene biguanide and chlorhexidine are not commercially available as ocular agents but can be prepared by a compounding pharmacy. Topical propamidine 0.1% q 1 to 2 h is often added for 3 days.

For all ulcers, treatment may also include a cycloplegic, such as atropine 1% or scopolamine 0.25% 1 drop tid, to decrease the ache of a corneal ulcer and to reduce the formation of posterior synechiae. In severe cases, debridement of the infected epithelium or even penetrating keratoplasty may be required. Patients who are poorly compliant or who have large, central, or refractory ulcers may need to be hospitalized.

Herpes Simplex Keratitis

(Herpes Simplex Keratoconjunctivitis)

Herpes simplex keratitis is corneal infection with herpes simplex virus (see also p. 1417). It may involve the iris. Symptoms and signs include foreign body sensation, lacrimation, photophobia, and conjunctival hyperemia. Recurrences are common and may lead to corneal hypoesthesia, ulceration, and permanent scarring. Diagnosis is based on the characteristic dendritic corneal ulcer and sometimes viral culture. Treatment is with topical and occasionally systemic antiviral drugs.

Herpes simplex usually affects the corneal surface but sometimes involves the deeper layers of the cornea (corneal stroma). Stromal involvement is probably an immunologic response to the virus.

As with all herpes simplex virus infections, there is a primary infection, followed by a latent phase, in which the virus goes into the nerve roots. Latent virus may reactivate, causing recurrent symptoms.

Symptoms and Signs

Primary infection: The initial (primary) infection is usually nonspecific self-limiting conjunctivitis, often in early childhood and sometimes without corneal involvement. If the cornea is involved, early symptoms include foreign body sensation, lacrimation, photophobia, and conjunctival hyperemia. Sometimes vesicular blepharitis (blisters on the eyelid) follows, symptoms worsen, vision blurs, and blisters break down and ulcerate, then resolve without scarring in about a week.

Recurrent infection: Recurrences usually take the form of epithelial keratitis (also called dendritic keratitis) with tearing, foreign body sensation, and a characteristic branching (dendritic or serpentine) lesion of the corneal epithelium with knoblike terminals that stain with fluorescein (see Plate 14). Multiple recurrences may result in corneal hypoesthesia or anesthesia, ulceration, and permanent scarring.

Stromal involvement: Most patients with disciform keratitis, which involves the corneal stroma, have a history of epithelial keratitis. Disciform keratitis is a deeper, disk-shaped, localized area of corneal edema and haze accompanied by anterior uveitis. This form may cause pain and vision loss.

Stromal keratitis can cause necrosis of the stroma and severe ache, photophobia, foreign body sensation, and decreased vision.

Diagnosis

Slit-lamp examination is mandatory. Finding a dendrite is enough to confirm the diagnosis in most cases. When the appearance is not conclusive, viral culture of the lesion can confirm the diagnosis.

Treatment

• Topical trifluridine

• Sometimes oral or IV acyclovir

• For stromal involvement or uveitis, topical corticosteroids in addition to antiviral drugs

Most patients are managed by an ophthalmologist. If stromal or uveal involvement occurs, treatment is more involved and referral to an ophthalmologist is mandatory.

Topical therapy (eg, trifluridine 1% drops 9 times/day) is usually effective. Occasionally, acyclovir 400 mg po 5 times/day is indicated. Immunocompromised patients may require IV antivirals (eg, acyclovir 5 mg/kg IV q 8 h for 7 days). If the epithelium surrounding the dendrite is loose and edematous, debridement by gentle swabbing with a cotton-tipped applicator before beginning drug therapy may speed healing.

Topical corticosteroids are contraindicated in epithelial keratitis but may be effective when used with an antiviral drug to manage later-stage stromal involvement (disciform or stromal keratitis) or uveitis. In such cases, patients may be given prednisolone acetate 1% instilled q 2 h initially, lengthening the interval to q 4 to 8 h as symptoms improve. Topical drugs to relieve photophobia include atropine 1% or scopolamine 0.25% tid.

Herpes Zoster Ophthalmicus

(Herpes Zoster Virus Ophthalmicus; Ophthalmic Herpes Zoster; Varicella-Zoster Virus Ophthalmicus)

Herpes zoster ophthalmicus is reactivation of a varicella-zoster virus infection (shingles) (see also p. 1420) involving the eye. Symptoms and signs, which may be intense, include dermatomal forehead rash and painful inflammation of all the tissues of the anterior and, rarely, posterior structures of the eye. Diagnosis is based on the characteristic appearance of the anterior structures of the eye plus zoster dermatitis of the first branch of the trigeminal nerve. Treatment is with oral antiviral drugs, mydriatics, and topical corticosteroids.

Herpes zoster of the forehead involves the globe in three fourths of cases when the nasociliary nerve is affected (as indicated by a lesion on the tip of the nose) and in one third of cases not involving the tip of the nose. Overall, the globe is involved in half of patients.

Symptoms and Signs

A prodrome of tingling of the forehead may occur. During acute disease, in addition to the forehead rash, symptoms and signs may include severe pain; marked eyelid edema; conjunctival, episcleral, and circumcorneal conjunctival hyperemia; corneal edema; and photophobia (see Plate 15).

Complications: Keratitis accompanied by uveitis may be severe and followed by scarring. Late sequelae —glaucoma, cataract, chronic or recurrent uveitis, corneal scarring, corneal neovascularization, and hypesthesia—are common and may threaten vision. Postherpetic neuralgia may develop late.

Diagnosis

• Zoster rash on the forehead or eyelid plus eye findings

Diagnosis is based on a typical acute herpes zoster rash on the forehead, eyelid, or both or on a characteristic history plus signs of previous zoster rash. Vesicular or bullous lesions in this distribution that do not yet involve the eye suggest significant risk and should prompt an ophthalmologic consultation to determine whether the eye is involved. Culture and immunologic or PCR studies of skin at initial evaluation or serial serologic tests are done only when lesions are atypical and the diagnosis uncertain.

Treatment

• Oral antivirals (eg, acyclovir, famciclovir, valacyclovir)

• Sometimes topical corticosteroids

Early treatment with acyclovir 800 mg po 5 times/day or famciclovir 500 mg or valacyclovir 1 g po tid for 7 days reduces ocular complications. Patients with keratitis or uveitis require topical corticosteroids (eg, prednisolone acetate 1% instilled qid initially, lengthening the interval as symptoms lessen). The pupil should be dilated with atropine 1% or scopolamine 0.25% 1 drop tid. Intraocular pressure must be monitored and treated if it rises significantly above normal values.

Use of a brief course of high-dose oral corticosteroids to prevent postherpetic neuralgia in patients > 60 yr who are in good general health remains controversial.

Interstitial Keratitis

(Parenchymatous Keratitis)

Interstitial keratitis is chronic, nonulcerative inflammation of the middle layers of the cornea (ie, mid-stroma) that is sometimes associated with uveitis. The cause is usually infectious. Symptoms are photophobia, pain, lacrimation, and vision blurring. Diagnosis is by slit-lamp examination and serologic tests to determine the cause. Treatment is directed at the cause and may require topical corticosteroids.

Interstitial keratitis, a manifestation of certain corneal infections, is rare in the US. Most cases occur in children or adolescents as a late complication of congenital syphilis (see p. 2821). Ultimately, both eyes may be involved. A similar but less dramatic bilateral keratitis occurs in Cogan's syndrome, Lyme disease, and Epstein-Barr virus infection. Rarely, acquired syphilis, herpes simplex, herpes zoster, or TB may cause a unilateral form in adults.

Symptoms and Signs

Photophobia, pain, lacrimation, and vision blurring are common. The lesion begins as patches of inflammation in the middle corneal layers (ie, mid-stroma) that cause opacification. Typically with syphilis and occasionally with other causes, the entire cornea develops a ground-glass appearance, obscuring the iris. New blood vessels grow in from the limbus (neovascularization) and produce orange-red areas (salmon patches). Anterior uveitis and choroiditis are common in syphilitic interstitial keratitis. Inflammation and neovascularization usually begin to subside after 1 to 2 mo. Some corneal opacity usually remains, causing mild to moderate vision impairment.

Diagnosis

• Corneal opacification and other typical findings on slit-lamp examination

• Serologic testing to determine etiology

The specific etiology must be determined. The stigmas of congenital syphilis, vestibuloauditory symptoms, history of an expanding rash, and tick exposure support a specific etiology. However, all patients should have serologic testing, including all of the following:

• Fluorescent treponemal antibody absorption test or the microhemagglutination assay for *Treponema pallidum*

• Lyme titer

• Epstein-Barr virus panel

Patients with negative serologic test results may have Cogan's syndrome, an idiopathic syndrome consisting of interstitial keratitis and vestibular and auditory deficits. To prevent permanent vestibuloauditory damage, symptoms of hearing loss, tinnitus, or vertigo require referral to an otolaryngologist.

Treatment

• Sometimes topical corticosteroids

Keratitis may resolve with treatment of the underlying condition. Additional topical treatment with a corticosteroid, such as prednisolone 1% qid, is often advisable. An ophthalmologist should be consulted.

Cogan's Syndrome

Cogan's syndrome is a rare autoimmune disease involving the eye and the inner ear.

Cogan's syndrome affects young adults, with 80% of patients between 14 and 47 yr. The disease appears to result from an autoimmune reaction directed against an unknown common autoantigen in the cornea and inner ear. About 10 to 30% of patients also have severe systemic vasculitis, which may include life-threatening aortitis.

Symptoms and Signs

The presenting symptoms involve the ocular system in 38% of patients, the vestibuloauditory system in 46%, and both in 15%. By 5 mo, 75% of patients have both ocular and vestibuloauditory symptoms. Nonspecific systemic complaints include fever, headache, joint pain, and myalgia.

Ocular: Ocular involvement includes any combination of the following:

• Bilateral interstitial keratitis or other corneal stromal keratitis

• Episcleritis or scleritis

• Uveitis

• Papillitis

• Other orbital inflammation (eg, vitritis, choroiditis)

Ocular symptoms include irritation, pain, photophobia, and decreased vision. Ocular examination shows a patchy corneal stromal infiltrate typical of interstitial keratitis (see p. 591), ocular redness, optic nerve edema, proptosis, or a combination of these symptoms.

Vestibuloauditory: Vestibuloauditory symptoms include sensorineural hearing loss, tinnitus, and vertigo.

Vascular: A diastolic heart murmur may be present when aortitis is significant. Claudication may be present if limb vessels are affected.

Diagnosis

Diagnosis is based on clinical findings and exclusion of other causes (eg, syphilis, Lyme disease, Epstein-Barr virus infection) by appropriate serologic tests. Evaluation by an ophthalmologist and otolaryngologist is important.

Treatment

• Initially topical and sometimes systemic corticosteroids

Untreated disease may lead to corneal scarring and visual loss and, in 60 to 80% of patients, permanent hearing loss. Keratitis, episcleritis, and anterior uveitis can usually be treated with topical prednisolone acetate 1% q 1 h to qid. To treat deeper ocular inflammation and especially to treat vestibuloauditory symptoms before they become permanent, prednisone 1 mg/kg po once/day is begun as soon as possible and continued for 2 to 6 mo. Some clinicians add cyclophosphamide, methotrexate, or cyclosporine for recalcitrant cases.

Keratoconjunctivitis Sicca

(Dry Eyes; Keratitis Sicca)

Keratoconjunctivitis sicca is chronic, bilateral desiccation of the conjunctiva and cornea due to an inadequate tear film. Symptoms include itching, burning, irritation, and photophobia. Diagnosis is clinical; the Schirmer test may be helpful. Treatment is with topical tear supplements and sometimes blockage of the nasolacrimal openings.

Etiology

There are 2 main types:

- Aqueous tear-deficient keratoconjunctivitis sicca is caused by inadequate tear volume.

- Evaporative keratoconjunctivitis sicca (more common) is caused by accelerated tear evaporation due to poor tear quality.

Aqueous tear-deficient keratoconjunctivitis sicca is most commonly an isolated idiopathic condition in postmenopausal women. It is also commonly part of Sjogren's syndrome (see p. 303), RA, or SLE. Less commonly, it is secondary to other conditions that scar the lacrimal ducts (eg, cicatricial pemphigoid, Stevens-Johnson syndrome, trachoma). It may result from a damaged or malfunctioning lacrimal gland due to graft-vs-host disease, HIV (diffuse infiltrative lymphocytosis syndrome), local radiation therapy, or familial dysautonomia.

Evaporative keratoconjunctivitis sicca is caused by loss of the tear film due to abnormally rapid evaporation caused by an inadequate oil layer on the surface of the aqueous layer of tears. Symptoms may result from abnormal oil quality (ie, meibomian gland dysfunction) or a degraded normal oil layer (ie, seborrheic blepharitis). Patients frequently have acne rosacea.

Drying can also result from exposure due to inadequate eye closure at night (nocturnal lagophthalmos) or, rarely, from inadequate tear volume due to an insufficient blink rate.

Symptoms and Signs

Patients report itching; burning; a gritty, pulling, or foreign body sensation; or photophobia. A sharp stabbing pain, eye strain or fatigue, and blurred vision may also occur. Some patients note a flood of tears after severe irritation. Typically, symptoms fluctuate in intensity and may be intermittent. Certain factors can worsen symptoms:

- Prolonged visual efforts (eg, reading, working on the computer, driving, watching television)

- Local environments that are dry, windy, dusty, or smoky

- Certain systemic drugs, including isotretinoin, sedatives, diuretics, antihypertensives, oral contraceptives, and all anticholinergics (including antihistamines and many GI drugs)

Symptoms lessen on cool, rainy, or foggy days or in other high-humidity environments, such as in the shower. Recurrent and prolonged blurring and frequent intense irritation can impair daily function. However, permanent impairment of vision is rare.

With both forms, the conjunctiva is hyperemic, and there is often scattered, fine, punctate loss of corneal epithelium (superficial punctate keratitis), conjunctival epithelium, or both. When the condition is severe, the involved areas, mainly between the eyelids (the intrapalpebral or exposure zone), stain with fluorescein. Patients often blink at an accelerated rate because of irritation.

With the aqueous tear-deficient form, the conjunctiva can appear dry and lusterless with redundant folds.

With the evaporative form, abundant tears may be present as well as foam at the eyelid margin. Very rarely, severe, advanced, chronic drying leads to significant vision loss due to keratinization of the ocular surface or loss of corneal epithelium, leading to sequelae such as scarring, neovascularization, infections, ulceration, and perforation.

Diagnosis

• Schirmer test and tear breakup tests

Diagnosis is based on characteristic symptoms and clinical appearance. The Schirmer test and tear breakup test may differentiate type.

The Schirmer test determines whether tear production is normal. After blotting the closed eye to remove excess tears, a strip of filter paper is placed, without topical anesthesia, at the junction of the middle and lateral third of the lower eyelid. If < 5.5 mm of wetting occurs after 5 min on 2 successive occasions, the patient has aqueous tear-deficient keratoconjunctivitis sicca.

With evaporative keratoconjunctivitis sicca, the Schirmer test is usually normal. The tear film can be made visible under cobalt blue light at the slit lamp by instillation of a small volume of highly concentrated fluorescein (made by wetting a fluorescein strip with saline and shaking the strip to remove any excess moisture). Blinking several times reapplies a complete tear film. The patient then stares, and the length of time until the first dry spot develops is determined (tear breakup test, or TBUT). An accelerated rate of intact tear film breakup (< 10 sec) is characteristic of evaporative keratoconjunctivitis sicca.

If aqueous tear-deficient keratoconjunctivitis sicca is diagnosed, Sjogren's syndrome (see p. 303) should be suspected, especially if xerostomia is also present. Serologic tests and labial salivary gland biopsy are used for diagnosis. Patients with primary or secondary Sjogren's syndrome are at increased risk of several serious diseases (eg, primary biliary cirrhosis, non-Hodgkin lymphoma). Therefore, proper evaluation and monitoring are essential.

Treatment

• Artificial tears

• Sometimes occlusion of nasolacrimal punctum or tarsorrhaphy

Frequent use of artificial tears can be effective for both forms. More viscous artificial tears coat the ocular surface longer, and artificial tears that contain polar lipids such as glycerin reduce evaporation; both types are particularly useful in evaporative keratoconjunctivitis sicca. Artificial tear ointments applied before sleep are particularly useful when patients have nocturnal lagophthalmos or irritation on waking. Most cases are treated adequately throughout the patient's life with such supplementation. Staying hydrated, using humidifiers, and avoiding dry, drafty environments can often help. Not smoking and avoiding secondary smoke are important. In recalcitrant cases, occlusion of the nasolacrimal punctum may be indicated. In severe cases, a partial tarsorrhaphy can reduce tear loss through evaporation. Topical cyclosporine and ω-3 fatty acid dietary supplements may be a useful adjunct in some patients.

Patients with evaporative keratoconjunctivitis sicca often benefit from treatment of concomitant blepharitis and associated rosacea with measures such as warm compresses, eyelid margin scrubs, and intermittent topical eyelid antibiotic ointments (eg, bacitracin at bedtime), systemic doxycycline 50 to 100 mg po once or twice/day (contraindicated in pregnant or nursing patients), or both.

Cyclosporine drops that decrease the inflammation associated with dryness of the eye are available. They lead to meaningful improvement but only in a fraction of patients. These drops sting and take months before an effect is noticed.

Keratoconus

Keratoconus is a bulging distortion of the cornea, leading to loss of visual acuity.

Keratoconus is a slowly progressive thinning and bulging of the cornea, usually bilateral, beginning between ages 10 and 25. Its cause is unknown.

The distorted cone shape of the cornea causes major changes in the refractive characteristics of the cornea (irregular astigmatism) that cannot be fully corrected with glasses. Progressing keratoconus necessitates frequent change of eyeglasses. Contact lenses may provide better vision correction and should be tried when eyeglasses are not satisfactory. Corneal transplant surgery may be necessary if visual acuity with contact lenses is inadequate, contact lenses are not tolerated, or a visually significant corneal scar (caused by tearing of stromal fibers) is present.

Newer treatments seem promising. Implantation of corneal ring segments appears to have the potential to save selected patients from transplantation. Corneal cross-linking, an ultraviolet light treatment that strengthens the cornea, has had positive results in European studies and may become more common.

Keratomalacia

(Xerotic Keratitis; Xerophthalmia)

Keratomalacia is degeneration of the cornea caused by nutritional deficiency.

Keratomalacia is caused by vitamin A deficiency typically in patients with protein-calorie undernutrition. It is characterized by a hazy, dry cornea. Corneal ulceration with secondary infection is common. The lacrimal glands and conjunctiva are also affected. Lack of tears causes extreme dryness of the eyes, and foamy spots appear on the temporal and often nasal bulbar conjunctiva (Bitot's spots). Night blindness may occur. For further details, including specific therapy, see Vitamin A Deficiency on p. 34.

Peripheral Ulcerative Keratitis

(Marginal Keratolysis; Peripheral Rheumatoid Ulceration)

Peripheral ulcerative keratitis is inflammation and ulceration of the cornea that often occurs with chronic connective tissue diseases. Irritation and decreased vision result.

Peripheral ulcerative keratitis is a serious corneal ulceration; it often occurs with autoimmune diseases that are active, long-standing, or both, such as RA, Wegener's granulomatosis, and relapsing polychondritis.

Patients often have decreased visual acuity, photophobia, and foreign body sensation. A crescentic area of opacification in the periphery of the cornea, due to infiltration by WBCs and ulceration, stains with fluorescein. Infectious causes, such as bacteria, fungi, and herpes simplex virus, must be ruled out by culturing the ulcer and eyelid margins.

Among patients with rheumatic disease and peripheral ulcerative keratitis, the 10-yr mortality rate is about 40% (usually due to MI) without treatment and about 8% with systemic cytotoxic therapy.

Any patient with peripheral ulcerative keratitis should be promptly referred to an ophthalmologist. Systemic cyclophosphamide or other immunosuppressants treat the keratitis, life-threatening vasculitis, and underlying autoimmune disease. Treatment also includes local approaches to control inflammation (eg, tissue adhesive and bandage contact lenses) and repair damage (eg, patch grafts). Other possibly helpful drugs include collagenase inhibitors, such as systemic tetracycline or topical 20% *N*-acetylcysteine.

Phlyctenular Keratoconjunctivitis

(Phlyctenular Conjunctivitis; Phlyctenulosis)

Phlyctenular keratoconjunctivitis, a hypersensitivity reaction of the cornea and conjunctiva to

bacterial antigens, is characterized by discrete nodular areas of corneal or conjunctival inflammation.

Phlyctenular keratoconjunctivitis results from a hypersensitivity reaction to bacterial antigens, primarily staphylococcal, but TB, *Chlamydia*, and other agents have been implicated. It is more common in children. Many patients also have blepharitis.

Patients have multiple lesions, consisting of small yellow-gray nodules (phlyctenules) that appear at the limbus, on the cornea, or on the bulbar conjunctiva and persist from several days to 2 wk. On the conjunctiva, these nodules ulcerate but heal without a scar. When the cornea is affected, severe lacrimation, photophobia, blurred vision, aching, and foreign body sensation may be prominent. Frequent recurrence, especially with secondary infection, may lead to corneal opacity and neovascularization with loss of visual acuity.

Diagnosis is by characteristic clinical appearance. Testing for TB may be indicated (eg, for patients at risk).

Treatment for nontuberculous cases is with a topical corticosteroid-antibiotic combination. If patients have seborrheic blepharitis, eyelid scrubs may help prevent recurrence.

Superficial Punctate Keratitis

Superficial punctate keratitis is corneal inflammation of diverse causes characterized by scattered, fine, punctate corneal epithelial loss or damage. Symptoms are redness, lacrimation, photophobia, and slightly decreased vision. Diagnosis is by slit-lamp examination. Treatment depends on the cause.

Superficial punctate keratitis is a nonspecific finding. Causes may include any of the following:

• Viral conjunctivitis (most commonly adenovirus)

• Blepharitis

• Keratoconjunctivitis sicca

• Trachoma

• Chemical burns

• Ultraviolet (UV) light exposure (eg, welding arcs, sunlamps, snow glare)

• Contact lens overwear

• Systemic drugs (eg, adenine arabinoside)

• Topical drug or preservative toxicity.

Symptoms include photophobia, foreign body sensation, lacrimation, redness, and slightly decreased vision. Slit-lamp or ophthalmoscope examination of the cornea reveals a characteristic hazy appearance with multiple punctate speckles that stain with fluorescein. With viral conjunctivitis, preauricular adenopathy is common and chemosis may occur.

Keratitis that accompanies adenovirus conjunctivitis resolves spontaneously in about 3 wk. Blepharitis (see p. 575), keratoconjunctivitis sicca (see p. 592), and trachoma (see p. 583) require specific therapy. When caused by overwearing contact lenses, keratitis is treated with discontinuation of the contact lens and an antibiotic ointment (eg, ciprofloxacin 0.3% qid), but the eye is not patched because serious infection may result. Contact lens wearers with superficial punctate keratitis should be examined the next day. Suspected causative topical drugs (active ingredient or preservative) should be stopped.

Ultraviolet keratitis: UVB light (wavelength < 300 nm) can burn the cornea, causing keratitis or keratoconjunctivitis. Arc welding is a common cause; even a brief, unprotected glance at a welding arc may result in a burn. Other causes include high-voltage electric sparks, artificial sun lamps, and sunlight reflected off snow at high altitudes. UV radiation increases 4 to 6% for every 1000-ft (305-m) increase in altitude above sea level, and snow reflects 85% of UVB.

Symptoms are usually not apparent for 8 to 12 h after exposure and last 24 to 48 h. Patients have lacrimation, pain, redness, swollen eyelids, photophobia, headache, foreign body sensation, and decreased vision. Permanent vision loss is rare.

Diagnosis is by history, presence of superficial punctate keratitis, and absence of a foreign body or infection.

Treatment consists of an antibiotic ointment (eg, bacitracin or gentamicin 0.3% ointment q 8 h) and occasionally a short-acting cycloplegic drug (eg, cyclopentolate 1% drop q 4 h). Severe pain may require systemic analgesics. The corneal surface regenerates spontaneously in 24 to 48 h. The eye must be rechecked in 24 h. Dark glasses or welder's helmets that block UV light are preventive.

Corneal Transplantation

(Corneal Graft; Penetrating Keratoplasty)

Indications: Corneal transplantations are done for several reasons:

- To reconstruct the cornea (eg, replacing a perforated cornea)
- To relieve intractable pain (eg, severe foreign body sensation due to recurrent ruptured bullae in bullous keratopathy)
- To treat a disorder unresponsive to medical management (eg, severe, uncontrolled fungal corneal ulcer)
- To improve the optical qualities of the cornea and thus improve vision (eg, replacing a cornea that is scarred after a corneal ulcer, is clouded because of edema as occurs in Fuchs' dystrophy or after cataract surgery, is opaque because of deposits of nontransparent abnormal corneal stromal proteins as occurs in hereditary corneal stromal dystrophy, or has irregular astigmatism as occurs with keratoconus)

The most common indications are the following:

- Bullous keratopathy (pseudophakic or aphakic, Fuchs' endothelial dystrophy)
- Keratoconus
- Repeat graft
- Keratitis or postkeratitis (caused by viral, bacterial, fungal, or *Acanthamoeba* infection or perforation)
- Corneal stromal dystrophies

Procedure: Tissue matching is not routinely done. Cadaveric donor tissue cannot be used from anyone suspected of having a communicable disease.

Corneal transplantation can be done using general anesthesia or local anesthesia plus IV sedation.

Topical antibiotics are used for several weeks postoperatively and topical corticosteroids for several months. To protect the eye from inadvertent trauma after transplantation, the patient wears shields, glasses, or sunglasses. If transplantation involves the full thickness of the cornea (as in penetrating

keratoplasty, or PKP), achievement of full visual potential may take up to 18 mo because of changing refraction with wound healing and after suture removal. If only the endothelium is replaced (as in Descemet's stripping endothelial keratoplasty), achievement of full visual potential usually occurs by 6 mo. In many patients, earlier and better vision is attained by wearing a rigid contact lens over the corneal transplant.

Complications: Complications include the following:

• Graft rejection

• Infection (intraocular and corneal)

• Wound leak

• Glaucoma

• Graft failure

• High refractive error (especially astigmatism, myopia, or both)

• Recurrence of disease (with herpes simplex or hereditary corneal stromal dystrophy)

Graft rejection rates are usually < 10% but may be up to 68% in higher-risk patients. Rejection symptoms include decreased vision, photosensitivity, ocular ache, and ocular redness. Graft rejection is treated with topical corticosteroids (eg, prednisolone 1% hourly), sometimes with a supplemental periocular injection (eg, triamcinolone acetonide 40 mg). If graft rejection is severe or if graft function is marginal, additional corticosteroids are given orally (eg, prednisone 1 mg/kg once/day) and occasionally IV (eg, methylprednisolone 3 to 5 mg/kg once). Typically, the rejection episode reverses, and graft function returns fully. The graft may fail if the rejection episode is unusually severe or long-standing or if multiple episodes of graft rejection occur. Regraft is possible, but the long-term prognosis is worse than for the original graft.

Prognosis

The chance of long-term transplant success is

• > 90% for keratoconus, corneal scars, early bullous keratopathy, or hereditary corneal stromal dystrophies

• 80 to 90% for more advanced bullous keratopathy or inactive viral keratitis

• 50% for active corneal infection

• 0 to 50% for chemical or radiation injury

The generally high rate of success of corneal transplantation is attributable to many factors, including the avascularity of the cornea and the fact that the anterior chamber has venous drainage but no lymphatic drainage. These conditions promote low-zone tolerance (an immunologic tolerance that results from constant exposure to low doses of an antigen) and a process termed anterior chamber-associated immune deviation, in which there is active suppression of intraocular lymphocytes and delayed-type hypersensitivity to transplanted intraocular antigens. Another important factor is the effectiveness of the corticosteroids used topically, locally, and systemically to treat graft rejection.

Corneal Limbal Stem Cell Transplantation

Corneal limbal stem cell transplantation surgically replaces critical stem cells at the limbus (the area where the conjunctiva meets the cornea). Host stem cells normally reside in this area. Transplantation is done when the host stem cells have been too severely damaged to recover from disease or injury.

Conditions such as severe chemical burns, Stevens-Johnson syndrome, and severe contact lens overwear may cause persistent nonhealing corneal epithelial defects. These defects result from failure of corneal epithelial stem cells to produce sufficient epithelial cells to repopulate the cornea. If untreated, persistent nonhealing corneal epithelial defects are vulnerable to infection, which can lead to scarring, perforation, or both. Under these circumstances, a corneal transplant, which replaces only the central cornea and not the limbus, is insufficient; stem cells are needed to produce new cells that repopulate the cornea, restoring the regenerative capacity of the ocular surface.

Corneal limbal stem cells can be transplanted from the patient's healthy eye or from a cadaveric donor eye. The patient's damaged corneal epithelial stem cells are removed by a partial-thickness dissection of the limbus (ie, all the epithelium and the superficial stroma of the limbus). Donor limbal tissue, which is prepared by a similar dissection, is sutured into the prepared bed.

Chapter 65. Glaucoma

Introduction

Glaucomas are a group of eye disorders characterized by progressive optic nerve damage at least partly due to increased intraocular pressure (IOP). Glaucoma is the 3rd most common cause of blindness worldwide and the 2nd most common cause of blindness in the US, where it is the leading cause of blindness for blacks and Hispanics. About 3 million Americans and 14 million people worldwide have glaucoma, but only half are aware of it. Glaucoma can occur at any age but is 6 times more common among people > 60 yr.

Glaucomas are categorized as open-angle or closed-angle (angle-closure)—see Tables 65-1, 65-2, and 65-3. The "angle" refers to the angle formed by the junction of the iris and cornea at the periphery of the anterior chamber (see Fig. 65-1). The angle is where > 98% of the aqueous humor exits the eye via either the trabecular meshwork and Schlemm's canal (the major pathway, particularly in the elderly) or the ciliary body face and choroidal vasculature. These outflow pathways are not simply a mechanical filter and drain but instead involve active physiologic processes.

Glaucomas are further subdivided into primary (cause of outflow resistance or angle closure is unknown) and secondary (outflow resistance results from another disorder), accounting for > 20 adult types.

Pathophysiology

Axons of retinal ganglion cells travel through the optic nerve carrying images from the eye to the brain. Damage to these axons causes ganglion cell death with resultant optic nerve atrophy and patchy vision loss. Elevated IOP (in unaffected eyes, the average range is 11 to 21 mm Hg) plays a role in axonal damage, either by direct nerve compression or diminution of blood flow. However, the relationship between pressure and nerve damage is variable. Of people with IOP > 21 mm Hg (ie, ocular hypertension), only about 1 to 2%/yr (about 10% over 5 yr) develop glaucoma. Additionally, about one third of patients with glaucoma do not have IOPs > 21 mm Hg (known as lowtension glaucoma or normal-tension glaucoma).

IOP is determined by the balance of aqueous secretion and drainage. Elevated IOP is caused by inhibited or obstructed outflow, not oversecretion. In open-angle glaucoma, IOP is elevated because outflow is inadequate despite an angle that appears unobstructed. In angle-closure glaucoma, IOP is elevated when a physical distortion of the peripheral iris mechanically blocks outflow.

Symptoms and Signs

Symptoms and signs vary with the type of glaucoma, but the defining characteristic is optic nerve damage as evidenced by an abnormal optic disk (see p. 601 and Plate 13) and certain types of visual field deficits (see p. 601).

IOP may be elevated or within the average range. (For techniques of measurement, see p. 540)

Diagnosis

• Characteristic visual field defects

• Exclusion of other causes

• IOP usually > 21 mm Hg (but not required for the diagnosis)

Glaucoma should be suspected in a patient with any of the following:

• Typical visual field defects

• Abnormal optic nerve on ophthalmoscopy

• Elevated IOP

Such patients (and those with any risk factors) should be referred to an ophthalmologist for a comprehensive examination that includes a thorough history, family history, examination of the optic disks (preferably using a binocular examination technique), formal visual field examination, IOP measurement, and gonioscopy (visualization of the anterior chamber angle with a special mirrored contact lens prism). Glaucoma is diagnosed when characteristic findings of optic nerve damage are present and other causes (eg, multiple sclerosis)

[Table 65-1. Open-Angle Glaucoma: Classification Based on Mechanisms of Outflow Obstruction*]

have been excluded. Elevated IOP makes the diagnosis more likely but is not essential.

Screening: Screening can be done by primary physicians by checking visual fields with frequency-doubling technology (FDT) perimetry and ophthalmoscopic evaluation of the optic nerve. FDT perimetry involves use of a desktop device that can screen for visual field abnormalities suggestive of glaucoma in 2 to 3 min per eye. Although IOP should be measured, screening based only on IOP has low sensitivity, low specificity, and low positive

[Table 65-2. Angle-Closure Glaucoma: Classification Based on Mechanisms of Outflow Obstruction*]

predictive value. Patients > 40 yr and those who have risk factors for open-angle or angle-closure glaucoma should receive a comprehensive eye examination every 1 to 2 yr.

Treatment

• Decreasing IOP by using drugs or laser or incisional surgery

[Table 65-3. Developmental Abnormalities of the Anterior Chamber Angle Causing Glaucoma: Classification Based on Mechanisms of Outflow Obstruction*]

Patients with characteristic optic nerve and corresponding visual field changes are treated regardless of IOP. Lowering the IOP is the only clinically proven treatment. For chronic adult and juvenile glaucomas, the initial target IOP is at least 20% below pretreatment readings.

Three methods are available: drugs, laser surgery, and incisional surgery. The type of glaucoma determines the appropriate method. Drugs and most laser surgeries (trabeculoplasty) modify the existing aqueous secretion and drainage system. Most incisional surgeries (eg, guarded filtration procedures [trabeculectomy], glaucoma drainage implant devices [tube shunts]) create a new drainage system.

Prophylactic IOP lowering in patients with ocular hypertension delays the onset of glaucoma. However, because the rate of conversion from ocular hypertension to glaucoma in untreated people is low, the decision to treat prophylactically should be individualized based on the presence of risk factors, magnitude of IOP elevation, and patient factors (ie, preference for drugs vs surgery, drug adverse effects). Generally, treatment is recommended for patients with IOP > 30 mm Hg even if the visual field is full and the optic nerve disk appears healthy because the likelihood of damage is significant at that IOP level.

[Fig. 65-1. Aqueous humor production and flow.]

Primary Open-Angle Glaucoma

Primary open-angle glaucoma is a syndrome of optic nerve damage associated with an open

anterior chamber angle and an elevated or sometimes average intraocular pressure (IOP). Symptoms occur late and involve visual field loss. Diagnosis is by ophthalmoscopy, gonioscopy, visual field examination, and measurement of IOP. Treatment includes topical drugs (eg, prostaglandin analogs, β-blockers) and often requires laser or incisional surgery to increase aqueous drainage.

Etiology

Although open-angle glaucomas can have numerous causes (see Table 65-1), 60 to 70% of cases have no identifiable cause and are termed primary open-angle glaucoma. Both eyes usually are affected, but typically not equally.

Risk factors include older age, positive family history, black race, thinner central corneal thickness, systemic hypertension, diabetes, and myopia. In blacks, glaucoma is more severe and develops at an earlier age, and blindness is 6 to 8 times more likely.

Pathophysiology

IOP can be elevated or within the average range.

Elevated-pressure glaucoma: Two thirds of patients with glaucoma have elevated (> 21 mm Hg) IOP. Aqueous humor drainage is inadequate, whereas production by the ciliary body is normal. Identifiable mechanisms (ie, secondary open-angle glaucomas) are not present. These mechanisms include developmental anomalies, scarring caused by trauma or infection, and plugging of channels by detached iris pigment (ie, pigment dispersion syndrome) or abnormal protein deposits (eg, pseudoexfoliation syndrome).

Normal- or low-pressure glaucoma: In at least one third of patients with glaucoma, IOP is within the average range, but optic nerve damage and visual field loss typical of glaucoma are present. These patients have a higher incidence of vasospastic diseases (eg, migraines, Raynaud's syndrome) than the general population, suggesting that a vascular disorder compromising blood flow to the optic nerve may play a role.

Symptoms and Signs

Early symptoms are uncommon. Usually, the patient becomes aware of visual field loss only when optic nerve atrophy is marked; the typically asymmetric deficits contribute to delay in recognition. However, some patients have complaints, such as missing stairs if their inferior visual field has been lost, noticing portions of words missing when reading, or having difficulty with driving.

Examination findings include an unobstructed open angle on gonioscopy and characteristic optic nerve appearance and visual field defects. IOP may be normal or high but is almost always higher in the eye with more optic nerve damage.

Optic nerve appearance: The optic nerve head (ie, disk) is normally a slightly vertically elongated circle with a centrally located depression called the cup. The neurosensory rim is the tissue between the margin of the cup and the edge of the disk and is composed of the ganglion cell axons from the retina.

Characteristic optic nerve changes include

- Increased cup:disk ratio
- Thinning of the neurosensory rim
- Pitting or notching of the rim
- Nerve fiber layer hemorrhage that crosses the disk margin (ie, Drance hemorrhage or splinter hemorrhages)

• Vertical elongation of the cup

• Quick angulations in the course of the exiting blood vessels

Thinning of the neurosensory rim over time alone can be diagnostic of glaucoma regardless of the IOP or visual field. However, most initial diagnoses of glaucoma involve some visual field change.

Visual field defects: Visual field changes caused by lesions of the optic nerve include

• Nasal step defects (which do not cross the horizontal meridian—an imaginary horizontal line between the upper and lower parts of the visual field)

• Arcuate (arc-shaped) scotomata extending nasally from the blind spot

• Temporal wedge defects

• Paracentral scotomata

In contrast, deficits of the more proximal visual pathways (ie, from the lateral geniculate nucleus to the occipital lobe) involve quadrants or hemispheres of the visual field; thus, deficits do not cross the vertical meridian.

Diagnosis

• Visual field testing

• Ophthalmoscopy

• Measurement of IOP

• Exclusion of other optic neuropathies

Diagnosis is suggested by the examination, but similar findings can result from other optic neuropathies (eg, caused by ischemia, cytomegalovirus infection, or vitamin B_{12} deficiency).

Before a diagnosis of normal-pressure glaucoma can be established, the following factors may need to be ruled out: inaccurate IOP readings, large diurnal fluctuations (causing intermittent normal readings), optic nerve damage caused by previously resolved glaucoma (eg, a previously elevated IOP due to corticosteroid use or uveitis), intermittent angle-closure glaucoma, and other ocular or neurologic disorders that cause similar visual field defects.

Optic disk photography or a detailed optic disk drawing is helpful for future comparison. The frequency of follow-up examinations varies from weeks to years, depending on the patient's reliability, severity of the glaucoma, and response to treatment.

Treatment

• Decreasing IOP 20 to 40%

• Initially, drugs (eg, prostaglandin analogs, β-blockers such as timolol)

• Sometimes surgery, such as laser trabeculoplasty or guarded filtration procedure

Vision lost by glaucoma cannot be recovered. The goal is to prevent further optic nerve and visual field damage by lowering IOP. The target level is 20 to 40% below pretreatment readings. In general, the greater the damage caused by glaucoma, the lower the IOP must be to prevent further damage. If damage progresses, the IOP goal is lowered further and additional therapy is initiated.

Initial treatment is usually drug therapy, proceeding to laser therapy and then incisional surgery if the target IOP is not met. Surgery may be the initial treatment if IOP is extremely high.

Drug therapy: Multiple drugs are available (see Table 65-4). Topical agents are preferred. The most popular are prostaglandin analogs, followed by β-blockers (particularly timolol). Other drugs include α_2-selective adrenergic agonists, cholinergic agonists, and carbonic anhydrase inhibitors. Oral carbonic anhydrase inhibitors are effective, but adverse effects limit their use.

Patients taking topical glaucoma drugs should be taught passive lid closure with punctal occlusion to help reduce systemic absorption and associated adverse effects, although the effectiveness of these maneuvers is controversial. Patients who have difficulty instilling drops directly onto the conjunctiva may place the drop on the nose just medial to the medial canthus, then roll the head slightly toward the eye so that the liquid flows into the eye.

Typically, to gauge effectiveness, clinicians start drugs in only one eye (one-eye trial); once improvement in the treated eye has been confirmed at a subsequent visit (typically 1 to 4 wk later), both eyes are treated.

Surgery: Surgery for primary open-angle and normal-pressure glaucoma includes laser trabeculoplasty, a guarded filtration procedure, and possibly tube shunts or ciliodestructive procedures.

Argon laser trabeculoplasty (ALT) may be the initial treatment for patients who do not respond to or who cannot tolerate drug therapy. Laser energy is applied to either 180° or 360° of the trabecular meshwork to improve the drainage of aqueous humor. Within 2 to 5 yr, about 50% of patients require additional drug therapy or surgery because of insufficient IOP control.

Selective laser trabeculoplasty (SLT) uses a pulsed double-frequency neodymium:yttrium-aluminum-garnet laser. SLT and ALT are equally effective initially, but SLT may have greater effectiveness in subsequent treatments.

A **guarded filtration procedure** is the most commonly used filtration procedure. A hole is made in the limbal sclera (trabeculectomy), which is covered by a partial-thickness scleral flap that controls egress of aqueous from the eye to the subconjunctival space, forming a filtration bleb. Adverse effects of glaucoma filtration surgery include acceleration of cataract growth, pressures that are too low, and transient swelling during the perioperative period. Patients with trabeculectomies are at increased risk of bacterial endophthalmitis and should be instructed to report any symptoms or signs of bleb infection (blebitis) or endophthalmitis immediately.

Viscocanalostomy, canaloplasty, and Trabectome® surgery are newer filtration procedures that do not involve creating a fistula between the anterior chamber and subconjunctival space. Viscocanalostomy and canaloplasty involve dilating Schlemm's canal. Trabectome® surgery uses a proprietary device to remove a portion of the inner aspect of one of the drains of the eye (trabecular meshwork). More long-term studies with these procedures are needed and are on-going. Currently, these new procedures do not appear as effective as trabeculectomy but seem to offer greater safety.

Angle-Closure Glaucoma

Angle-closure glaucoma is glaucoma associated with a physically obstructed anterior chamber angle, which may be chronic or, rarely, acute. Symptoms of acute angle closure are severe ocular pain and redness, decreased vision, colored halos around lights, headache, nausea, and vomiting. Intraocular pressure (IOP) is elevated. Immediate treatment of the acute condition with multiple topical and systemic drugs is required to prevent permanent vision loss, followed by the definitive treatment, iridotomy.

Angle-closure glaucoma accounts for about 10% of all glaucomas in the US.

Etiology

Angle-closure glaucoma is caused by factors that either pull or push the iris up into the angle (ie, junction of the iris and cornea at the periphery of the anterior chamber), physically blocking drainage of aqueous and raising IOP (see Table 65-2). Elevated IOP damages the optic nerve.

Pathophysiology

Angle closure may be primary (cause is unknown) or secondary to another condition (see Table 65-2) and can be acute, subacute (intermittent), or chronic.

[**Table 65-4.** Drugs Used to Treat Glaucoma]

Primary angle-closure glaucoma: Narrow angles are not present in young people. As people age, the lens of the eye continues to grow. In some but not all people, this growth pushes the iris forward, narrowing the angle. Risk factors for developing narrow angles include Asian ethnicity, hyperopia, family history, and advanced age.

In people with narrow angles, the distance between the pupillary iris and the lens is also very narrow. When the iris dilates, forces pull it centripetally and posteriorly causing iris-lens contact, which prevents aqueous from passing between the lens and iris into the anterior chamber (this mechanism is termed pupillary block). Pressure from the continued secretion of aqueous into the posterior chamber by the ciliary body pushes the peripheral iris anteriorly (causing a forward-bowing iris called iris bombe), closing the angle. This closure blocks aqueous outflow, resulting in rapid (within hours) and severe (> 40 mm Hg) elevation of IOP. Because of the rapid onset, this condition is called primary acute angle-closure glaucoma and is an ophthalmic emergency requiring immediate treatment.

Intermittent angle-closure glaucoma occurs if the episode of pupillary block resolves spontaneously after several hours, usually after sleeping supine.

Chronic angle-closure glaucoma occurs if the angle narrows slowly, allowing scarring between the peripheral iris and trabecular meshwork; IOP elevation is slow.

Pupillary dilation (mydriasis) can push the iris into the angle and precipitate acute angle-closure glaucoma in any person with narrow angles. This development is of particular concern when applying topical agents to dilate the eye for examination (eg, cyclopentolate, phenylephrine) or for treatment (eg, homatropine) or when giving systemic drugs that have the potential to dilate the pupils (eg, scopolamine, α-adrenergic agonists commonly used to treat urinary incontinence, drugs with anticholinergic effects).

Secondary angle-closure glaucomas: The mechanical obstruction of the angle is due to a coexisting condition, such as proliferative diabetic retinopathy (PDR), ischemic central vein occlusion, uveitis, or epithelial down-growth. Contraction of a neovascular membrane (eg, in PDR) or inflammatory scarring associated with uveitis can pull the iris into the angle.

Symptoms and Signs

Acute angle-closure glaucoma: Patients have severe ocular pain and redness, decreased vision, colored halos around lights, headache, nausea, and vomiting. The systemic complaints may be so severe that patients are misdiagnosed as having a neurologic or GI problem. Examination typically reveals conjunctival hyperemia, a hazy cornea, a fixed mid-dilated pupil, and anterior chamber inflammation. Vision is decreased. IOP is usually 40 to 80 mm Hg. The optic nerve is difficult to visualize because of corneal edema, and visual field testing is not done because of discomfort.

Chronic angle-closure glaucoma: This type of glaucoma manifests similarly to open-angle glaucoma (see p. 600). Some patients have ocular redness, discomfort, blurred vision, or headache that lessens with sleep (perhaps because of sleep-induced miosis and posterior displacement of the lens by gravity). On gonioscopy, the angle is narrow, and peripheral anterior synechiae (PAS) may be seen. IOP may be normal but is usually higher in the affected eye.

Diagnosis

- **Acute:** Measurement of IOP and clinical findings

- **Chronic:** Gonioscopy showing peripheral anterior synechiae and characteristic optic nerve and visual field abnormalities

Diagnosis of acute angle-closure glaucoma is clinical and by measurement of IOP. Gonioscopy may be difficult to perform in the involved eye because of a clouded cornea with friable corneal epithelium. However, examination of the other eye reveals a narrow or occludable angle. If the other eye has a wide angle, a diagnosis other than primary angle-closure glaucoma should be considered.

Diagnosis of chronic angle-closure glaucoma is based on the presence of PAS on gonioscopy and characteristic optic nerve and visual field changes (see p. 601).

Treatment

- **Acute:** Timolol, pilocarpine, and apraclonidine drops and a systemic osmotic drug followed promptly by laser peripheral iridotomy

- **Chronic:** Similar to primary open-angle glaucoma except that laser peripheral iridotomy may be done if the clinician feels that the procedure may slow the mechanical closing of the angle

Acute angle-closure glaucoma: Treatment must be initiated immediately because vision can be lost quickly and permanently. The patient should receive several drugs at once. A suggested regimen is timolol 0.5% one drop q 30 min for 2 doses; pilocarpine 2 to 4% one drop q 15 min for the first 1 to 2 h; apraclonidine 0.5 to 1% one drop q 30 min for 2 doses; acetazolamide 500 mg po initially followed by 250 mg q 6 h; and an osmotic agent, such as oral glycerol 1 mL/kg diluted with an equal amount of cold water, mannitol 1.0 to 1.5 mg/kg IV, or isosorbide 100 g po (220 mL of a 45% solution [NOTE: This form of isosorbide is not isosorbide dinitrate.]). Response is evaluated by measuring IOP. Miotics are generally not effective when IOP is > 40 or 50 mm Hg because of an anoxic pupillary sphincter.

Definitive treatment is with laser peripheral iridotomy (LPI), which opens another pathway for fluid to pass from the posterior to the anterior chamber, breaking the pupillary block. It is done as soon as the cornea is clear and inflammation has subsided. In some cases the cornea clears within hours of lowering the IOP; in other cases, it can take 1 to 2 days. Because the chance of having an acute attack in the other eye is 80%, LPI is done on both eyes.

The risk of complications with LPI is extremely low compared with its benefits. Glare, which can be bothersome, may occur if the iridotomy is not placed superiorly enough for the upper lid to cover it.

Chronic angle-closure glaucoma: Patients with chronic, subacute, or intermittent angle-closure glaucoma should also have LPI. Additionally, patients with a narrow angle, even in the absence of symptoms, should undergo prompt LPI to prevent angle-closure glaucoma.

The drug and surgical treatments are the same as with open-angle glaucoma. Laser trabeculoplasty is relatively contraindicated if the angle is so narrow that additional PAS may form after the laser procedure.

Chapter 66. Cataract

(For developmental or congenital cataracts, see p. 2920.)

A cataract is a congenital or degenerative opacity of the lens. The main symptom is gradual, painless vision blurring. Diagnosis is by ophthalmoscopy and slit-lamp examination. Treatment is surgical removal and placement of an intraocular lens.

Lens opacity can develop in several locations:

• Central lens nucleus (nuclear cataract)

• Beneath the posterior lens capsule (posterior subcapsular cataract)

Etiology

Cataracts occur with aging. Other risk factors may include the following:

• Trauma (sometimes causing cataracts years later)

• Smoking

• Alcohol use

• Exposure to x-rays

• Heat from infrared exposure

• Systemic disease (eg, diabetes)

• Uveitis

• Systemic drugs (eg, corticosteroids)

• Undernutrition

• Dark eyes

• Possibly chronic ultraviolet exposure

Many people have no risk factors other than age. Some cataracts are congenital, associated with numerous syndromes and diseases.

Symptoms and Signs

Cataracts generally develop slowly over years. Early symptoms may be loss of contrast, glare (halos and starbursts around lights), needing more light to see well, and problems distinguishing dark blue from black. Painless blurring eventually occurs. The degree of blurring depends on the location and extent of the opacity. Double vision occurs rarely.

With a nuclear cataract (see Plate 4), distance vision worsens. Near vision may improve in the early stages because of changes in the refractive index of the lens; presbyopic patients may be temporarily able to read without glasses (second sight).

A posterior subcapsular cataract disproportionately affects vision because the opacity is located at the crossing point of incoming light rays. Such cataracts reduce visual acuity more when the pupil constricts (eg, in bright light, during reading). They are also the type most likely to cause loss of contrast as well as

glare, especially from bright lights or from car headlights while driving at night.

Rarely, the cataract swells, occluding the trabecular drainage meshwork and causing secondary closed-angle glaucoma and pain.

Diagnosis

• Ophthalmoscopy followed by slit-lamp examination

Diagnosis is best made with the pupil dilated. Well-developed cataracts appear as gray, white, or yellow-brown opacities in the lens. Examination of the red reflex through the dilated pupil with the ophthalmoscope held about 30 cm away usually discloses subtle opacities. Small cataracts stand out as dark defects in the red reflex. A large cataract may obliterate the red reflex. Slit-lamp examination provides more details about the character, location, and extent of the opacity.

Treatment

• Surgical removal of the cataract

• Placement of an intraocular lens

Frequent refractions and corrective lens prescription changes may help maintain useful vision during cataract development. Occasionally, long-term pupillary dilation (with phenylephrine 2.5% q 4 to 8 h) is helpful for small centrally located cataracts. Indirect lighting while reading minimizes pupillary constriction and may optimize vision for close tasks. Polarized lenses reduce glare.

Usual indications for surgery include the following:

• Best vision obtained with glasses is worse than 20/40 (< 6/12), or vision is significantly decreased under glare conditions (eg, oblique lighting while trying to read a chart) in a patient with bothersome halos or starbursts.

• Patients sense that vision is limiting (eg, by preventing activities of daily living such as driving, reading, hobbies, and occupational activities).

• Vision could potentially be meaningfully improved if the cataract is removed (ie, a significant portion of the vision loss must be caused by the cataract).

Far less common indications include cataracts that cause glaucoma or that obscure the fundus in patients who need periodic fundus examinations for management of diseases such as diabetic retinopathy and glaucoma. There is no advantage to removing a cataract early.

Cataract extraction is usually done using a topical or local anesthetic and IV sedation. There are 3 extraction techniques. In **intracapsular cataract extraction**, the cataract and lens capsule are removed in one piece; this technique is rarely used. In **extracapsular cataract extraction**, the hard central nucleus is removed in one piece and then the soft cortex is removed in multiple small pieces. In **phacoemulsification**, the hard central nucleus is dissolved by ultrasound and then the soft cortex is removed in multiple small pieces. Phacoemulsification requires the smallest incision, thus enabling the fastest healing, and is usually the preferred procedure. In extracapsular extraction and phacoemulsification, the lens capsule is not removed.

A plastic or silicone lens is almost always implanted intraocularly to replace the optical focusing power lost by removal of the crystalline lens. The lens implant is usually placed on or within the lens capsule (posterior chamber lens). The lens can also be placed in front of the iris (anterior chamber lens) or attached to the iris and within the pupil (iris plane lens). Iris plane lenses are rarely used in the US because many designs led to a high frequency of postoperative complications. Multifocal intraocular lenses are newer and have different focusing zones that may reduce dependence on glasses after surgery. Patients occasionally experience glare or halos with these lenses, especially under low-light

conditions.

In most cases, a tapering schedule of topical antibiotics (eg, moxifloxacin 0.5% 1 drop qid) and topical corticosteroids (eg, prednisolone acetate 1% 1 drop qid) is used for up to 4 wk postsurgery. Patients often wear an eye shield while sleeping and should avoid the Valsalva maneuver, heavy lifting, excessive forward bending, and eye rubbing for several weeks.

Major complications of cataract surgery are rare. Complications include the following:

- Intraoperative: Bleeding beneath the retina, causing the intraocular contents to extrude through the incision (choroidal hemorrhage), vitreous prolapsing out of the incision (vitreous loss), fragments of the cataract dislocating into the vitreous, incisional burn, and detachment of corneal endothelium and its basement membrane (Descemet's membrane)

- Within the first week: Endophthalmitis (infection within the eye) and glaucoma

- Within the first month: Cystoid macular edema

- Months later: Bullous keratopathy (ie, swelling of the cornea due to damage to the corneal pump cells during cataract surgery), retinal detachment, and posterior capsular opacification (common, but treatable with laser)

After surgery, vision returns to 20/40 (6/12) or better in 95% of eyes if there are no preexisting disorders such as amblyopia, retinopathy, macular degeneration, and glaucoma. If an intraocular lens is not implanted, contact lenses or thick glasses are needed to correct the resulting hyperopia.

Prevention

Many ophthalmologists recommend ultraviolet-coated eyeglasses or sunglasses as a preventive measure. Reducing risk factors such as alcohol, tobacco, and corticosteroids and controlling blood glucose in diabetes delay onset. A diet high in vitamin C, vitamin A, and carotenoids (contained in vegetables such as spinach and kale) may protect against cataracts.

Chapter 67. Uveitis

Introduction

Uveitis is inflammation of the uveal tract—the iris, ciliary body, and choroid. Most cases are idiopathic, but identifiable causes include various infections and systemic diseases, many of which are autoimmune. Symptoms include decreased vision, ocular ache, redness, photophobia, and floaters. Although intraocular inflammation is identified clinically, identifying the cause of the inflammation typically requires testing. Treatment depends on cause but typically includes topical, locally injected, or systemic corticosteroids with a topical cycloplegic-mydriatic drug. Noncorticosteroid immunosuppressive drugs may be used in severe and refractory cases. Infectious causes require antimicrobial therapy.

Inflammation of the uvea (uveitis) may occur with or without vitreitis, retinitis, papillitis, or optic neuritis. Uveitis is classified anatomically as anterior, intermediate, or posterior uveitis or panuveitis.

Anterior uveitis is localized primarily to the anterior segment of the eye and includes iritis (inflammation in the anterior chamber alone) and iridocyclitis (inflammation in the anterior chamber and anterior vitreous).

Intermediate uveitis (peripheral uveitis or chronic cyclitis) occurs in the vitreous.

Posterior uveitis refers to any form of retinitis, choroiditis, or inflammation of the optic disk.

Panuveitis (also called diffuse uveitis) implies inflammation in both the anterior and posterior chambers.

Etiology

Most cases are idiopathic and presumed to be autoimmune in origin. Identifiable causes include

• Trauma

• Ocular and systemic infections

• Systemic autoimmune disorders

The most common cause of anterior uveitis is trauma (traumatic iridocyclitis). Other causes are spondyloarthropathies (20 to 25%), juvenile idiopathic arthritis, and herpesvirus (herpes simplex and varicella-zoster) infection. Half of all cases of anterior uveitis are idiopathic.

Most intermediate uveitis is idiopathic. Uncommon identifiable causes include multiple sclerosis, sarcoidosis, TB, syphilis, and, in endemic regions, Lyme disease.

Most posterior uveitis (retinitis) is idiopathic. The most commonly recognized cause of posterior uveitis in immunocompetent patients is toxoplasmosis; the most commonly recognized cause in patients with HIV/AIDS is cytomegalovirus (CMV).

The most commonly identified cause of panuveitis is sarcoidosis, but most cases remain idiopathic despite appropriate testing.

Infrequently, systemic drugs cause uveitis (usually anterior). Examples are sulfonamides, pamidronate (an inhibitor of bone resorption), rifabutin, and cidofovir.

Systemic diseases causing uveitis and their treatment are discussed elsewhere in THE MANUAL.

Symptoms and Signs

Symptoms and signs may be subtle and vary depending on the site and severity of inflammation.

Anterior uveitis tends to be the most symptomatic, usually manifesting with pain (ocular ache), redness, photophobia, and, to a variable degree, decreased vision. Signs include hyperemia of the conjunctiva adjacent to the cornea (ciliary flush or limbal injection). Slit-lamp findings include cells and flare (a haze) in the anterior chamber (aqueous humor), keratic precipitates (WBC clumps on the inner corneal surface), and posterior synechiae. With severe anterior uveitis, WBCs may layer in the anterior chamber (hypopyon).

Intermediate uveitis is typically painless and manifests with floaters and decreased vision. The primary sign is cells in the vitreous humor. Aggregates and condensations of inflammatory cells often occur over the pars plana (near the junction of the iris and sclera), forming snowballs. Vision may be decreased because of floaters or cystoid macular edema, which results from fluid leakage from blood vessels in the macula. Confluent and condensed vitreous cells and snowballs over the pars plana may cause a classic snowbank appearance, which can be associated with neovascularization of the retinal periphery.

Posterior uveitis may give rise to diverse symptoms but most commonly causes floaters and decreased vision as occurs in intermediate uveitis. Signs include cells in the vitreous humor; white or yellow-white lesions in the retina (retinitis), underlying choroid (choroiditis), or both; exudative retinal detachments; retinal vasculitis; and optic disk edema.

Panuveitis may cause any combination of the previously mentioned symptoms and signs.

Consequences: Consequences of uveitis include profound and irreversible vision loss, especially when uveitis is unrecognized, inadequately treated, or both. The most frequent complications include cataract; glaucoma; retinal detachment; neovascularization of the retina, optic nerve, or iris; and cystoid macular edema (the most common cause of decreased vision in patients with uveitis).

Diagnosis

• Slit-lamp examination

• Ophthalmoscopy after pupil dilation

Uveitis should be suspected in any patient who has ocular ache, redness, photophobia, floaters, or decreased vision. Patients with anterior uveitis have ocular ache in the affected eye if light is shined in the unaffected eye (true photophobia), which is uncommon in conjunctivitis. Diagnosis of anterior uveitis is by recognizing cells and flare in the anterior chamber. Cells and flare are seen with a slit lamp and are most evident when using a narrow, intensely bright light focused on the anterior chamber in a dark room. Findings of intermediate and posterior uveitis are most easily seen after dilating the pupil (see p. 538). Indirect ophthalmoscopy (usually done by an ophthalmologist) is more sensitive than direct ophthalmoscopy. (NOTE: If uveitis is suspected, patients should be referred immediately for complete ophthalmologic evaluation.)

Many conditions that cause intraocular inflammation can mimic uveitis and should be considered in the appropriate clinical settings. Such conditions include intraocular cancers in the very young (typically retinoblastoma and leukemia) and in the elderly (intraocular lymphoma). Less commonly, retinitis pigmentosa (see p. 618) can manifest with mild inflammation, which may be confused with uveitis.

Treatment

• Corticosteroids (usually topical)

• Cycloplegic-mydriatic drugs

Treatment of active inflammation usually involves corticosteroids given topically or by periocular or intraocular injection along with a cycloplegic-mydriatic drug (eg, homatropine 2% or 5% drops bid to qid depending on severity). Antimicrobial drugs are used to treat infectious uveitis. Particularly severe or chronic cases may require systemic corticosteroids, systemic noncorticosteroid immunosuppressive

drugs, laser phototherapy, cryotherapy applied transsclerally to the retinal periphery, or surgical removal of the vitreous (vitrectomy).

Uveitis Caused by Connective Tissue Disease

A number of connective tissue diseases cause inflammation of the uveal tract.

Spondyloarthropathies: The seronegative spondyloarthropathies (see p. 341) are a common cause of anterior uveitis. RA, in contrast, is not associated with uveitis. Ocular inflammation is most common with ankylosing spondylitis but also occurs with reactive arthritis, inflammatory bowel disease (ulcerative colitis and Crohn's disease), and psoriatic arthritis. Uveitis is classically unilateral, but recurrences are common and active inflammation may alternate between eyes. Men are affected more commonly than women. Most patients, regardless of sex, are HLA-B27 positive.

Treatment requires a topical corticosteroid and a cycloplegic-mydriatic drug. Occasionally, periocular corticosteroids are required.

Juvenile idiopathic arthritis (JIA, also known as juvenile RA): JIA characteristically causes chronic bilateral iridocyclitis in children, particularly those with the pauciarticular variety (see p. 339). Unlike most forms of anterior uveitis, however, JIA tends not to cause pain, photophobia, and conjunctival injection but only blurring and meiosis and is, therefore, often referred to as white iritis. JIA-associated uveitis is more common among girls.

Recurrent bouts of inflammation are best treated with a topical corticosteroid and a cycloplegic-mydriatic drug. Long-term control often requires use of a noncorticosteroid immunosuppressive drug (eg, methotrexate, mycophenolate mofetil).

Sarcoidosis: Sarcoidosis (see also p. 1965) accounts for 10 to 20% of cases of uveitis, and about 25% of patients with sarcoidosis develop uveitis. Sarcoid uveitis is more common among blacks and the elderly.

Virtually any symptoms and signs of anterior, intermediate, posterior, or panuveitis can occur. Suggestive findings include conjunctival granulomas, large keratic precipitates on the corneal endothelium (so-called granulomatous or mutton fat precipitates), iris granulomas, and retinal vasculitis. Biopsy of suggestive lesions, which provides the most secure diagnosis, is usually done on the conjunctiva; it is rarely done on intraocular tissues because of the risk associated with the procedure.

Treatment usually involves topical, periocular, intraocular, or systemic corticosteroids, or a combination, along with a topical cycloplegic-mydriatic drug. Patients with moderate to severe inflammation may require a noncorticosteroid immunosuppressive drug (eg, methotrexate, mycophenolate mofetil, azathioprine).

Behcet's syndrome: This condition is rare in North America but is a fairly common cause of uveitis in the Middle East and Far East (see also p. 315).

Typical findings include severe anterior uveitis with hypopyon, retinal vasculitis, and optic disk inflammation. The clinical course is usually severe with multiple recurrences.

Diagnosis requires the presence of associated systemic manifestations, such as oral aphthous or genital ulcers; dermatitis, including erythema nodosum; thrombophlebitis; or epididymitis. Oral aphthae may be biopsied to show an occlusive vasculitis. There are no laboratory tests for Behcet's syndrome.

Treatment with local and systemic corticosteroids and a cycloplegic-mydriatic drug may alleviate acute exacerbations, but most patients eventually require systemic corticosteroids and a noncorticosteroid immunosuppressive drug (eg, cyclosporine, chlorambucil) to control the inflammation and avoid the serious complications of long-term corticosteroid treatment. Biologic agents such as interferons and tumor necrosis factor inhibitors have been effective in selected patients unresponsive to other therapies.

Vogt-Koyanagi-Harada (VKH) syndrome: VKH syndrome is an uncommon systemic disorder

characterized by uveitis accompanied by cutaneous and neurologic abnormalities. VKH syndrome is particularly common among people of Asian, Asian Indian, and American Indian descent. Women in their 20s and 30s are affected more often than men. The etiology is unknown, although an autoimmune reaction directed against melanin-containing cells in the uveal tract, skin, inner ear, and meninges is strongly suspected.

Neurologic symptoms tend to occur early and include tinnitus, dysacusis (auditory agnosia), vertigo, headache, and meningismus. Cutaneous findings frequently occur later and include patchy vitiligo (especially common on the eyelids, low back, and buttocks), poliosis (a localized patch of white hair), and alopecia, often involving the head and neck. Common findings include serous retinal detachment, optic disk edema, and choroiditis. Long-term complications include cataracts, glaucoma, subretinal fibrosis, and choroidal neovascularization.

Early treatment includes local and systemic corticosteroids and a cycloplegic-mydriatic drug. Many patients also require a noncorticosteroid immunosuppressive drug (eg, methotrexate, azathioprine, mycophenolate mofetil).

Endophthalmitis

Endophthalmitis is an acute panuveitis resulting most often from bacterial infection.

Most cases of endophthalmitis are caused by gram-positive bacteria, such as *Staphylococcus epidermidis* or *S. aureus*. Gram-negative organisms can also cause endophthalmitis, tend to be more virulent, and predict a poorer prognosis. Fungal and protozoan causes of endophthalmitis are rare. Most cases occur after penetrating ocular trauma or intraocular surgery (exogenous). Less commonly, infection reaches the eye via the bloodstream after systemic surgery or dental procedures or when IV lines or IV drugs are used (endogenous).

Endophthalmitis is a medical emergency because vision prognosis is directly related to the time from onset to treatment. Rarely, untreated intraocular infections extend beyond the confines of the eye to involve the orbit and CNS.

Exogenous endophthalmitis typically causes severe ocular ache and decreased vision. Signs include intense conjunctival hyperemia and intraocular inflammation within the anterior chamber and vitreous, occasionally with eyelid edema.

Diagnosis requires a high index of suspicion in at-risk patients, especially those with recent eye surgery or trauma. Gram stain and culture of aspirates from the anterior chamber and vitreous are standard. Patients with suspected endogenous endophthalmitis should also have blood and urine cultures.

Initial treatment includes broad-spectrum intravitreal antibiotics, most commonly vancomycin and ceftazidime. Patients with endogenous endophthalmitis should receive both intravitreal and IV antibiotics. Therapy is modified based on culture and sensitivity results.

Vision prognosis is often poor, even with early and appropriate treatment. Patients with count-fingers or worse vision at presentation should be considered for vitrectomy and use of intraocular corticosteroids. Corticosteroids are, however, contraindicated in fungal endophthalmitis.

Infectious Uveitis

A number of infectious diseases cause uveitis (see Table 67-1). The most common are

[**Table 67-1.** Infectious Causes of Uveitis]

herpes simplex virus, varicella-zoster virus, and CMV infection and toxoplasmosis. Different organisms affect different parts of the uveal tract.

Herpesvirus: Herpes simplex virus (see also p. 1417) causes anterior uveitis. Varicellazoster virus does so less commonly, although the prevalence of zoster-associated anterior uveitis increases with age. Symptoms include ocular ache, photophobia, and decreased vision. Signs include redness; conjunctival injection and anterior chamber inflammation (cells and flare), often accompanied by corneal inflammation (keratitis); decreased corneal sensation; and patchy or sectorial iris atrophy. Intraocular pressure may be elevated as well; elevation can be detected by using applination tonometry with a Schiotz tonometer, a Goldmann tonometer, or a pneumotonometer.

Treatment should generally be initiated by an ophthalmologist and should include a topical corticosteroid and a cycloplegic-mydriatic drug. Acyclovir (400 mg po 5 times/day for herpes simplex virus and 800 mg po 5 times/day for herpes zoster virus) may also be given. Drops to lower intraocular pressure may be required in patients with ocular hypertension.

Much less commonly, varicella-zoster and herpes simplex viruses cause a rapidly progressing form of retinitis called acute retinal necrosis (ARN), which typically manifests as confluent retinitis, occlusive retinal vasculitis, and moderate to severe vitreous inflammation. One third of ARN cases become bilateral, and in three fourths of eyes, retinal detachment occurs. ARN may also occur in patients with HIV/AIDS, but severely immunocompromised patients can have less prominent vitreous inflammation. Vitreous biopsy for culture and PCR analysis may be useful in diagnosing ARN. Treatment options include IV acyclovir, IV ganciclovir or foscarnet, intravitreal ganciclovir or foscarnet, and oral valacyclovir or valganciclovir.

Toxoplasmosis: Toxoplasmosis (see also p. 1390) is the most common cause of retinitis in immunocompetent patients. Most cases are transmitted congenitally, although acquired cases occur. Symptoms of floaters and decreased vision may be due to cells in the vitreous humor or to retinal lesions or scars. Concurrent anterior segment involvement can occur and may cause ocular ache, redness, and photophobia. Laboratory testing should include serum anti-*Toxoplasma* antibody titers.

Treatment is recommended for patients with posterior lesions that threaten vital visual structures, such as the optic disk or macula, and for immunocompromised patients. Multidrug therapy is commonly prescribed; it includes pyrimethamine, sulfonamides, clindamycin, and, in select cases, systemic corticosteroids. Corticosteroids should not, however, be used without concurrent antimicrobial coverage. Long-acting periocular and intraocular corticosteroids (eg, triamcinolone acetonide) should be avoided. Patients with small peripheral lesions that do not directly threaten vital visual structures may be observed without treatment and should begin to show slow improvement in 1 to 2 mo.

Cytomegalovirus: CMV (see also p. 1416) is the most common cause of retinitis in immunocompromised patients, affecting ≤ 5% of patients with HIV/AIDS receiving highly active antiretroviral therapy (HAART). Most affected patients have a CD4+ count < 100 cells/µL. CMV retinitis may also occur in neonates and in pharmacologically immunosuppressed patients but is uncommon.

The diagnosis is largely clinical based on direct or indirect ophthalmoscopic examination; serologic tests are of limited use. Treatment in patients with HIV/AIDS is with systemic or local (implant) ganciclovir, systemic foscarnet, or valganciclovir. Therapy is typically continued indefinitely, unless immune reconstitution is achieved with combination antiretroviral therapy (typically a CD4+ count > 100 cells/µL for at least 3 mo).

Sympathetic Ophthalmia

Sympathetic ophthalmia is inflammation of the uveal tract after trauma or surgery to the other eye.

Sympathetic ophthalmia is a rare granulomatous uveitis that occurs after penetrating trauma or surgery to the other eye. Sympathetic ophthalmia has been estimated to occur in up to 0.5% of nonsurgical and in < 0.1% of surgical penetrating eye wounds. The underlying mechanism is thought to be an autoimmune reaction directed against melanin-containing cells in the uvea. Uveitis appears within 2 to 12 wk after injury in about 80% of cases. Isolated cases of sympathetic ophthalmia have occurred as early as 1 wk or as late as 30 yr after the initial injury or surgery.

Symptoms typically include floaters and decreased vision. Choroiditis, often with overlying exudative retinal detachment, is common.

Treatment typically requires oral corticosteroids plus a long-term noncorticosteroid immunosuppressive drug. Prophylactic enucleation of a severely injured eye should be considered within 2 wk of vision loss to minimize the risk of sympathetic ophthalmia developing in the other eye, but only when the injured eye has no vision potential.

Chapter 68. Retinal Disorders

Introduction

(For Retinopathy of Prematurity, see p. 2781.)

The retina is the light-sensing layer of tissue at the back of the eye; it contains the rods, cones, and nerve endings that transform light into neural impulses. Retinal disorders may be inherited or caused by vascular disease, inflammation, infection, cancer, or trauma. Visual rehabilitation is indicated for all patients who have severe vision loss.

Age-Related Macular Degeneration

(Senile Macular Degeneration)

Age-related macular degeneration (AMD) is the most common cause of irreversible central vision loss in elderly patients. Funduscopic findings are diagnostic; fluorescein angiography and optical coherence tomography assist in directing treatment. Treatment is with dietary supplements, intravitreal injection of anti-vascular endothelial growth factor, laser photocoagulation, photodynamic therapy, and low-vision devices.

AMD is a leading cause of permanent, irreversible vision loss in the elderly. It is more common among whites.

Etiology

Risk factors include the following:

• Genetic variants (eg, abnormal complement factor H)

• Smoking

• Cardiovascular disease

• Hypertension

• A diet low in ω-3 fatty acids and dark green leafy vegetables

• Age

Pathophysiology

Two different forms occur:

• Dry (atrophic), in about 90% of cases

• Wet (exudative or neovascular), in about 10% of cases

Ninety percent of the blindness caused by AMD occurs in patients who have the wet form.

Dry AMD causes retinal pigmentation changes, yellow spots (drusen—see Plate 3), and areas of chorioretinal atrophy (referred to as geographic atrophy). There is no elevated macular scar, edema, hemorrhage, or exudation.

Wet AMD begins as dry AMD. Choroidal neovascularization (abnormal new vessel formation) occurs under the retina. Localized macular edema or hemorrhage may elevate an area of the macula or cause a localized retinal pigment epithelial detachment. Eventually, neovascularization causes an elevated scar under the macula.

Symptoms and Signs

Dry AMD: The loss of central vision is slow, painless, and usually mild. Central blind spots (scotomas) usually occur late and can sometimes become severe. Symptoms are usually bilateral.

Funduscopic changes include the following:

• Pigment changes

• Drusen

• Areas of chorioretinal atrophy

Wet AMD: Rapid vision loss is more typical of wet AMD. The first symptom is usually visual distortion, such as a central blind spot (scotoma) or curving of straight lines (metamorphopsia). Peripheral vision and color vision are generally unaffected; however, the patient may become legally blind (< 20/200 vision) in the affected eye or eyes, particularly if AMD is not treated. Wet macular degeneration usually affects one eye at a time; thus, symptoms of wet AMD are often unilateral.

Funduscopic changes include the following:

• Subretinal hemorrhage in or around the macula

• Localized retinal elevation

• Retinal edema

• Gray discoloration of the subretinal space

• Exudates in or around the macula

• Detachment of retinal pigment epithelium

Diagnosis

• Funduscopic examination

• Fluorescein angiography

• Optical coherence tomography

Both forms of AMD are diagnosed by funduscopic examination. Visual changes can often be detected with an Amsler grid (see p. 539). Fluorescein angiography is done when findings suggest wet AMD. Angiography demonstrates and characterizes subretinal choroidal neovascular membranes and can delineate areas of geographic atrophy. Optical coherence tomography (OCT) aids in identifying intraretinal and subretinal fluid and can help assess response to treatment.

Treatment

• Dietary supplements for dry or unilateral wet AMD

• Intravitreal anti-vascular endothelial growth factor drugs or laser treatments for wet AMD

• Supportive measures

Dry AMD: There is no way to reverse damage caused by dry AMD, but patients with extensive drusen, pigment changes, or geographic atrophy benefit from daily supplements of the following:

• Zinc oxide 80 mg

• Copper 2 mg

• Vitamin C 500 mg

• Vitamin E 400 IU

• β-Carotene 15 mg (or vitamin A 28,000 IU)

Vitamin A is sometimes substituted for β-carotene. In smokers, β-carotene and vitamin A can increase the risk of lung cancer. For this reason, they are contraindicated in patients who have smoked in the previous 7 yr. Reducing cardiovascular risk factors, including eating foods high in ω-3 fatty acids and dark green leafy vegetables may help.

Wet AMD: Patients with wet AMD in one eye may benefit from daily supplements that are recommended for dry AMD. The choice of other treatment depends on the size, location, and type of neovascularization. Intravitreal injection of anti-vascular endothelial growth factor (VEGF) drugs (usually ranibizumab or bevacizumab or, occasionally, pegaptanib) can substantially reduce the risk of vision loss and can help restore reading vision in up to one third of patients. Thermal laser photocoagulation of neovascularization outside the fovea may prevent severe vision loss. Photodynamic therapy, a type of laser treatment, helps under specific circumstances. Corticosteroids (eg, triamcinolone) are sometimes injected intraocularly along with an anti-VEGF drug. Other treatments, including transpupillary thermotherapy, subretinal surgery, and macular translocation surgery, are seldom used.

Supportive measures: For patients who have lost central vision, low-vision devices such as magnifiers, high-power reading glasses, computer monitors, and telescopic lenses, are available. Also, certain types of software can display computer data in large print or read information aloud in a synthetic voice. Low-vision counseling is advised.

Central Retinal Artery Occlusion

(Retinal Artery Occlusion)

Central retinal artery occlusion is blockage of the central retinal artery, usually due to an embolism. Its symptom is sudden, painless, unilateral blindness. Diagnosis is by history and characteristic retinal findings on funduscopy. Decreasing intraocular pressure can be attempted within the first 24 h of occlusion. If patients present within the first few hours of occlusion, some centers catheterize the carotid artery and selectively inject thrombolytic drugs.

Etiology

Retinal artery occlusion may be due to embolism or thrombosis.

Emboli may come from any of the following:

• Atherosclerotic plaques

• Endocarditis

• Fat

• Atrial myxoma

Giant cell arteritis (see p. 319) is another important cause of arterial occlusion.

Occlusion can affect a branch of the retinal artery as well as the central retinal artery.

Neovascularization (abnormal new vessel formation) of the retina or iris (rubeosis iridis) with secondary (neovascular) glaucoma can occur weeks to months after occlusion. Vitreous hemorrhage may result from retinal neovascularization.

Symptoms and Signs

Retinal artery occlusion causes sudden, painless blindness or visual field defect, usually unilaterally.

The pupil may respond poorly to direct light but constricts briskly when the other eye is illuminated (relative afferent pupillary defect). In acute cases, funduscopy discloses a pale, opaque fundus with a red fovea (cherry-red spot—see Plate 5). Typically, the arteries are attenuated and may even appear bloodless. An embolic obstruction is sometimes visible. If a major branch is occluded rather than the entire artery, fundus abnormalities and vision loss are limited to that sector of the retina.

Patients who have giant cell arteritis often have headache, a tender and palpable temporal artery, jaw claudication, fatigue, or a combination.

Diagnosis

• Clinical evaluation

• Sometimes fluorescein angiography

The diagnosis is suspected when a patient has acute, painless vision loss. Funduscopy is usually confirmatory. Fluorescein angiography is often done and shows obstruction clearly.

Once the diagnosis is made, carotid Doppler ultrasonography and echocardiography should be done to locate any embolic source so that further embolization can be prevented.

If giant cell arteritis is suspected, ESR, C-reactive protein, and platelet count are done.

Prognosis

Patients with a branch artery occlusion often maintain good to fair vision, but vision loss is often profound with central artery occlusion, even with treatment. Once retinal infarction occurs (possibly in < 2 h, almost always by 24 h), vision loss is permanent.

Treatment

• Sometimes reduction of intraocular pressure

Immediate treatment is indicated if occlusion occurred within 24 h of presentation. Reduction of intraocular pressure by ocular hypotensive drugs (eg, topical timolol 0.5%, acetazolamide 500 mg IV or po), intermittent digital massage over the closed eyelid, or anterior chamber paracentesis may dislodge an embolus and allow it to enter a smaller branch of the artery, thus reducing the area of retinal ischemia. Some centers have tried infusing thrombolytics into the carotid artery to dissolve the obstructing clot. Nonetheless, treatments for retinal artery occlusions rarely improve visual acuity. Surgical or laser-mediated embolectomy is available but not commonly done.

Patients with occlusion secondary to temporal arteritis should receive high-dose systemic corticosteroids.

Central Retinal Vein Occlusion

(Retinal Vein Occlusion)

Central retinal vein occlusion is a blockage of the central retinal vein by a thrombus. It causes

painless vision loss, usually suddenly. Diagnosis is by funduscopy. Most treatments are ineffective.

Etiology

Major risk factors include

• Hypertension

• Age

Other risk factors include

• Glaucoma

• Diabetes

• Increased blood viscosity

Occlusion may also be idiopathic. The condition is uncommon among young people. Occlusion may affect a branch of the retinal vein or the central retinal vein.

Neovascularization of the retina or iris (rubeosis iridis) with secondary (neovascular) glaucoma can occur weeks to months after occlusion. Vitreous hemorrhage may result from retinal neovascularization.

Symptoms and Signs

Painless visual loss is usually sudden, but it can also occur gradually over a period of days to weeks. Funduscopy reveals hemorrhages throughout the retina, engorgement and tortuousness of the retinal veins, and, usually, significant retinal edema (see
Plate 6). These changes are limited to one quadrant if obstruction involves only a branch of the central retinal vein.

Diagnosis

• Funduscopy

The diagnosis is suspected in patients with painless visual loss, particularly those at risk. Funduscopy confirms the diagnosis. Patients with a central retinal vein occlusion are evaluated for hypertension and glaucoma and tested for diabetes. Young patients are tested for increased blood viscosity (with a CBC and other coagulable factors as deemed necessary).

Prognosis

Most patients have some visual deficit. In mild cases, there can be spontaneous improvement to near-normal vision over a variable period of time. Visual acuity at presentation is a good indicator of final vision. If visual acuity is at least 20/40, visual acuity will likely remain good, occasionally near normal. If visual acuity is worse than 20/200, it will remain at that level or worsen in 80% of patients.

Treatment

• Panretinal photocoagulation if neovascularization develops

There is no generally accepted medical therapy for occlusion itself. However, if neovascularization develops, panretinal photocoagulation should be initiated because it may decrease vitreous hemorrhages and prevent neovascular glaucoma.

Clinical trials are investigating intravitreal injection of corticosteroids and anti-vascular endothelial growth

factor drugs.

Diabetic Retinopathy

Diabetic retinopathy includes microaneurysms, intraretinal hemorrhage, exudates, macular edema, macular ischemia, neovascularization, vitreous hemorrhage, and traction retinal detachment. Symptoms may not develop until late in the disease. Diagnosis is by funduscopy; further details are elucidated by fluorescein angiography and optical coherence tomography. Treatment includes control of diabetes and BP and ocular laser photocoagulation, intravitreal injection of drugs, vitrectomy, or a combination.

Pathophysiology

Diabetic retinopathy is a major cause of blindness. The degree of retinopathy is highly correlated with

• Duration of diabetes

• Blood glucose levels

• BP levels

Pregnancy can impair blood glucose control and thus worsen retinopathy.

Nonproliferative retinopathy: (also called background retinopathy) develops first and causes increased capillary permeability, microaneurysms, hemorrhages, exudates, macular ischemia, and macular edema (thickening of the retina caused by fluid leakage from capillaries).

Proliferative retinopathy: develops after nonproliferative retinopathy and is more severe; it may lead to vitreous hemorrhage and traction retinal detachment. Proliferative retinopathy is characterized by abnormal new vessel formation (neovascularization), which occurs on the inner (vitreous) surface of the retina and may extend into the vitreous cavity and cause vitreous hemorrhage. The neovascularization is often accompanied by preretinal fibrous tissue, which, along with the vitreous humor, can contract, resulting in traction retinal detachment. Neovascularization may also occur in the anterior segment of the eye on the iris; neovascular membrane growth in the angle of the eye at the peripheral margin of the iris can result, leading to neovascular glaucoma. Vision loss with proliferative retinopathy may be severe.

Clinically significant macular edema can occur with nonproliferative or proliferative retinopathy and is the most common cause of vision loss due to diabetic retinopathy.

Symptoms and Signs

Nonproliferative retinopathy: Vision symptoms accompany macular edema or macular ischemia. However, patients may be unaware of vision loss. The first signs of nonproliferative retinopathy are

• Capillary microaneurysms

• Dot and blot retinal hemorrhages

• Hard exudates

• Cotton-wool spots (soft exudates)

Hard exudates are discrete, yellow, and generally deeper than retinal vessels and suggest retinal edema. Cotton-wool spots are areas of microinfarction that lead to retinal opacification; they are fuzzy-edged and white and obscure underlying vessels (see
Plate 10).

Signs in later stages are

• Macular edema (seen on slit-lamp biomicroscopy as elevation and blurring of retinal layers)

• Venous dilation and intraretinal microvascular abnormalities

Proliferative retinopathy: Symptoms may include blurred vision, black spots or flashing lights in the field of vision, and sudden, severe painless vision loss. Some of these symptoms may be caused by vitreous hemorrhage or traction retinal detachment.

Proliferative retinopathy, unlike nonproliferative retinopathy, causes fine preretinal capillaries (newly developed capillaries) to appear on the optic nerve or retinal surface (see Plates 11 and 23). Macular edema or retinal hemorrhage may be visible on funduscopy.

Diagnosis

• Funduscopy

• Fluorescein angiography

• Sometimes optical coherence tomography

Diagnosis is by funduscopy. Fluorescein angiography is used to determine the extent of damage, to develop a treatment plan, and to monitor the results of treatment. Optical coherence tomography is also useful to assess severity of macular edema and treatment response.

Screening: Because early detection is important, all patients with diabetes should have an annual dilated ophthalmologic examination. Pregnant patients with diabetes should be examined every trimester. Vision symptoms are indications for ophthalmologic referral.

Treatment

• Control of blood glucose and BP

• For macular edema, focal laser and possibly vitrectomy or intravitreal drugs

• For high-risk or complicated proliferative retinopathy, panretinal laser photocoagulation and sometimes vitrectomy

Control of blood glucose and BP are critical; intensive control of blood glucose slows progression of retinopathy. Clinically significant diabetic macular edema is treated with focal laser. Intravitreal injection of triamcinolone, as well as anti-vascular endothelial growth factor (VEGF) drugs, may help in more severe cases. Vitrectomy can help in recalcitrant diabetic macular edema. In select cases of severe nonproliferative retinopathy, panretinal laser photocoagulation may be used; however, most patients can be followed closely until proliferative retinopathy develops.

Proliferative diabetic retinopathy with high-risk characteristics of vitreous hemorrhage, extensive preretinal neovascularization, or anterior segment neovascularization/neovascular glaucoma, should be treated with panretinal laser photocoagulation. This treatment reduces the risk of severe vision loss significantly.

Vitrectomy can help preserve and often restore lost vision in patients with any of the following:

• Vitreous hemorrhage that persists for 3 mo

• Extensive preretinal membrane formation

• Traction retinal detachment

Prevention

Control of blood glucose and BP is critical; intensive control of blood glucose delays onset of retinopathy.

Hypertensive Retinopathy

Hypertensive retinopathy is retinal vascular damage caused by hypertension. Symptoms develop late. Funduscopic examination shows arteriolar constriction, arteriovenous nicking, vascular wall changes, flame-shaped hemorrhages, cotton-wool spots, yellow hard exudates, and papilledema. Treatment is directed at controlling BP and, when vision loss occurs, treating the retina.

Pathophysiology

Acute BP elevation typically causes reversible vasoconstriction in retinal blood vessels, and hypertensive crisis may cause papilledema. More prolonged or severe hypertension leads to exudative vascular changes, a consequence of endothelial damage and necrosis. Other changes (eg, arteriole wall thickening) typically require years of elevated BP to develop. Smoking compounds the adverse effects of hypertension on the retina.

Hypertension is a major risk factor for other retinal disorders (eg, retinal artery or vein occlusion, diabetic retinopathy). Also, hypertension combined with diabetes greatly increases risk of vision loss. Patients with hypertensive retinopathy are at high risk of hypertensive damage to other end organs.

Symptoms and Signs

Symptoms usually do not develop until late in the disease.

In the early stages, funduscopy identifies arteriolar constriction, with a decrease in the ratio of the width of the retinal arterioles to the retinal venules.

Chronic, poorly controlled hypertension causes the following:

• Permanent arterial narrowing

• Arteriovenous crossing abnormalities (arteriovenous nicking)

• Arteriosclerosis with moderate vascular wall changes (copper wiring) to more severe vascular wall hyperplasia and thickening (silver wiring)

Sometimes total vascular occlusion occurs. Arteriovenous nicking is a major predisposing factor to the development of a branch retinal vein occlusion.

If acute disease is severe, the following can develop:

• Superficial flame-shaped hemorrhages

• Small white superficial foci of retinal ischemia (cotton-wool spots—see Plate 18)

• Yellow hard exudates

• Optic disk edema (papilledema)

Yellow hard exudates represent intraretinal lipid deposition from leaking retinal vessels. These exudates can form a star-shaped lesion in the macula, particularly when hypertension is severe (see Plate 17). In severe hypertension, the optic disk becomes congested and edematous (papilledema

indicating hypertensive crisis).

Diagnosis

Diagnosis is by history (duration and severity of hypertension) and funduscopy.

Treatment

Hypertensive retinopathy is managed primarily by controlling hypertension. Other vision-threatening conditions should also be aggressively controlled. If vision loss occurs, treatment of the retinal edema with laser or with intravitreal injection of corticosteroids or anti-vascular endothelial growth factor (VEGF) drugs may be useful.

Retinal Detachment

Retinal detachment is separation of the neural retina from the underlying retinal pigment epithelium. The most common cause is a retinal tear. Symptoms are decreased peripheral or central vision, often described as a curtain or dark cloud coming across the field of vision. Associated symptoms can include painless vision disturbances, including flashing lights and excessive floaters. Traction and serous retinal detachments cause either central or peripheral vision loss. Diagnosis is by funduscopy; ultrasonography may help determine the presence and type of retinal detachment if it cannot be seen with funduscopy. Immediate treatment is imperative if rhegmatogenous retinal detachment is acute and threatens central vision. Treatment of rhegmatogenous detachment may include sealing retinal holes (by laser, diathermy, or cryotherapy), supporting the holes with scleral buckling, pneumatic retinopexy, and vitrectomy.

Etiology

There are 3 types of detachment: rhegmatogenous, which involves a retinal tear, and traction and serous (exudative) detachment, which do not involve a tear (nonrhegmatogenous).

Rhegmatogenous detachment is the most common. Risk factors include the following:

• Myopia

• Previous cataract surgery

• Ocular trauma

Traction retinal detachment can be caused by vitreoretinal traction due to preretinal fibrous membranes as may occur in proliferative diabetic or sickle cell retinopathy.

Serous detachment results from transudation of fluid into the subretinal space. Causes include severe uveitis, especially in Vogt-Koyanagi-Harada syndrome, choroidal hemangiomas, and primary or metastatic choroidal cancers (see p. 619).

Symptoms and Signs

Retinal detachment is painless. Early symptoms of rhegmatogenous detachment may include dark or irregular vitreous floaters (particularly in large numbers), flashes of light (photopsias), and blurred vision. As detachment progresses, the patient notices a curtain, veil, or grayness in the field of vision. If the macula is involved, central vision becomes poor. Patients may have simultaneous vitreous hemorrhage. Traction and exudative (serous) retinal detachments can cause blurriness of vision, but they may not cause any symptoms in the early stages.

Diagnosis

• Indirect funduscopy with pupillary dilation

Retinal detachment should be suspected in patients, particularly those at risk, who have any of the following:

• Sudden increase or change in floaters

• Photopsias

• Curtain or veil across the visual field

• Any sudden, unexplained loss of vision

• Vitreous hemorrhage that obscures the retina

Funduscopy shows the retinal detachment and can differentiate the subtypes of retinal detachment in nearly all cases. Direct funduscopy using a handheld ophthalmoscope can miss some retinal detachments, which may be peripheral. Peripheral fundus examination, using either indirect ophthalmoscopy with scleral depression or using a 3-mirror lens, should be done.

If vitreous hemorrhage (which may be due to a retinal tear), cataract, corneal opacification, or traumatic injury obscures the retina, retinal detachment should be suspected and B-scan ultrasonography should be done.

Treatment

• Sealing retinal holes

• Scleral buckling

• Pneumatic retinopexy

• Vitrectomy

Although often localized, retinal detachments due to retinal tears can expand to involve the entire retina if they are not treated promptly. *Any patient with a suspected or established retinal detachment should be examined urgently by an ophthalmologist*.

Rhegmatogenous detachment is treated with one or more methods, depending on the cause and location of the lesion. One method involves sealing the retinal holes by laser, diathermy, or cryotherapy. The eye may be treated by scleral buckling (which indents the sclera, pushing the retina inward and thereby relieving vitreous traction on the retina); during this procedure, fluid may be drained from the subretinal space. Pneumatic retinopexy (intravitreal injection of gas) and vitrectomy are other treatments. Retinal tears without detachment can be sealed by laser photocoagulation or transconjunctival cryopexy. Nearly all rhegmatogenous detachments can be reattached surgically.

Nonrhegmatogenous detachments due to vitreoretinal traction may be treated by surgical vitrectomy; transudative detachments due to uveitis may respond to systemic corticosteroids, systemic corticosteroid-sparing drugs (eg, methotrexate, azathioprine, anti-tumor necrosis factor drugs), or a slow-release corticosteroid implant, which is surgically implanted into the eye. Primary and metastatic choroidal cancers also require treatment. Choroidal hemangiomas may respond to localized photocoagulation.

Retinitis Pigmentosa

Retinitis pigmentosa is a slowly progressive, bilateral degeneration of the retina and retinal pigment epithelium caused by various genetic mutations. Symptoms include night blindness and loss of peripheral vision. Diagnosis is by funduscopy, which demonstrates pigmentation in a bone-spicule configuration in the equatorial retina, narrowing of the retinal arterioles, a waxy

pallor of the optic disk, posterior subcapsular cataracts, and cells in the vitreous. Electroretinography helps confirm the diagnosis.

Abnormal gene coding for retinal proteins appears to be the cause of retinitis pigmentosa; several genes have been identified. Transmission may be autosomal recessive, autosomal dominant, or, infrequently, X-linked. It may occur as part of a syndrome (eg, Bassen-Kornzweig, Laurence-Moon). Some of these syndromes include congenital hearing loss as well.

Symptoms and Signs

Retinal rods are affected, causing defective night vision that becomes symptomatic at varying ages, sometimes in early childhood. Night vision may eventually be lost. A peripheral ring scotoma (detectable by visual field testing) widens gradually, so that central vision may also be affected in advanced cases.

The most conspicuous funduscopic finding is hyperpigmentation in a bone-spicule configuration in the midperipheral retina. Other findings include the following:

• Narrowing of the retinal arterioles

• Cystoid macular edema

• Waxy yellow appearance of the disk

• Posterior subcapsular cataracts

• Cells in the vitreous (less commonly)

• Myopia

Diagnosis

• Funduscopy

• Electroretinography

The diagnosis is suspected in patients with poor night vision or a family history. Diagnosis is by funduscopy, usually supplemented with electroretinography. Other retinopathies that can simulate retinitis pigmentosa should be excluded; they include retinopathies associated with syphilis, rubella, phenothiazine or chloroquine toxicity, and nonocular cancer. Family members should be examined and tested as necessary or desired to establish the hereditary pattern. Patients with a hereditary syndrome may wish to seek genetic counseling before having children.

Treatment

• Vitamin A

There is no way to reverse damage caused by retinitis pigmentosa, but vitamin A palmitate 20,000 units po once/day may help slow disease progression in some patients. Patients taking vitamin A palmitate should have regular liver function tests. Vision decreases as the macula becomes increasingly involved and can evolve to legal blindness.

Epiretinal Membrane

(Macular Pucker; Cellophane Maculopathy; Premacular Fibrosis)

Epiretinal membrane is formation of a thin membrane over the retina, which interferes with vision.

Epiretinal membrane typically occurs after age 50 and is most common among people > 75. An epiretinal membrane is a thin fibrotic membrane that forms over the retina and contracts, wrinkling the retina underneath.

Risk factors for epiretinal membrane are the following:

• Diabetic retinopathy

• Uveitis

• Retinal detachment

• Ocular injury

Most cases are idiopathic.

Symptoms may include blurred vision or distorted vision (eg, straight lines may appear wavy). Many patients say that it seems like they are looking through plastic wrap or cellophane. Diagnosis is by funduscopy. Fluorescein angiography and optical coherence tomography may also be helpful.

Most people need no treatment. If problems with vision are significant, the membrane can be removed surgically (membrane peel).

Cancers Affecting the Retina

Cancers affecting the retina usually begin in the choroid. Because the retina depends on the choroid for its support and half of its blood supply, damage to the choroid by a cancer is likely to affect vision.

Choroidal melanoma: Choroidal melanoma originates in the choroidal melanocytes. Choroidal melanoma is the most common cancer originating in the eye, with an incidence of about 1 in 2500 whites. It is less common among darker-skinned people. It occurs most frequently at age 55 to 60. It may spread locally or metastasize and be fatal.

Symptoms tend to develop late and include loss of vision and symptoms of retinal detachment (see p. 617).

Diagnosis is by funduscopy, supplemented, when indicated, by other tests, such as ultrasonography, CT, fluorescein angiography, and serial photographs.

Small cancers are treated with laser, radiation, or radioactive implants, which may preserve vision and save the eye. Rarely, local resection is used. Large cancers require enucleation.

Choroidal metastases: Choroidal metastases are common because the choroid is highly vascular. The most common primary cancers are those of the breast in women and of the lung and prostate in men.

Symptoms tend to develop late and include loss of vision and symptoms of retinal detachment.

Diagnosis is often incidental during routine ophthalmoscopy. Ultrasonography is usually done, and the diagnosis is confirmed using fine-needle biopsy.

Treatment is usually with chemotherapy, radiation therapy, or both.

Chapter 69. Optic Nerve Disorders

Introduction

The optic pathway includes the retina, optic nerve, optic chiasm, optic radiations, and occipital cortex (see Fig. 69-1). Damage along the optic pathway causes a variety of visual field changes (see Table 60-1 on p. 540).

Hereditary Optic Neuropathies

Hereditary optic neuropathies are genetic defects that cause vision loss, occasionally with cardiac or neurologic abnormalities. There is no effective treatment.

Hereditary optic neuropathies typically manifest in childhood or adolescence with

[**Fig. 69-1.** Higher visual pathways—lesion sites and corresponding visual field defects.]

bilateral, symmetric central vision loss. Optic nerve damage is usually permanent and in some cases progressive. By the time optic atrophy is detected, substantial optic nerve injury has already occurred.

Dominant optic atrophy: This disorder is inherited in an autosomal dominant fashion. It is believed to be the most common of the hereditary optic neuropathies, with prevalence in the range of 1:10,000 to 1:50,000. It is thought to be optic abiotrophy, premature degeneration of the optic nerve leading to progressive vision loss. Onset is in the 1st decade of life.

Leber's hereditary optic neuropathy: This disorder involves a mitochondrial DNA abnormality that affects cellular respiration. Although mitochondrial DNA throughout the body is affected, vision loss is the primary manifestation. Most cases (80 to 90%) occur in males. The disease is inherited with a maternal inheritance pattern, meaning that all offspring of a woman with the abnormality inherit the abnormality, but only females can pass on the abnormality because the zygote receives mitochondria only from the mother.

Symptoms and Signs

Dominant optic atrophy: Most patients have no associated neurologic abnormalities, although nystagmus and hearing loss have been reported. The only symptom is slowly progressive bilateral vision loss, usually mild until late in life. The entire optic disk or, at times, only the temporal part is pale without visible vessels. A blue-yellow color vision deficit is characteristic.

Leber's hereditary optic neuropathy: Vision loss typically begins between 15 and 35 yr (range, 1 to 80 yr). Painless central vision loss in one eye is usually followed weeks to months later by loss in the other eye. Simultaneous vision loss has been reported. Most patients lose vision to worse than 20/200 acuity. Ophthalmoscopic examination may show telangiectatic microangiopathy, swelling of the nerve fiber layer around the optic disk, and an absence of leakage on fluorescein angiography. Eventually, optic atrophy supervenes.

Some patients with Leber's hereditary optic neuropathy have cardiac conduction defects. Other patients have minor neurologic abnormalities, such as a postural tremor, loss of ankle reflexes, dystonia, spasticity, or a multiple sclerosis-like illness.

Diagnosis

Molecular genetic testing is available to confirm the diagnosis of dominant optic atrophy.

Diagnosis of Leber's hereditary optic atrophy is mainly clinical. ECG should be done to diagnose occult cardiac conduction defects.

Treatment

• Symptomatic treatment

There is no effective treatment for the hereditary optic neuropathies. Low-vision aids (eg, magnifiers, large-print devices, talking watches) may be helpful. Genetic counseling is suggested.

Leber's hereditary optic neuropathy: Corticosteroids, vitamin supplements, and antioxidants have been tried without success. A small study found benefits from quinone analogs (ubiquinone and idebenone) during the early phase. Suggestions to avoid agents that might stress mitochondrial energy production (eg, alcohol) have no proven benefit but are theoretically reasonable. Patients should avoid tobacco products and excessive alcohol intake. Cardiac and neurologic abnormalities should be referred to a specialist.

Ischemic Optic Neuropathy

Ischemic optic neuropathy is infarction of the optic disk. The only constant symptom is painless vision loss. Diagnosis is clinical. Treatment is ineffective.

Two varieties of optic nerve infarction exist: nonarteritic and arteritic. The nonarteritic variant occurs more frequently, typically affecting people about 50 yr and older. Vision loss tends not to be as severe as in the arteritic variant, which typically affects an older group, typically about 70 yr and older.

Most ischemic optic neuropathy is unilateral. Bilateral, sequential cases occur in about 20%, but bilateral simultaneous involvement is uncommon. Atherosclerotic narrowing of the posterior ciliary arteries may predispose to nonarteritic optic nerve infarction, particularly after a hypotensive episode. Any of the inflammatory arteritides, especially giant cell arteritis (see p. 319), can precipitate the arteritic form.

Acute ischemia causes nerve edema, which further worsens ischemia. A small optic cup to optic disk ratio is a risk factor for nonarteritic ischemic optic neuropathy but not for the arteritic variety. Usually, no medical condition is apparent to cause the nonarteritic variety, although diabetes and hypertension are present in some patients and are thought to be risk factors. Vision loss on awakening leads investigators to suspect nocturnal hypotension as a potential cause of the nonarteritic variety.

Symptoms and Signs

Vision loss with both varieties is typically rapid (over minutes, hours, or days) and painless. Some patients notice the loss on awakening. Symptoms such as general malaise, muscle aches and pains, headaches over the temple, pain when combing hair, jaw claudication, and tenderness over the temporal artery may be present with temporal arteritis; however, such symptoms may not occur until after vision is lost. Visual acuity is reduced, and an afferent pupillary defect is present. The optic disk is swollen with surrounding hemorrhages. Visual field examination often shows a defect in the inferior and central visual fields.

Diagnosis

• ESR

• CT or MRI if vision loss is progressive

Diagnosis is based mainly on a clinical evaluation, but ancillary testing may be needed. Most important is to exclude the arteritic variety because the other eye is at risk if treatment is not started quickly. ESR is usually dramatically elevated in the arteritic variety and is normal in the nonarteritic variety. C-reactive protein is also a useful monitoring test. If temporal arteritis is suspected, temporal artery biopsy should be done. For isolated cases of progressive vision loss, CT or MRI should be done to rule out compressive lesions.

Prognosis

There is no effective treatment, and most lost vision is not recovered; however, in the nonarteritic variety,

up to 40% of patients spontaneously recover some useful vision.

Treatment

• Corticosteroids for the arteritic variety

The arteritic variety is treated with oral corticosteroids (prednisone 80 mg po once/day and tapered based on ESR) to protect the other eye. Treatment should not be delayed while awaiting biopsy results. Treatment of the nonarteritic variety with aspirin or corticosteroids has not been helpful. Risk factors are controlled. Low-vision aids (eg, magnifiers, large-print devices, talking watches) may be helpful in both types.

Optic Neuritis

Optic neuritis is inflammation of the optic nerve. Symptoms are usually unilateral, with eye pain and partial or complete vision loss. Diagnosis is primarily clinical. Treatment is directed at the underlying condition; most cases resolve spontaneously.

Etiology

Optic neuritis is most common among adults 20 to 40 yr. Most cases result from demyelinating disease, particularly multiple sclerosis (see p. 1779), in which case there may be recurrences. Optic neuritis is often the presenting manifestation of multiple sclerosis. Other causes include the following:

• Infectious diseases (eg, viral encephalitis [particularly in children], sinusitis, meningitis, TB, syphilis, HIV)

• Tumor metastasis to the optic nerve

• Chemicals and drugs (eg, lead, methanol, quinine, arsenic, antibiotics)

Rare causes include diabetes, pernicious anemia, Graves' disease, bee stings, and trauma. Often, the cause remains obscure despite thorough evaluation.

Symptoms and Signs

The main symptom is vision loss, frequently maximal within 1 or 2 days and varying from a small central or paracentral scotoma to complete blindness. Most patients have mild eye pain, which often feels worse with eye movement.

If the optic disk is swollen, the condition is called papillitis. Otherwise, it is called retrobulbar neuritis. The most characteristic findings include reduced visual acuity, a visual field deficit, and disturbed color vision (often out of proportion to loss of visual acuity). An afferent pupillary defect is usually detectable if the contralateral eye is unaffected or involved to a lesser degree. Testing of color vision is a useful adjunct. In about two thirds of patients, inflammation is entirely retrobulbar, causing no visible changes in the optic fundus. In the rest, disk hyperemia, edema in or around the disk, vessel engorgement, or a combination is present. A few exudates and hemorrhages may be present near or on the optic disk.

Diagnosis

• Clinical evaluation

• MRI

Optic neuritis is suspected in patients with characteristic pain and vision loss. Neuroimaging, preferably with gadolinium-enhanced MRI, is usually done and may show an enlarged, enhancing optic nerve. MRI may also help diagnose multiple sclerosis. Fluid attenuating inversion recovery (FLAIR) MRI sequences may show typical demyelinating lesions in a periventricular location if optic neuritis is related to demyelination.

Prognosis

Prognosis depends on the underlying condition. Most episodes resolve spontaneously, with return of vision in 2 to 3 mo. Most patients with a typical history of optic neuritis and no underlying systemic disease, such as a connective tissue disease, recover vision, but > 25% have a recurrence in the same eye or in the other eye. MRI is used to determine future risk of demyelinating disease.

Treatment

• Corticosteroids

Corticosteroids are an option, especially if multiple sclerosis is suspected. Treatment with methylprednisolone (500 mg to 1000 mg IV once/day) for 3 days followed by prednisone (1 mg/kg po once/day) for 11 days may speed recovery, but ultimate vision results are no different from those with observation alone. IV corticosteroids have been reported to delay onset of multiple sclerosis for at least 2 yr. Treatment with oral prednisone alone does not improve vision outcome and may increase the rate of recurrent episodes. Low-vision aids (eg, magnifiers, large-print devices, talking watches) may be helpful.

Papilledema

Papilledema is swelling of the optic disk due to increased intracranial pressure. All other causes of optic disk swelling, such as that caused by malignant hypertension or thrombosis of the central retinal vein, do not involve increased intracranial pressure and therefore are not causes of papilledema. There are no early symptoms, although vision may be disturbed for a few seconds. Papilledema requires an immediate search for the cause. Diagnosis is by ophthalmoscopy with further tests, usually brain imaging, to determine cause. Treatment is directed at the underlying condition.

Papilledema is a sign of elevated intracranial pressure and is almost always bilateral. Causes include the following:

• Brain tumor or abscess

• Cerebral trauma or hemorrhage

• Meningitis

• Arachnoidal adhesions

• Cavernous or dural sinus thrombosis

• Encephalitis

• Idiopathic intracranial hypertension (pseudotumor cerebri), a condition with elevated CSF pressure and no mass lesion

Symptoms and Signs

Vision is usually not affected initially, but seconds-long graying out of vision, flickering, or blurred or double vision may occur. Patients may have symptoms of increased intracranial pressure, such as headache or nausea and vomiting.

Ophthalmoscopic examination reveals engorged and tortuous retinal veins, a hyperemic and swollen optic disk (optic nerve head), and retinal hemorrhages around the disk but not into the retinal periphery (see Plate 19). Isolated disk edema (eg, caused by optic neuritis or ischemic optic neuropathy) without elevated CSF pressure is not considered papilledema.

In the early stages, visual acuity and pupillary response to light are usually normal and become abnormal only after the condition is well advanced. Visual field testing may detect an enlarged blind spot. Later, nerve fiber bundle defects may be apparent.

Diagnosis

• Clinical evaluation

• Immediate neuroimaging

The degree of disk swelling can be quantified by comparing the plus lens numbers needed to focus an ophthalmoscope on the most elevated portion of the disk and on the unaffected portion of the retina.

Differentiating papilledema from other causes of a swollen optic disk, such as optic neuritis, ischemic optic neuropathy, hypotony, central retinal vein occlusion, uveitis, or pseudo swollen disks (eg, optic nerve drusen), requires a thorough ophthalmologic evaluation. If papilledema is suspected clinically, MRI with gadolinium contrast or CT with contrast is done immediately to exclude causes such as an intracranial mass. Lumbar puncture and measurement of CSF pressure should be done if a mass lesion has been ruled out. Lumbar puncture in patients with intracranial mass lesions can result in brain stem herniation. B-scan ultrasonography is the best diagnostic tool for the pseudo disk edema of optic nerve drusen.

Treatment

• Treatment of underlying disorder

Urgent treatment of the underlying disorder is indicated to decrease intracranial pressure. If intracranial pressure is not reduced, secondary optic nerve atrophy and vision loss eventually occur, along with other serious neurologic sequelae.

Toxic Amblyopia

(Nutritional Amblyopia)

Toxic amblyopia is reduction in visual acuity believed to be the result of a toxic reaction in the orbital portion (papillomacular bundle) of the optic nerve. It can be caused by various toxic and nutritional factors and probably unknown factors. The main symptom is painless vision loss. Diagnosis is by history and visual field examination. Treatment is avoiding suspected toxic agents and improving nutrition.

Etiology

Toxic amblyopia is usually bilateral and symmetric. In alcoholics, undernutrition may be the cause. True tobacco-induced amblyopia is rare. Lead, methanol, chloramphenicol, digoxin, ethambutol, and many other chemicals can damage the optic nerve. Deficiencies of protein and antioxidants are likely risk factors. Toxic amblyopia may occur with other nutritional disorders, such as Strachan's syndrome (polyneuropathy and orogenital dermatitis).

Symptoms and Signs

Vision blurring and dimness typically develop over days to weeks. An initially small central or pericentral scotoma slowly enlarges, typically involving both the fixation and the blind spot (centrocecal scotoma), and progressively interferes with vision. Total blindness may occur in methanol ingestion, but other nutritional causes typically do not cause profound vision loss. Retinal abnormalities do not usually occur, but temporal disk pallor may develop late.

Diagnosis

• Mainly clinical evaluation

A history of undernutrition or toxic or chemical exposure combined with typical bilateral scotomata on visual field testing justifies treatment. Laboratory testing for lead, methanol, and other suspected toxins is done.

Prognosis

Vision may improve if the cause is treated or removed quickly. Once the optic nerve has atrophied, vision usually does not recover.

Treatment

The cause is treated. Exposure to toxic substances should stop immediately. Chelation therapy is indicated in lead poisoning. Dialysis, fomepizole, ethanol, or a combination is used for methanol poisoning. Treatment with oral or parenteral B vitamins before vision loss becomes severe may reverse the condition when undernutrition is the presumed cause.

Low-vision aids (eg, magnifiers, large-print devices, talking watches) may be helpful.

The role of antioxidants has not been fully characterized. Their use could be justified on a theoretic basis; however, there is no proof of efficacy, and the at-risk population that should receive such supplements has not been defined.

Chapter 70. Orbital Diseases

Introduction

Orbital diseases may be vascular, thyroid-related (Graves' disease), infectious, inflammatory, or neoplastic. Cavernous sinus thrombosis causes many of the same symptoms and signs as orbital diseases. Infiltrative ophthalmopathy due to Graves' disease, the most frequent cause of orbital disease, is discussed on p. 780. Orbital fractures are discussed on p. 3232. (See Fig. 60-1 on p. 537 for anatomy of the orbit.)

Cavernous Sinus Thrombosis

Cavernous sinus thrombosis (CST) is a very rare, typically septic thrombosis of the cavernous sinus, usually caused by bacterial sinusitis. Symptoms and signs include pain, proptosis, ophthalmoplegia, vision loss, papilledema, and fever. Diagnosis is confirmed by CT or MRI. Treatment is with IV antibiotics. Complications are common, and prognosis is poor.

Etiology

The cavernous sinuses are trabeculated sinuses located at the base of the skull that drain venous blood from facial veins. CST is an extremely rare complication of common facial infections, most notably nasal furuncles (50%), sphenoidal or ethmoidal sinusitis (30%), and dental infections (10%). Most common pathogens are *Staphylococcus aureus* (70%), followed by *Streptococcus* sp; anaerobes are more common when the underlying condition is dental or sinus infection.

Thrombosis of the lateral sinus (related to mastoiditis) and thrombosis of the superior sagittal sinus (related to bacterial meningitis) occur but are rarer than CST.

Pathophysiology

The 3rd, 4th, and 6th cranial nerves and the ophthalmic and maxillary branches of the 5th cranial nerve are adjacent to the cavernous sinus and are commonly affected. Complications include meningoencephalitis, brain abscess, stroke, blindness, and pituitary insufficiency.

Symptoms and Signs

Initial symptoms are progressively severe headache or facial pain, usually unilateral and localized to retro-orbital and frontal regions. High fever is common. Later, ophthalmoplegia (initially the 6th cranial nerve, lateral gaze), proptosis, and lid edema develop and often become bilateral. Facial sensation may be diminished or absent. Decreased level of consciousness, confusion, seizures, and focal neurologic deficits are signs of CNS spread. Patients may also have anisocoria or mydriasis (3rd cranial nerve dysfunction), papilledema, and vision loss.

Diagnosis

• MRI or CT

CST is often misdiagnosed because it is rare. It should be considered in patients who have signs consistent with orbital cellulitis. Features that distinguish CST from orbital cellulitis include cranial nerve dysfunction, bilateral eye involvement, and mental status changes.

Diagnosis is based on neuroimaging. MRI is the better study, but CT is also helpful. Useful adjunct testing may include blood cultures and lumbar puncture. Lumbar puncture may show inflammatory cells (PMNs, lymphocytes, monocytes); other possible abnormalities include low glucose, high protein, and positive CSF cultures. Cultures of any suspected source infections are also done.

Prognosis

Mortality is 30% in all patients and 50% in those with underlying sphenoid sinusitis. An additional 30% develop serious sequelae (eg, ophthalmoplegia, blindness, disability due to stroke, pituitary insufficiency), which may be permanent.

Treatment

• IV high-dose antibiotics

• Sometimes corticosteroids

Initial antibiotics can include nafcillin or oxacillin 1 to 2 g q 4 to 6 h combined with a 3rd-generation cephalosporin (eg, ceftriaxone 1 g q 12 h). In areas where methicillin-resistant *S. aureus* is prevalent, vancomycin 1 g IV q 12 h should be substituted for nafcillin or oxacillin. A drug for anaerobes (eg, metronidazole 500 mg q 8 h) should be added if an underlying sinusitis or dental infection is present.

In cases with underlying sphenoid sinusitis, surgical sinus drainage is indicated, especially if there is no clinical response to antibiotics within 24 h.

Secondary treatment may include corticosteroids (eg, dexamethasone 10 mg po q 6 h) for cranial nerve dysfunction; anticoagulation is controversial because most patients respond to antibiotics, and adverse effects may exceed benefits.

Inflammatory Orbital Disease

Orbital inflammation (inflammatory orbital pseudotumor) can affect any or all structures within the orbit. The inflammatory response can be nonspecific, granulomatous, or vasculitic. The inflammation can be part of an underlying medical disorder or can exist in isolation. Patients of all ages can be affected. The process can be acute or chronic and can recur.

Symptoms and Signs

Symptoms and signs typically include a sudden onset of pain along with swelling and erythema of the eyelids. Proptosis, diplopia, and vision loss are also possible.

Diagnosis

• CT or MRI

Similar findings occur with orbital infection, but there is no history of trauma or adjacent focus of infection (eg, sinusitis). Neuroimaging with CT or MRI is required. For chronic or recurrent disease, biopsy may be used to find evidence of an underlying medical condition.

Treatment

Treatment depends on the type of inflammatory response and may include oral corticosteroids, radiation therapy, and one of several immunomodulating drugs. In difficult cases, some initial success has occurred with monoclonal antibodies against tumor necrosis factor α or with another monoclonal antibody that causes lymphocyte depletion.

Preseptal and Orbital Cellulitis

Preseptal cellulitis (periorbital cellulitis) is infection of the eyelid and surrounding skin anterior to the orbital septum. Orbital cellulitis (postseptal cellulitis) is infection of the orbital tissues posterior to the orbital septum. Either can be caused by an external focus of infection (eg, a wound), infection that extends from the nasal sinuses or teeth, or metastatic spread from infection elsewhere. Symptoms include eyelid pain, discoloration, and swelling; orbital cellulitis also causes fever, malaise, proptosis, impaired ocular movement, and impaired vision. Diagnosis is based on history, examination, and CT or MRI. Treatment is with antibiotics and

sometimes surgical drainage.

Preseptal cellulitis and orbital cellulitis are 2 distinct diseases that share a few clinical symptoms and signs. Preseptal cellulitis usually begins superficial to the orbital septum. Orbital cellulitis usually begins deep to the orbital septum. Both are more common among children; preseptal cellulitis is far more common than orbital cellulitis.

Etiology

Preseptal cellulitis is caused by contiguous spread of infection from local facial or eyelid injuries, insect or animal bites, conjunctivitis, chalazion, or sinusitis.

Orbital cellulitis is most often caused by extension of infection from adjacent sinuses, especially the ethmoid sinus (75 to 90%); it is less commonly caused by direct infection accompanying local trauma (eg, insect or animal bite, penetrating eyelid injuries) or contiguous spread of infection from the face or teeth or by hematogenous spread.

Pathogens vary by etiology and patient age. *Streptococcus pneumoniae* is the most frequent pathogen associated with sinus infection, whereas *Staphylococcus aureus* and *Streptococcus pyogenes* predominate when infection arises from local trauma. *Haemophilus influenzae* type b, once a common cause, is now less common because of widespread vaccination. Fungi are uncommon pathogens, causing orbital cellulitis in diabetic or immunosuppressed patients. Infection in children < 9 yr is typically with a single aerobic organism; patients > 15 yr typically have polymicrobial mixed aerobic and anaerobic (*Bacteroides*, *Peptostreptococcus*) infections.

Pathophysiology

Because orbital cellulitis originates from large adjacent foci of fulminant infection (eg, sinusitis) separated by only a thin bone barrier, orbital infection can be extensive and severe. Subperiosteal fluid collections, some quite large, can accumulate; they are called subperiosteal abscesses, but many are sterile initially.

Complications include vision loss (3 to 11%) due to ischemic retinopathy and optic neuropathy caused by increased intraorbital pressure; restricted ocular movements (ophthalmoplegia) caused by soft-tissue inflammation; and intracranial sequelae from central spread of infection, including cavernous sinus thrombosis, meningitis, and cerebral abscess.

Symptoms and Signs

Symptoms and signs of preseptal cellulitis include tenderness, swelling, warmth, and redness or discoloration (violaceous in the case of *H. influenzae*) of the eyelid. Patients may be unable to open their eyes because of swelling, but visual acuity is not affected.

Symptoms and signs of orbital cellulitis include swelling and redness of the eyelid and surrounding soft tissues, conjunctival hyperemia and chemosis, decreased ocular motility, pain with eye movements, decreased visual acuity, and proptosis caused by orbital swelling. Signs of the primary infection are also often present (eg, nasal discharge and bleeding with sinusitis, periodontal pain and swelling with abscess). Fever, malaise, and headache should raise suspicion of associated meningitis. Some or all of these findings may be absent early in the course of the infection.

Subperiosteal abscesses, if large enough, can contribute to symptoms of orbital cellulitis such as swelling and redness of the eyelid, decreased ocular motility, proptosis, and decreased visual acuity.

Diagnosis

• Mainly clinical evaluation

• CT or MRI if orbital cellulitis is possible

Diagnosis is suspected clinically. Other disorders to consider include trauma, insect or animal bites without cellulitis, retained foreign bodies, allergic reactions, tumors, and inflammatory orbital pseudotumor.

Eyelid swelling may require the use of lid retractors for evaluation of the globe, and initial signs of complicated infection may be subtle. An ophthalmologist should be consulted when orbital cellulitis is suspected.

Preseptal cellulitis and orbital cellulitis are often distinguishable clinically. Preseptal cellulitis is likely if eye findings are normal except for eyelid swelling. The presence of a local nidus of infection on the skin makes preseptal cellulitis even more likely.

If findings are equivocal, if the examination is difficult (as in young children), or if nasal discharge is present (suggesting sinusitis), CT or MRI should be done to confirm orbital cellulitis, to exclude tumor and pseudotumor, and to diagnose sinusitis if present. MRI is better than CT if cavernous sinus thrombosis is being considered.

The direction of proptosis may be a clue to the site of infection; eg, extension from the frontal sinus pushes the globe down and out, and extension from the ethmoid sinus pushes the globe laterally and out.

Blood cultures are often done (ideally before beginning antibiotics) in patients with orbital cellulitis but are positive in less than one third. Lumbar puncture is done if meningitis is suspected. Cultures of the paranasal sinus fluid are done if sinusitis is the suspected source. Other laboratory tests are not particularly helpful.

Treatment

• Antibiotics

Preseptal cellulitis: Initial therapy should be directed against sinusitis pathogens (*S. pneumoniae*, nontypable *H. influenzae*, *S. aureus*, *Moraxella catarrhalis*); however, in areas where methicillin-resistant *S. aureus* is prevalent, clinicians should add appropriate antibiotics (eg, clindamycin, trimethoprim/sulfamethoxazole, or doxycycline for oral treatment and vancomycin for inpatient treatment). In patients with dirty wounds, gram-negative infection must be considered.

Outpatient treatment is an option if orbital cellulitis has been definitively excluded; children should have no signs of systemic infection and should be in the care of responsible parents or guardians. Patients should be closely followed by an ophthalmologist. Outpatient treatment options include amoxicillin/clavulanate 30 mg/kg po q 8 h (for children < 12 yr) or 500 mg po tid or 875 mg po bid (for adults) for 10 days.

For inpatients, ampicillin/sulbactam 50 mg/kg IV q 6 h (for children) or 1.5 to 3 g (for adults) IV q 6 h (maximum 8 g ampicillin/day) for 7 days is an option.

Orbital cellulitis: Patients with orbital cellulitis should be hospitalized and treated with meningitis-dose antibiotics. A 2nd- or 3rd-generation cephalosporin, such as cefotaxime 50 mg/kg IV q 6 h (for children < 12 yr) or 1 to 2 g IV q 6 h (for adults) for 14 days, is an option when sinusitis is present; imipenem, ceftriaxone, and piperacillin/tazobactam are other options. If cellulitis is related to trauma or foreign body, treatment should cover gram-positive (vancomycin 1 g IV q 12 h) and gram-negative (eg, ertapenem 100 mg IV once/day) pathogens and be taken for 7 to 10 days or until clinical improvement.

Surgery to decompress the orbit, drain an abscess, open infected sinuses, or a combination is indicated in any of the following circumstances:

• Vision is compromised.

• Suppuration or foreign body is suspected.

• Imaging shows orbital or large subperiosteal abscess.

• The infection does not resolve with antibiotics.

Tumors of the Orbit

Orbital tumors can be benign or malignant and arise primarily within the orbit or secondarily from an adjacent source, such as the eyelid, paranasal sinus, or intracranial compartment.

Causes differ by age group. The more common benign pediatric tumors include dermoid tumors and vascular lesions such as capillary hemangioma and lymphangioma. In adults, cavernous hemangiomas predominate.

Some orbital tumors usually cause proptosis and displacement of the globe in a direction opposite the tumor. Pain, diplopia, and vision loss may also be present. Diagnosis, in most cases, is based on the history, examination, and neuroimaging (CT, MRI, or both).

Treatment

Treatment varies by tumor type. Treatment of dermoid tumors is excision. Capillary hemangiomas tend to spontaneously involute and therefore do not need any treatment; however, especially when located on the upper eyelid, they may affect vision and require treatment with interlesional injection of corticosteroids or surgical debulking.

Children: The common pediatric malignant tumors include rhabdomyosarcoma and metastatic lesions related to leukemia or neuroblastoma. If rhabdomyosarcoma is resectable, surgery is done, followed by chemotherapy and orbital radiation therapy. Leukemic disease is usually managed by orbital radiation therapy, chemotherapy, or both.

Adults: The most common benign tumors are meningiomas, mucoceles, and cavernous hemangiomas. When symptomatic, sphenoid wing meningiomas are treated with debulking via craniotomy, sometimes followed by a course of radiation therapy. Because meningioma cells infiltrate bone of the skull base, complete resection usually is not possible. Mucoceles are treated by draining them into the nose because they most commonly arise from the ethmoid or frontal sinus. Cavernous hemangiomas are excised.

Common malignant tumors include lymphoma, squamous cell carcinoma, and metastatic disease. Lymphomas involving the orbit are typically B-cell and characteristically low grade. Lymphomas can be bilateral and simultaneous and can be part of a systemic process or exist in the orbit in isolation. Radiation therapy effectively treats orbital lymphomas with few adverse effects, although the addition of monoclonal antibodies against a surface receptor (CD20) on the lymphocyte is also effective. Most squamous cell carcinomas arise from the adjacent paranasal sinuses. Surgery, radiation therapy, or both form the backbone of therapy. Metastatic disease is usually treated with radiation therapy. Metastatic disease involving the orbit is usually an unfavorable prognostic sign; carcinoid tumors are a notable exception.