بهترین نرم افزار مطب

دسترسی سریع به پرونده بیماران/ دارای سامانه پیگیری بیماران

سازمان تامین اجتماعی

سازمان نظام پزشکی ایران

اکسیر

Disorders of the Eye

PART XXVII

Chapter 658
Growth and Development of the Eye

Scott E. Olitsky and Justin D. Marsh

The eye of a normal full-term infant at birth is approximately 65% of adult size. Postnatal growth is maximal during the first year, proceeds at a rapid but decelerating rate until the third year, and continues at a slower rate thereafter until puberty, after which little change occurs. The anterior structures of the eye are relatively large at birth but thereafter grow proportionately less than the posterior structures. This results in a progressive change in the shape of the globe such that it becomes more spherical.

In an infant, the sclera is thin and translucent, with a bluish tinge. The cornea is relatively large in newborns (averaging 10 mm) and attains adult size (nearly 12 mm) by the age of 2 years or earlier. Its curvature tends to flatten with age, resulting in a progressive change in the refractive properties of the eye. A normal cornea is perfectly clear. In infants born prematurely, however, the cornea may have a transient opalescent haze. The anterior chamber in a newborn appears shallow, and the angle structures, important in the maintenance of normal intraocular pressure, must undergo further differentiation after birth. The iris, typically light blue or gray at birth in White individuals, undergoes progressive change of color as the pigmentation of the stroma increases in the first 6 months of life. The pupils of a newborn infant tend to be small and are often difficult to dilate. This is the result of an immature iris dilator muscle. Remnants of the **pupillary membrane** (anterior vascular capsule) are often evident on ophthalmoscopic examination, appearing as cobweb-like lines crossing the pupillary aperture, especially in preterm infants.

The lens of a newborn infant is more spherical than that of an adult; its greater refractive power helps to compensate for the relative shortness of the young eye. The lens continues to grow throughout life, as new peripheral fibers continually push older fibers toward the center of the lens. With age, the lens becomes progressively denser and more resistant to the change of shape that occurs during accommodation (focusing of the lens).

The fundus of a newborn's eye is less pigmented than that of an adult; the choroidal vascular pattern is highly visible, and the retinal pigment pattern often has a fine peppery or mottled appearance. In some darkly pigmented infants, the fundus has a gray or opalescent sheen. In a newborn, the macular landmarks, particularly the foveal light reflex, are less well defined due to incomplete maturation of the retinal layers. The peripheral retina appears pale or grayish, and the peripheral retinal vasculature is immature, especially in premature infants. The optic nerve head color varies from pink to slightly pale, sometimes grayish. Within 4-6 months, the appearance of the fundus approximates that of the mature eye.

Superficial retinal hemorrhages may be observed in many newborn infants. These are usually absorbed promptly and rarely leave any permanent effect. The majority of birth-related retinal hemorrhages resolve within 2 weeks, with complete resolution of all such hemorrhages within 4-6 weeks of birth. Conjunctival hemorrhages also may occur at birth and are resorbed spontaneously without consequence.

Remnants of the primitive **hyaloid vascular system** may appear as small tufts or wormlike structures projecting from the disc (Bergmeister papilla) or as a fine strand traversing the vitreous; in some cases, only a small dot (Mittendorf dot) remains on the posterior aspect of the lens capsule.

An infant's eye is somewhat **hyperopic** (farsighted). The general trend is for hyperopia to increase from birth until age 7 years. Thereafter, the level of hyperopia tends to decrease rapidly until age 14 years. Elimination of the hyperopic state may occur during this time. If the process continues, a child may become **myopic** (nearsighted). A slower continuation of the decrease in hyperopia, or increase in myopia, continues into the third decade of life. The refractive state at any time in life depends on the net effect of many factors: the size of the eye, the state of the lens, and the curvature of the cornea.

Newborn infants tend to keep their eyes closed much of the time, but normal newborns can see, respond to changes in illumination, and fixate points of contrast. The visual acuity in newborns is estimated to be approximately 20/400. This poor vision is a result of the immature, multilayered foveal anatomy. Retinal development continues postnatally, maturing completely during the first few years of life. One of the earliest responses to a formed visual stimulus is an infant's regard for the mother's face, evident especially during feeding. By 2 weeks of age, an infant shows more sustained interest in large objects, and by 8-10 weeks of age, a normal infant can follow an object through an arc of 180 degrees. The acuity improves rapidly and may reach 20/30-20/20 by the age of 2-3 years.

Many normal infants may have imperfect coordination of the eye movements and alignment during the early days and weeks, but proper coordination should be achieved by 3-6 months, usually sooner. Persistent deviation of an eye in an infant at 6 months of age requires evaluation.

Tears often are not present with crying until after 1-3 months. Preterm infants have reduced reflex and basal tear secretion, which may allow topically applied medications to become concentrated and lead to rapid drying of their corneas.

Visit Elsevier eBooks+ at eBooks.Health.Elsevier.com for Bibliography.

Chapter 659
Examination of the Eye

Scott E. Olitsky and Justin D. Marsh

The eye exam is a routine part of pediatric well childcare, which begins in the newborn period. The primary care physician plays a critical role in the detection of both obvious and insidious asymptomatic eye diseases. School and community screening programs can also be effective in identifying problems at an early age. The American Academy of Ophthalmology recommends preschool vision screening during well child visits as a means of reducing preventable visual loss (Table 659.1). Referrals to an ophthalmologist should be

made when a significant ocular abnormality or visual acuity deficit is suspected. An ophthalmologist should also examine high-risk children, such as those with a family history of eye disease, or various systemic or genetic disorders, such as Down syndrome or juvenile idiopathic arthritis.

The basic eye exam, whether performed by a pediatrician or an ophthalmologist, must include visual acuity and visual field testing, assessment of pupils, ocular motility and alignment, a general external/facial examination, and finally, examination of the media and fundus via ophthalmoscopy.

The periodicity for visual assessment should occur beginning in the newborn to 6 month age group and continue at ages 6-12 months, 1-3 years, 4-5 years, and 6 years and older. The assessments include an ocular history, inspection of the lids and eyes, red reflex testing, pupil examination, ocular motility testing, and assessment of visual acuity.

When indicated, biomicroscopy (slit-lamp examination), cycloplegic refraction, and tonometry are performed by an ophthalmologist. Special diagnostic procedures, such as ultrasound, fluorescein angiography, electroretinography, or visual evoked response testing, are also indicated for specific conditions.

VISUAL ACUITY

There are various means of assessing visual acuity in the pediatric population. A child's age and ability to cooperate, as well as clinician preference, all factor into deciding which test to use. The most common visual acuity test in infants is an assessment of their ability to fixate and follow a target. If appropriate targets are used, this response can be demonstrated by approximately 6 weeks of age.

The test begins by seating the child comfortably in the caretaker's lap. The object of visual interest, usually a bright-colored toy or target with lights, is slowly moved to the right and to the left. The examiner observes whether the infant's eyes turn toward the object and follow its movements. The examiner can use a thumb or palm of the hand to occlude one of the infant's eyes to test each eye separately. Although a sound-producing object might compromise the purity of the visual stimulus, in practice, toys that squeak or rattle heighten an infant's awareness and interest in the test.

The human face is a better target than test objects. The examiner can exploit this by moving his or her face slowly in front of the infant's face. If the appropriate following movements are not elicited, the test should be repeated with the caretaker's face as the test stimulus. It should be remembered that even children with poor vision can follow a large object without apparent difficulty, especially if only one eye is affected.

An objective measurement of visual acuity is usually possible when children reach the age of 2.5-3 years. Children this age are tested using a schematic picture or other illiterate eye chart. Examples include Allen or Lea symbols and tumbling E. Each eye should be tested separately. It is essential to prevent peeking. The examiner should hold the occluder in place and observe the child throughout the test. The child should be reassured and encouraged throughout the test because many children are intimidated by the process and fear a "bad grade" or punishment for errors. In addition, many children may be too timid to verbally identify figures being tested and may be more willing to participate if given the opportunity to match the presented symbols to identical symbols provided on a handout during the exam. Matching is often preferred at this age, particularly in randomized control trials, because it also allows the clinician to test visual acuity using letters instead of figures, even if a child has not yet learned the alphabet.

An adult-type **Snellen acuity chart** can be used at 5-6 years of age if the child knows letters. A visual acuity of 20/40 is generally accepted as normal for 3-year-old children. At 4 years of age, 20/30 is acceptable. By 5 or 6 years of age, most children attain 20/20 vision.

Optokinetic nystagmus (the response to a sequence of moving targets; "railroad" nystagmus) can also be used to assess vision; this can be calibrated by targets of various sizes (stripes or dots) or by a rotating drum (known as an OKN drum) at specified distances.

The visual evoked response, an electrophysiologic method of evaluating the response to light and special visual stimuli, such as calibrated stripes or a checkerboard pattern, can also be used to study visual function in selected cases.

Preferential looking tests are used for evaluating vision in infants and children who cannot respond verbally to standard acuity tests. This is a behavioral technique based on the observation that, given a choice, an infant prefers to look at patterned rather than unpatterned stimuli. Because these tests require the presence of a skilled examiner, their use is often limited to research protocols involving preverbal children.

VISUAL FIELD ASSESSMENT

Visual field assessment must be geared to a child's age and abilities. Formal visual field examination (perimetry and scotometry) can often be accomplished in school-age children. In younger children and in the pediatrician's office, the examiner must often rely on confrontation techniques and finger counting in quadrants of the visual field. In many such children, only testing by attraction can be accomplished; the examiner observes a child's response to familiar objects brought into each of the four quadrants of the visual field of each eye in turn. The child's bottle, a favorite toy, and lollipops are particularly effective attention-getting items. These gross methods can often detect diagnostically significant field changes such as the bitemporal hemianopia of a chiasmal lesion or the homonymous hemianopia of a cerebral lesion.

COLOR VISION TESTING

Color vision testing can be accomplished when a child is able to name or trace the test figures, which include numbers, shapes, or other symbols. The common color vision testing tools include Ishihara color plates or Hardy Rand Littler. Color vision testing is not frequently necessary in young children; however, parents may request testing, particularly if their child seems to be slow in learning colors or if there is a family history of color vision deficiency. It is important to keep in mind and reassure parents that "color-deficient" children do not misname colors, and that true "color blindness" is very rare and not compatible with normal vision. **Color deficiency** is common in male patients but rare in females because the gene is transmitted in an X-linked manner. **Achromatopsia**, which may be encountered occasionally, is a condition of complete color blindness associated with subnormal visual acuity, nystagmus, and photophobia.

Color discrimination is a means of assessing the intensity of a hue, typically red. Patients describe the intensity of red depicted from the test object. A change in color discrimination (often referred to as color "desaturation") can be a sign of optic nerve or retinal disease.

PUPILLARY EXAMINATION

The pupil exam includes evaluations of both the direct and consensual responses to light, accommodation (a near target), and reduced illumination, noting the size and symmetry of the pupils under each testing condition. Special care must be taken to differentiate the reaction to light from the reaction to near gaze. A child's natural tendency is to look directly at the approaching light, inducing the near gaze reflex when one is attempting to test only the reaction to light; accordingly, every effort must be made to control fixation on a distance target. The swinging flashlight test is especially useful for detecting unilateral or asymmetric prechiasmatic afferent defects in children (see "Marcus Gunn Pupil" in Chapter 662).

OCULAR MOTILITY

Ocular motility testing assesses alignment and extraocular muscle function. This is tested by having a child follow an object in various positions of gaze, known as the *cardinal positions*. The cardinal positions are those in which one extraocular muscle predominantly functions and a deficit can be identified if present. Movements of each eye individually **(ductions)** and of the two eyes together (**versions**, conjugate movements, and convergence) are assessed.

Alignment can be assessed in two ways. The first is symmetry of the corneal light reflexes. The second method is to occlude each eye in an

Table 659.1 Vision Screening Guidelines

FUNCTION	RECOMMENDED TESTS	REFERRAL CRITERIA	COMMENTS
AGES 3-5 YEARS			
Distance visual acuity	Snellen letters Snellen numbers Tumbling E test HOTV test (contains only these 4 letters)	<4 of 6 correct on 20-ft line with either eye tested at 10 ft monocularly (i.e., <10/20 or 20/40), or Two-line difference between eyes, even within the passing range (i.e., 10/12.5 and 10/20 or 20/25 and 20/40)	Tests are listed in decreasing order of cognitive difficulty; the highest test that the child is capable of performing should be used; in general, Lea symbols or the HOTV test should be used for ages 3-5 years and Snellen letters or numbers for ages 6 years and older
	Picture tests		Testing distance of 3 m (10 ft) is recommended for all visual acuity tests
	Allen figures		A line of figures is preferred over a single figure
	Lea symbols		The nontested eye should be covered by an occluder held by the examiner or by an adhesive occluder patch applied to eye; the examiner must ensure that it is not possible to peek with the nontested eye
Ocular alignment	Cross cover test at 3 m (10 ft) or Random dot E stereo test at 40 cm (630 sec of arc)	Any eye movement <4 of 6 correct	
	Simultaneous red reflex test (Bruckner test)	Any asymmetry of pupil color, size, brightness	Direct ophthalmoscope used to view both red reflexes simultaneously in a darkened room from 2-3 ft away; detects asymmetric refractive errors as well
Ocular media clarity (cataracts, tumors, etc.)	Red reflex	White pupil, dark spots, absent reflex	Direct ophthalmoscope, darkened room. View eyes separately at 12-18 inches; white reflex indicates possible retinoblastoma
AGES 6 YEARS AND OLDER			
Distance visual acuity	Snellen letters Snellen numbers Tumbling E test HOTV test	<4 of 6 correct on 4.5 m (15 ft) line with either eye tested at 3 m (10 ft) monocularly (i.e., <10/15 or 20/30)	Tests are listed in decreasing order of cognitive difficulty; the highest test that the child is capable of performing should be used; in general, Lea symbols or the HOTV test should be used for ages 3-5 years and Snellen letters or numbers for ages 6 years and older
	Picture tests	Two-line difference between eyes, even within the passing range (i.e., 10/10 and 10/15 or 20/20 and 20/30)	Testing distance of 3 m (10 ft) is recommended for all visual acuity tests
	Allen figures		A line of figures is preferred over a single figure
	Lea symbols		The nontested eye should be covered by an occluder held by the examiner or by an adhesive occluder patch applied to the eye; the examiner must ensure that it is not possible to peek with the nontested eye
Ocular alignment	Cross cover test at 3 m (10 ft) or Random dot E stereo test at 40 cm (630 sec of arc)	Any eye movement <4 of 6 correct	

alternating fashion and observe for a change in fixation of the viewing eye (see discussion on cover testing for strabismus in Chapter 663).

BINOCULAR VISION

Attaining binocular visual function is one of the primary goals of amblyopia therapy and ocular realignment surgery. Just as there are multiple methods for assessing visual acuity, there are various means of testing the level of binocular vision. The Titmus test is probably the most frequently used test; a series of three-dimensional images are shown to the child while he or she wears a set of polarized glasses. The level of difficulty with which these images can be detected correlates with the degree of binocular vision present.

EXTERNAL EXAMINATION

The external examination begins with general inspection, paying close attention to size, shape, and symmetry of the orbits, in addition to the position and movement of the lids and position and symmetry of the globes. Viewing the eyes and lids in such a manner aids in detecting orbital asymmetry, lid masses, proptosis (exophthalmos), and abnormal pulsations. Palpation is also important in detecting orbital and lid masses. Orbital dermoids and capillary hemangiomas are frequently evaluated during the external examination.

The lacrimal system is assessed by looking for evidence of tear deficiency, overflow of tears (epiphora), erythema, and swelling in the region of the tear sac or gland. The lacrimal gland is located in the superotemporal orbit, beneath the eyebrow. The tear drainage system, which includes the lacrimal sac, is located within the medial wall of the orbit, where the eyelids meet the bridge of the nose. The sac is massaged to check for reflux when obstruction is suspected. The presence and position of the puncta are also checked.

The lids and conjunctivae are specifically examined for focal lesions, foreign bodies, and inflammatory signs; loss and misdirection of lashes should also be noted. When necessary, the lids can be everted in the following manner: (1) instruct the patient to look down; (2) grasp the lashes of the patient's upper lid between the thumb and index finger of one hand; (3) place a probe, a cotton-tipped applicator, or the thumb of the other hand at the upper margin of the tarsal plate; and (4) pull the lid down and outward and evert it over the probe, using the instrument as a fulcrum. Foreign bodies commonly lodge in the concavity just above the lid margin and are exposed only by fully everting the lid.

The anterior segment of the eye is then evaluated with oblique focal illumination, noting the luster and clarity of the cornea, the depth and clarity of the anterior chamber, and the features of the iris. Transillumination of the anterior segment aids in detecting opacities and in demonstrating atrophy or hypopigmentation of the iris; these latter signs are important when ocular albinism is suspected. When necessary, fluorescein dye can be used to aid in diagnosing abrasions, ulcerations, and foreign bodies.

BIOMICROSCOPY (SLIT-LAMP EXAMINATION)

The slit-lamp exam provides a highly magnified view of the various structures of the eye and an optical section through the media of the eye—the cornea, aqueous humor, lens, and vitreous. Lesions can be identified and localized according to their depth within the eye; the resolution is sufficient to detect individual inflammatory cells in the aqueous and anterior vitreous. With the addition of special lenses and prisms, the angle of the anterior chamber and components of the fundus also can be examined with a slit lamp. Biomicroscopy is often crucial in trauma and in examining for iritis. It is also helpful in diagnosing many metabolic and genetic diseases of childhood.

FUNDUS EXAMINATION (OPHTHALMOSCOPY)

The ideal setting for ophthalmoscopy is with a well-dilated pupil unless there are neurologic or other contraindications. Tropicamide (Mydriacyl) 0.5–1% and phenylephrine (Neo-Synephrine) 2.5% are recommended as mydriatics of short duration. These are safe for most children, but the possibility of adverse systemic effects must be recognized. For very small infants, especially 6 months or younger, more dilute preparations may be advisable. Beginning with posterior landmarks, the disc, the macula, and the four quadrants are systematically examined by following each of the major vessel groups to the periphery. Retinal hemorrhages, vascular anomalies, and posterior uveitis are often appreciated during this segment of the examination. Color, cup, and contour of the optic nerve should be noted as well. Abnormalities are frequently followed with further imaging studies such as a CT or MRI or diagnostic testing such as automated perimetry (see "Visual Field Assessment" earlier). The midperipheral retina can be seen if a child is directed to look up and down and to the right and left. Even with care, only a limited fraction of the fundus can be seen with a direct or handheld ophthalmoscope. For examination of the far periphery, an indirect ophthalmoscope is used, and full dilation of the pupil is essential.

REFRACTION

Refraction determines the focusing power of the eye: the degree of nearsightedness (myopia), farsightedness (hypermetropia), or astigmatism. Retinoscopy provides an objective determination of the amount of correction needed and can be performed at any age, including the newborn period. In young children, it is best done with cycloplegia using cyclopentolate 1% eye drops in an ophthalmologist's office. Subjective refinement of refraction involves asking patients for preferences in the strength and axis of corrective lenses; it can be accomplished in many school-age children. Refraction and determination of visual acuity with appropriate corrective lenses in place are essential steps in deciding whether a patient has a visual defect or amblyopia. Photoscreening cameras aid ancillary medical personnel in screening for refractive errors in preverbal children. The accuracy and practical usefulness of these devices are still being investigated.

TONOMETRY

Tonometry is the method of assessing intraocular pressure. It may be performed with a portable, stand-alone instrument or by the applanation method during slit-lamp examination. Alternative methods are pneumatic, electronic, or rebound tonometry. When accurate measurement of the pressure is necessary in a child who cannot cooperate, it may be performed with sedation or general anesthesia. A gross estimate of pressure can be made by palpating the globe with the index fingers placed side by side on the upper lid above the tarsal plate.

Visit Elsevier eBooks+ at eBooks.Health.Elsevier.com for Bibliography.

Chapter 660

Abnormalities of Refraction and Accommodation

Scott E. Olitsky and Justin D. Marsh

Emmetropia is the normal state in which parallel rays of light come to focus on the retina with the eye at rest (nonaccommodating). Even though such an ideal optical state is common, the opposite condition, ametropia, often occurs. Three principal types of **ametropia** exist: **hyperopia** (farsightedness), **myopia** (nearsightedness), and **astigmatism** (Fig. 660.1). Most children are physiologically hyperopic at birth. Nevertheless, myopia and astigmatism may develop early in childhood, particularly when associated with previous prematurity or numerous medical diagnoses. With growth, the refractive state tends to change and should be evaluated periodically.

Measurement of the refractive state of the eye (refraction) can be accomplished both objectively and subjectively. The objective method involves directing a beam of light from a retinoscope onto a patient's retina. Using loose lenses of various strengths held in front of the eye, the retinal light reflex (viewed through the pupil) can be neutralized, yielding a precise refraction. An objective refraction is obtainable at any age because it requires no response from the patient. In infants and children, it is generally more accurate to perform a refraction after instillation of eye drops that produce **mydriasis** (dilation of the pupil) and **cycloplegia** (paralysis of accommodation); those used most commonly are tropicamide (Mydriacyl), cyclopentolate (Cyclogyl), and atropine sulfate. A subjective refraction involves placing lenses in front of the eye and having the patient report which lenses provide the clearest image of the letters on a chart. This method is dependent on a patient's ability to discriminate and communicate, but it can be used for some children and may be helpful in determining the best refractive correction for children who are developmentally capable.

HYPEROPIA

If parallel rays of light come to focus posterior to the retina with the eye in a neutral state, hyperopia or farsightedness exists. This may result from a shorter anteroposterior diameter of the eye or a lower refractive power of the cornea or lens.

In hyperopia, the additional refracting power needed to bring objects into focus at distance and near is generated through the accommodative mechanism. If the accommodative effort required for focus is within that child's accommodative amplitude, the vision is clear. In

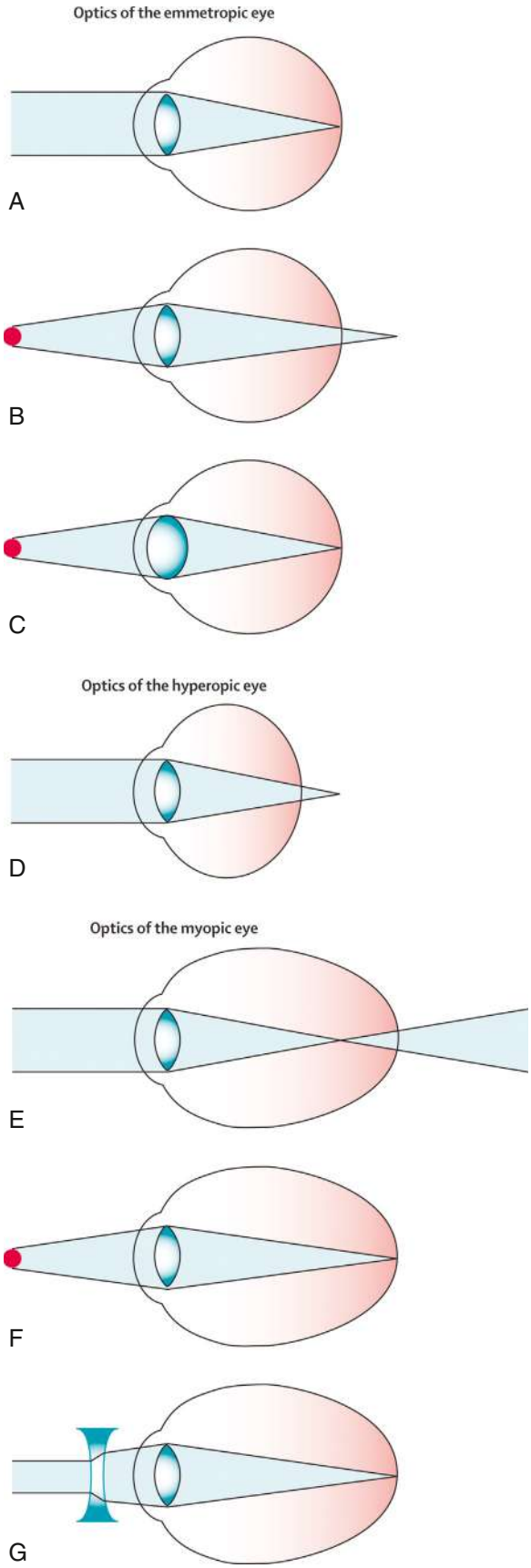

Fig. 660.1 Schematic optics of the eye. **A-C,** Emmetropic eyes. **D,** Hyperopic eyes. **E-G,** Myopic eyes. **A,** In emmetropic eyes, the parallel rays of a distant object are focused on the photoreceptors. **B,** When a closer object is viewed, the image is in focus behind the photoreceptors. The image can be brought forward into focus on the photoreceptors by the process of accommodation—increasing the optical power of the lens **(C).** In hyperopic eyes **(D),** the eye is too short, and the image of a distant object is focused behind the photoreceptors and can be brought into focus by accommodation. Myopic eyes are eyes that have grown too long **(E),** and the image of a distant object falls in front of the photoreceptors and cannot be brought into focus by accommodation. When closer objects are viewed, the image moves back toward the photoreceptors, and at a certain distance (the far point), which is related inverse to the severity of the myopia, it comes into focus **(F).** Closer objects can then be brought into focus using accommodation. Optical correction for myopia is achieved with concave (diverging) lenses, which move the image into focus on the photoreceptors (G). Contact lenses work in a similar way, whereas refractive surgery reduces the power of the cornea to bring the image of distant objects into focus. For equal corneal power, myopic eyes have longer axial lengths than emmetropic eyes, with deeper anterior and vitreal chambers. Their lenses tend to be thinner and of lower power than those of emmetropic eyes. *(From Morgan IG, Ohno-Matusi K, Saw SM. Myopia. Lancet. 2012;379:1739-1746, Fig. 1, p. 1740.)*

high degrees of hyperopia requiring greater accommodative effort, vision may be blurred, and the child may complain of eyestrain, headaches, or fatigue. Squinting, eye rubbing, and lack of interest in reading are frequent manifestations. If the induced discomfort is great enough, a child may not make the effort to focus and may develop bilateral amblyopia (ametropic amblyopia). Esotropia may also be associated (see discussion on convergent strabismus, accommodative esotropia in Chapter 663). Convex lenses (spectacles or contact lenses) of sufficient strength to provide clear vision and comfort are prescribed when indicated. Even children who have high degrees of hyperopia but who have good vision will happily wear glasses because they provide comfort by eliminating the excessive accommodation required to see well. Preverbal children should also be given glasses for high levels of hyperopia to prevent the development of esotropia or amblyopia. Children with normal levels of hyperopia do not require correction in the majority of cases.

MYOPIA

In myopia, parallel rays of light come to focus anterior to the retina. This is a result of either a long anteroposterior diameter of the eye or a higher refractive power of the cornea or lens. The principal symptom is blurred vision for distant objects. The far point of clear vision varies inversely with the degree of myopia; as the myopia increases, the far point of clear vision moves closer to the eye. For example, an individual with one diopter of myopia has a far point of clear focus that is 1 m from the eye. Any object located farther than 1 m from the eye will begin to appear blurry. Similarly, for an individual with 3 diopters of myopia, the far point of clear vision is now ⅓ m from the eye, as the far point is the inverse of the power of myopia, as measured in meters. Thus myopic children tend to hold objects and reading material closer, prefer to be close to the blackboard, and may be uninterested in distant activities. Squinting is common because the visual acuity is improved when the lid aperture is reduced, also known as the *pinhole effect*.

Myopia is infrequent in infants and preschool-age children. It is more common in infants with a history of **retinopathy of prematurity.** A hereditary tendency to myopia is also observed, and children of myopic parents should be examined at an early age. Nonsyndromic myopia is associated in some families with variants in the high-grade myopia-1 locus *(MYP1)* as well as in *SLITRK6* and *RASGRF1* genes. The incidence of myopia increases during the school years, especially during the preteen and teen years. The degree of myopia also increases with age during periods of rapid growth.

Concave lenses (spectacles or contact lenses) of appropriate strength are provided to allow for clear vision. Changes are usually needed periodically, from every few months to every 1-2 years. Globally the prevalence of myopia appears to be increasing, leading to heightened interest in myopia prevention treatment. Numerous therapies, including cycloplegic agents (topical atropine sulfate), peripheral defocus contact lenses, and reading addition spectacle lenses (bifocal lenses) are under investigation in an attempt to prevent or slow the progression of myopia.

Excimer laser correction for myopia has been approved for adults since 1995. The laser is applied to the corneal stroma to reshape the cornea, changing its refractive power (Fig. 660.2). Laser-assisted in situ keratomileusis (LASIK) uses either a microkeratome or a femtosecond laser to produce an epithelial-stromal flap, permitting the underlying corneal tissue to be ablated. The flap is then reseated and assumes the altered corneal shape. Photorefractive keratectomy (PRK) requires manual removal of the epithelium after treatment with alcohol to expose the Bowman layer and stroma, allowing the corneal surface to then be treated by the excimer laser. The epithelium regenerates to cover the defect over a period of 4-10 days. Reduction or elimination of refractive error is usually significant and remains stable over time. Risks are greatest with high degrees of myopia (>10 diopters) and include starbursts, halos, and distorted images or multiple images (usually at night). Refractive surgery is not approved for pediatric patients but is occasionally used off-label to treat certain forms of amblyopia or other high refractive error states in children who are unable to wear proper refractive correction.

In most cases, myopia is not a result of pathologic alteration of the eye and is referred to as simple or physiologic myopia. Some children may have **pathologic myopia**, a rare condition caused by a pathologically abnormal axial length of the eye; this is usually associated with thinning of the sclera, choroid, and retina and often with some degree of uncorrectable visual impairment. Tears or breaks in the retina may occur as it becomes increasingly thin, leading to the development of retinal detachments. Myopia may also occur as a result of other ocular abnormalities, such as keratoconus, ectopia lentis, congenital stationary night blindness, and glaucoma. Myopia is also a major feature of Stickler syndrome, a genetic disorder of connective tissue involving problems with vision, hearing, and facial and skeletal development; it is also common in Marfan syndrome, homocystinuria, and Weill-Marchesani syndrome.

ASTIGMATISM

In astigmatism, the refractive powers of the various meridians of the eye differ. Most cases are caused by irregularity in the curvature of the cornea, although some astigmatism results from changes in the lens. Mild degrees of astigmatism are common and may produce no symptoms. With greater degrees, distortion of vision can occur. To achieve a clearer image, a person with astigmatism uses accommodation or squints to obtain a pinhole effect. Symptoms include eyestrain, headache, and fatigue. Cylindrical or spherocylindrical lenses are used to provide optical correction when indicated. Glasses may be needed constantly or only part time, depending on the degree of astigmatism and the severity of the attendant symptoms. In some cases, contact lenses are used.

Infants and children with corneal irregularity resulting from injury, ptosis, or hemangiomas of the periorbita or eyelid are at increased risk of astigmatism and associated amblyopia.

ANISOMETROPIA

When the refractive state of one eye is significantly different from the refractive state of the other eye, **anisometropia** exists. If uncorrected, one eye may always be out of focus, leading to the development of amblyopia. Early detection and correction are essential if normal visual development in both eyes is to be achieved.

ACCOMMODATION

During accommodation, the ciliary muscle contracts, the suspensory fibers of the lens relax, and the lens assumes a more rounded shape, adding power to the lens. The amplitude of accommodation is greatest during childhood and gradually diminishes with age. The physiologic decrease in accommodative ability that occurs with age is called **presbyopia**.

Disorders of accommodation in children are relatively rare. Premature presbyopia is occasionally encountered in young children. The most common cause of paralysis of accommodation in children is

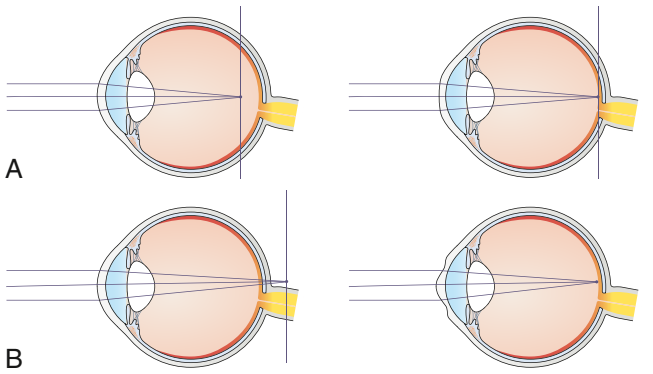

Fig. 660.2 Refractive errors before *(left)* and after *(right)* surgery. A, Refractive eye surgery corrects myopia using central ablation to flatten the corneal curvature (B) and corrects hyperopia using mid-peripheral ablation to steepen the corneal curvature. *(Modified from Kim T, Alió del Barrio, Wilkins M, et al. Refractive surgery. Lancet. 2019;393:2085-2094, Fig. 1, p. 2086.)*

intentional or inadvertent use of cycloplegic substances, topically or systemically; included are all the anticholinergic drugs and poisons, as well as plants and plant substances having these effects. Neurogenic causes of accommodative paralysis include lesions affecting the oculomotor nerve (third cranial nerve) along any part of its course. Differential diagnoses include tumors, degenerative diseases, vascular lesions, trauma, and infectious etiologies. Systemic disorders that may cause impairment of accommodation include botulism, diphtheria, Wilson disease, diabetes mellitus, and syphilis. Adie tonic pupil may also lead to a deficiency of accommodation after some viral illnesses (see Chapter 662). An apparent defect in accommodation may be psychogenic in origin; it is common for a child to feign inability to read when it can be demonstrated that visual acuity and ability to focus are normal.

Visit Elsevier eBooks+ at eBooks.Health.Elsevier.com for Bibliography.

Chapter 661

Disorders of Vision

Scott E. Olitsky and Justin D. Marsh

Severe visual impairment (corrected vision poorer than **6/60**) and blindness in children have many etiologies and may be caused by multiple defects affecting any structure or function along the visual pathways (Tables 661.1, 661.2, 661.3). The overall incidence is approximately 2.5/100,000 children; the incidence is higher in developing countries, in low birthweight infants, and in the first year of life. The most common causes occur during the prenatal and perinatal time periods; the cerebral-visual pathways, optic nerve (hypoplasia, atrophy), and retinal (Leber amaurosis) sites are most often affected. Important prenatal causes include microphthalmia/anophthalmia as well as autosomal recessive (most common), autosomal dominant, and X-linked genetic disorders and hypoxia or chromosomal syndromes. Perinatal/neonatal causes include retinopathy of prematurity, hypoxia-ischemia, and infection. Severe visual impairment starting in older children may be due to central nervous system or retinal tumors, infections, hypoxia-ischemia, injuries, neurodegenerative disorders, or juvenile idiopathic arthritis.

AMBLYOPIA

This is a decrease in visual acuity, unilateral or bilateral, that occurs in visually immature children as a result of a lack of a clear image projecting onto the retina. The unformed retinal image may occur secondary to a deviated eye **(strabismic amblyopia)**, an unequal need for vision correction between the eyes **(anisometropic amblyopia)**, a high refractive error in both eyes **(ametropic amblyopia)**, or a media opacity within the visual axis **(deprivation amblyopia)**.

The development of visual acuity normally proceeds rapidly in infancy and early childhood. Anything that interferes with the formation of a clear retinal image during this early developmental period can produce amblyopia. Amblyopia occurs only during the critical period of development before the cortex has become visually mature, within the first decade of life. The younger the child, the more susceptible he or she is to the development of amblyopia.

The **diagnosis** of amblyopia is confirmed when a complete ophthalmologic examination reveals reduced acuity that is unexplained by an organic abnormality. If the history and ophthalmologic examination do not support the diagnosis of amblyopia in a child with poor vision, consideration must be given to other causes (neurologic, psychologic). *Amblyopia is usually asymptomatic and can avoid detection until vision screening, which may delay diagnosis as screening programs often target school-age children.* This is problematic because amblyopia is more resistant to treatment at an older age, being reversed more rapidly in younger children whose visual system is less mature. Thus one key to the successful treatment of amblyopia is early detection and prompt intervention.

Most often, **treatment** first consists of removing any media opacity or prescribing appropriate glasses, if needed, so that a well-focused retinal image can be produced in each eye. The sound eye is then covered (occlusion therapy) or blurred with glasses (fogging) or drops (penalization therapy) to stimulate proper visual development of the more severely affected eye. Occlusion therapy may provide a more rapid improvement in vision, but some children may better tolerate atropine penalization. The best treatment for any one patient should be selected on an individual basis. The goals of treatment should be thoroughly understood and the treatment carefully supervised. Close monitoring of amblyopia therapy by an ophthalmologist is essential, especially in the very young, to avoid deprivation amblyopia in the good eye. Many families need reassurance and support throughout the trying course of treatment. Although full-time occlusion has historically been considered the best way to treat children with amblyopia, a series of prospective studies has shown that some children can achieve similar results with part-time patching, or the use of atropine drops. Historical thought was that older children would not respond to amblyopia therapy. Studies suggest older children and adolescents deemed visually mature who demonstrate amblyopia, particularly refractive or anisometropic in etiology, can demonstrate improvement in vision with appropriate therapy.

DIPLOPIA

Diplopia, or double vision, is generally a result of a misalignment of the visual axes. Occluding either eye relieves the diplopia if it is binocular in origin. Affected children commonly squint, cover one eye with a hand, or assume an abnormal head posture (a face turn or head tilt) to alleviate the bothersome sensation. These behaviors, especially in preverbal children, are important clues to diplopia. *The onset of diplopia in any child warrants prompt evaluation; it may signal the onset of a serious problem such as increased intracranial pressure, a brain tumor, infection (Lyme disease), migraine, Guillain-Barré syndrome, or an orbital mass* (Fig. 661.1).

Monocular diplopia is less common and results from refractive error, dislocation of the lens, cataract, dry eyes, or some defect in the media or macula. With this type of diplopia, occluding the nondiplopic eye will not relieve the symptoms. Monocular diplopia may also often have psychologic causes.

SUPPRESSION

In the presence of strabismus, diplopia occurs secondary to the same image falling on different regions of the retina in each eye. In a visually immature child, a process may occur in the cortex that eliminates the disability of seeing double. This is an active process and is termed **suppression**. It typically only develops in children. Although suppression eliminates the annoying symptom of diplopia, frequent suppression may not only place the patient at risk for amblyopia but also increase the risk for worsening strabismus. Once suppression develops, it may allow an intermittent strabismus to become constant or strabismus to redevelop later in life, even after successful treatment during childhood.

AMAUROSIS

Amaurosis is partial or total loss of vision; the term is usually reserved for profound impairment, blindness, or near blindness. When amaurosis exists from birth, primary consideration in the differential diagnosis must be given to developmental malformations, damage consequent to gestational or perinatal infection, anoxia or hypoxia, perinatal trauma, and the genetically determined diseases that can affect the eye itself or the visual pathways (see Table 661.3). Often the reason for amaurosis can be readily determined by objective ophthalmic examination; examples are severe microphthalmia, corneal opacification, dense cataracts, chorioretinal scars, macular defects, retinal dysplasia, and severe optic nerve hypoplasia. In other cases, an intrinsic retinal disease may not be apparent on initial ophthalmoscopic examination, or the defect may involve the brain and not the eye. Neuroradiologic (MRI or CT) and electrophysiologic (electroretinography) evaluation are helpful in these cases.

Amaurosis that develops in a child who once had useful vision has different implications. In the absence of obvious ocular disease (cataract, chorioretinitis, retinoblastoma, retinitis pigmentosa), consideration must be given to many neurologic and systemic disorders that can affect the visual pathways (see Table 661.1). Amaurosis of rather

Table 661.1 Causes of Childhood Severe Visual Impairment or Blindness

CONGENITAL
- Optic nerve hypoplasia or aplasia
- Holoprosencephaly
- Septo-optic dysplasia
- Optic coloboma
- Congenital hydrocephalus
- Hydranencephaly
- Porencephaly
- Microcephaly
- Encephalocele, particularly occipital
- Morning glory disc
- Aniridia
- Microphthalmia/anophthalmia syndromes
- Persistent pupillary membrane
- Cataracts
- Persistent hyperplastic primary vitreous
- Anterior segment dysgenesis syndromes
- Peters anomaly
- Axenfeld-Rieger anomaly
- Glaucoma syndromes (see Table 661.2)

PHAKOMATOSES
- Tuberous sclerosis
- Neurofibromatosis (special association with optic glioma)
- Sturge-Weber syndrome
- von Hippel-Lindau disease

TUMORS
- Retinoblastoma
- Optic glioma
- Perioptic meningioma
- Craniopharyngioma
- Cerebral glioma
- Astrocytoma
- Posterior and intraventricular tumors when complicated by hydrocephalus
- Pseudotumor cerebri

NEURODEGENERATIVE DISEASES
- Cerebral storage disease
- Gangliosidoses, particularly Tay-Sachs disease, Sandhoff variant, generalized gangliosidosis
- Other lipidoses and ceroid lipofuscinoses, particularly the late-onset disorders such as those of Jansky-Bielschowsky and of Batten-Mayou-Spielmeyer-Vogt
- Mucopolysaccharidoses, particularly Hurler syndrome and Hunter syndrome
- Leukodystrophies (dysmyelination disorders), particularly metachromatic leukodystrophy and Canavan disease
- Demyelinating sclerosis (myelinoclastic diseases), especially Schilder disease and Devic neuromyelitis optica
- *Special types:* Dawson disease, Leigh disease, the Bassen-Kornzweig syndrome, Refsum disease
- *Retinal degenerations:* retinitis pigmentosa and its variants and Leber congenital type (see Table 661.3)
- *Optic atrophies:* congenital autosomal recessive type, infantile and congenital autosomal dominant types, Leber disease, and atrophies associated with hereditary ataxias: Behr, Marie, and Sanger-Brown

INFECTIOUS/INFLAMMATORY PROCESSES
- Encephalitis, especially in the prenatal infection syndromes caused by *Toxoplasma gondii*, cytomegalovirus, rubella virus, *Treponema pallidum*, herpes simplex virus, Zika virus
- Meningitis or arachnoiditis
- Chorioretinitis
- Endophthalmitis
- Trachoma
- Keratitis
- Uveitis
- Sarcoidosis
- Optic neuritis
- Hemophagocytic lymphohistiocytosis
- Granulomatosis with polyangiitis

HEMATOLOGIC DISORDERS
- Leukemia with central nervous system involvement
- Langerhans cell histiocytosis

VASCULAR AND CIRCULATORY DISORDERS
- Collagen vascular diseases
- Arteriovenous malformations—intracerebral hemorrhage, subarachnoid hemorrhage
- Central retinal occlusion
- Retinal vasculitis
- Coats disease
- Susac syndrome

TRAUMA
- Contusion or avulsion of optic nerves, chiasm, globe, cornea
- Cerebral contusion or laceration
- Intracerebral, subarachnoid, or subdural hemorrhage
- Retinal detachment
- Laser injury

DRUGS AND TOXINS
- Quinine
- Ethambutol
- Methanol
- Many others

OTHER
- Retinopathy of prematurity
- Sclerocornea
- Conversion reaction
- Osteopetrosis
- Susac syndrome: branch retinal artery occlusions, hearing loss, CNS dysfunction
- Coats disease: poor vision, retinal telangiectasias and exudation

Modified from Kliegman R. *Practical Strategies in Pediatric Diagnosis and Therapy*. Philadelphia: WB Saunders;1996.

rapid onset may indicate an encephalopathy (hypertension), infectious or inflammatory (optic neuritis) processes, vasculitis, migraine, leukemia, drugs or toxins, eclampsia, or trauma. It may be caused by acute demyelinating disease affecting the optic nerves, chiasm, or cerebrum. In some cases, precipitous loss of vision is a result of increased intracranial pressure, rapidly progressive hydrocephalus, or dysfunction of a ventricular shunt. More slowly progressive visual loss suggests tumor or neurodegenerative disease. Gliomas of the optic nerve and chiasm and craniopharyngiomas are primary diagnostic considerations in children who show progressive loss of vision.

Clinical manifestations of impairment of vision vary with the age and abilities of a child, the mode of onset, and the laterality and severity of the deficit. The first clue to amaurosis in an infant may be **nystagmus** or **strabismus,** with the vision deficit itself passing undetected for some time. Timidity, clumsiness, or behavioral change may be the initial clues in the very young. Deterioration in school progress and indifference to school activities are common signs in an older child. School-age children often try to hide their disability and, in the case of very slowly progressive disorders, may not themselves realize the severity of the problem; some detect and promptly report small changes in their vision.

Any evidence of loss of vision requires prompt and thorough ophthalmic evaluation. Complete delineation of childhood amaurosis and its cause may require extensive investigation involving neurologic evaluation, electrophysiologic tests, neuroradiologic procedures, and sometimes metabolic and genetic studies. Furthermore, attendant special educational, social, and emotional needs must be met.

Table 661.2 Congenital Glaucoma and Anterior Segment Dysgenesis*

OMIM NUMBER	GENE SYMBOL	PROTEIN	PHENOTYPE	MODE OF INHERITANCE	SYNDROMIC (S) OR ISOLATED (I)
105650	*RPS19*	Ribosomal protein S19	Diamond-Blackfan anemia 1	AD	S
137600	*PITX2*	Paired like homeodomain 2	Anterior segment dysgenesis 4	AD	I
175780	*COL4A1*	Collagen type IV alpha 1 chain	Brain small vessel disease with or without ocular anomalies including congenital glaucoma	AD	S
180849	*CREBBP*	CREB binding protein	Rubinstein-Taybi syndrome 1	AD	S
236670	*POMT1*	Protein O-mannosyltransferase 1	Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 1; muscular dystrophy-dystroglycanopathy (congenital with cognitive disabilities), type B, 1; muscular dystrophy-dystroglycanopathy (limb-girdle), type C, 1	AR	S
249420	*SH3PXD2B*	SH3 and PX domains 2B	Frank-Ter Haar syndrome with or without glaucoma	AR	S
251750	*LTBP2*	Latent transforming growth factor beta binding protein 2	Weill-Marchesani syndrome 3; glaucoma 3, primary congenital, D; microspherophakia and/or megalocornea, with ectopia lentis and with or without secondary glaucoma	AR	S or I
253280	*POMGNT1*	Protein O-linked mannose N-acetylglucosaminyltransferase 1 (beta 1,2-)	Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 3	AR	S
600221	*TEK*	TEK receptor tyrosine kinase	Glaucoma 3, primary congenital, E; Venous malformations, multiple cutaneous and mucosal	AD	S or I
601090	*FOXC1*	Forkhead box C1	Anterior segment dysgenesis 3, multiple subtypes; Axenfeld-Rieger syndrome, type 3	AD	S or I
601631	*FOXC1*	Forkhead box C1	Anterior segment dysgenesis 3, multiple subtypes; Axenfeld-Rieger syndrome, type 3	AD	S or I
601652	*MYOC*	Myocilin	Glaucoma 1A, primary open angle	AD	I
601771	*CYP1B1*	Cytochrome P450 family 1 subfamily B member 1	Anterior segment dysgenesis 6, multiple subtypes; glaucoma 3A, primary open angle, congenital, juvenile, or adult onset	AR	I
602091	*LTBP2*	Latent transforming growth factor beta binding protein 2	Weill-Marchesani syndrome 3; Glaucoma 3, primary congenital, D; microspherophakia and/or megalocornea, with ectopia lentis and with or without secondary glaucoma	AR	S or I
603474	*RPS19*	Ribosomal protein S19	Diamond-Blackfan anemia 1	AD	S
604563	*SBF2*	SET binding factor 2	Charcot-Marie-Tooth disease, type 4B2	AR	S
607423	*POMT1*	Protein O-mannosyltransferase 1	Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 1; muscular dystrophy-dystroglycanopathy (congenital with cognitive disabilities), type B, 1; muscular dystrophy-dystroglycanopathy (limb-girdle), type C, 1	AR	S
610192	*GLIS3*	GLIS family zinc finger 3	Diabetes mellitus, neonatal, with congenital hypothyroidism. Additional features include congenital glaucoma	AR	S
610199	*GLIS3*	GLIS family zinc finger 3	Diabetes mellitus, neonatal, with congenital hypothyroidism. Additional features include congenital glaucoma	AR	S

Continued

Table 661.2 Congenital Glaucoma and Anterior Segment Dysgenesis*—cont'd

OMIM NUMBER	GENE SYMBOL	PROTEIN	PHENOTYPE	MODE OF INHERITANCE	SYNDROMIC (S) OR ISOLATED (I)
613150	*POMT2*	Protein O-mannosyltransferase 2	Muscular dystrophy-dystroglycanopathy (congenital with brain and eye anomalies), type A, 2	AR	S
613293	*SH3PXD2B*	SH3 and PX domains 2B	Frank-Ter Haar syndrome with or without glaucoma	AR	S
617315	*CYP1B1*	Cytochrome P450 family 1 subfamily B member 1	Anterior segment dysgenesis 6, multiple subtypes; glaucoma 3A, primary open angle, congenital, juvenile, or adult onset	AR	I

*There are 55 entries in Online Mendelian Inheritance in Man (OMIM, https://www.ncbi.nlm.nih.gov/omim) for congenital glaucoma. This table only lists those with strong association to congenital glaucoma or diseases with congenital glaucoma as one of the major clinical features.
AD, Autosomal dominant; AR, autosomal recessive.
From Chen HY, Lehmann OJ, Swaroop A. Genetics and therapy for pediatric eye diseases. *EBioMedicine*. 2021;67:103360(Table 1b)

Table 661.3 Leber Congenital Amaurosis (LCA)*

OMIM NUMBER	GENE SYMBOL	PROTEIN	PHENOTYPE	MODE OF INHERITANCE	SYNDROMIC (S) OR ISOLATED (I)
204000	*GUCY2D*	Guanylate cyclase 2D, retinal	Leber congenital amaurosis 1	AD or AR	I
601777			Cone-rod dystrophy 6		
204100	*RPE65*	Retinoid isomerohydrolase RPE65	Leber congenital amaurosis 2	AR	I
613794			Retinitis pigmentosa 20		
618697			Retinitis pigmentosa 87 with choroidal involvement	AD	
604232	*SPATA7*	Spermatogenesis associated 7	Leber congenital amaurosis 3; Retinitis pigmentosa, juvenile	AR	I
604393	*AIPL1*	Aryl hydrocarbon receptor interacting protein like 1	Cone-rod dystrophy; Retinitis pigmentosa, juvenile; Leber congenital amaurosis 4	AD or AR	I
604537	*LCA5*	Lebercilin LCA5	Leber congenital amaurosis 5	AR	I
613826	*RPGRIP1*	RPGR interacting protein 1	Leber congenital amaurosis 6	AR	I
613829	*CRX*	Cone-rod homeobox	Leber congenital amaurosis 7	AD	I
613835	*CRB1*	Crumbs cell polarity complex component 1	Leber congenital amaurosis 8	AR	I
600105			Retinitis pigmentosa-12		
608553	*NMNAT1*	Nicotinamide nucleotide adenylyltransferase 1	Leber congenital amaurosis 9	AR	I
611755	*CEP290*	Centrosomal protein 290	Leber congenital amaurosis 10	AR	I or S
610188			Joubert syndrome 5		
610189			Senior-Loken syndrome 6		
613837	*IMPDH1*	Inosine monophosphate dehydrogenase 1	Leber congenital amaurosis 11	AR	I
180105			Retinitis pigmentosa 10	AD	
610612	*RD3*	RD3 regulator of GUCY2D	Leber congenital amaurosis 12	AR	I
612712	*RDH12*	Retinol dehydrogenase 12	Leber congenital amaurosis 13	AD or AR	I
613341	*LRAT*	Lecithin retinol acyltransferase	Retinitis pigmentosa, juvenile; Leber congenital amaurosis 14; Retinal dystrophy, early-onset severe	AR	I
613843	*TULP1*	TUB like protein 1	Leber congenital amaurosis 15	AR	I
600132					

Table 661.3 Leber Congenital Amaurosis (LCA)*—cont'd

OMIM NUMBER	GENE SYMBOL	PROTEIN	PHENOTYPE	MODE OF INHERITANCE	SYNDROMIC (S) OR ISOLATED (I)
614186	*KCNJ13*	Potassium inwardly rectifying channel subfamily J member 13	Leber congenital amaurosis 16	AR	I
615360	*GDF6*	Growth differentiation factor 6	Leber congenital amaurosis 17	AR	I
608133	*PRPH2*	Peripherin 2	Leber congenital amaurosis 18; Retinitis pigmentosa 7 and digenic form	AD or AR	I or S
169150			Macular dystrophy, patterned, 1		
618513	*USP45*	Ubiquitin specific peptidase 45	Leber congenital amaurosis 19	AR	I
617879	*TUBB4B*	Tubulin beta 4B class IVb	Leber congenital amaurosis with early-onset deafness	AD	S
609237	*IQCB1*	IQ motif-containing protein B1	Leber congenital amaurosis	AR	I or S
609254			Senior-Loken syndrome 5	AR	

*There are 101 entries in Online Mendelian Inheritance in Man (OMIM; https://www.ncbi.nlm.nih.gov/omim) for LCA. This table only lists the genes with strong association to LCA or diseases with LCA as one of the major clinical attributes.
AD, Autosomal dominant; AR, autosomal recessive; DR, digenic recessive.
From Chen HY, Lehmann OJ, Swaroop A. Genetics and therapy for pediatric eye diseases. *EBioMedicine* .2021;67:103360(Table 1c)

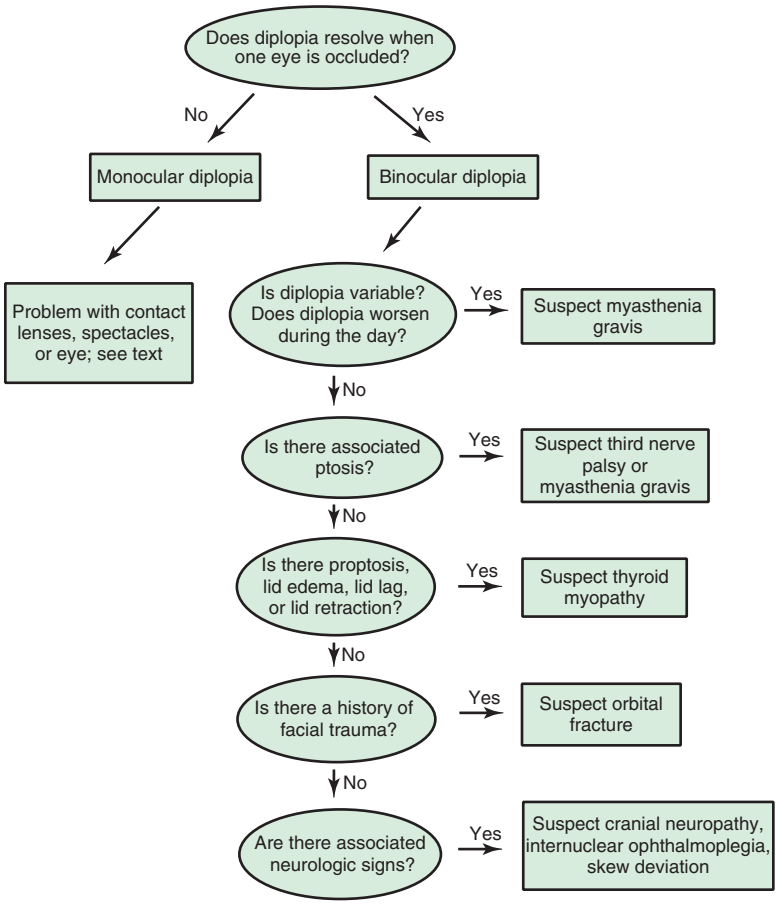

Fig. 661.1 General approach to diplopia. The clinician should first distinguish monocular from binocular diplopia and, in patients with binocular diplopia, address the five questions on the right side of the figure. Only then should the clinician identify which muscle is weak, although this is unnecessary if the clinician already suspects myasthenia (from fatigability) or full third nerve palsy (from weakness of the medial rectus, superior rectus, inferior rectus, and inferior oblique muscles, with or without a dilated pupil). Uncommon causes of diplopia and associated ptosis, not presented in the figure, are botulism, the Fisher variant of Guillain-Barre syndrome, and aberrant regeneration of the third nerve. Uncommon causes of diplopia and associated orbital findings (e.g., proptosis) are carotid-cavernous fistula (which causes an orbital bruit), orbital tumor, and pseudotumor. *(From McGee S. Evidence-Based Physical Diagnosis, 3rd ed. Elsevier; 2012. Fig. 57.1, p. 522.)*

NYCTALOPIA

Nyctalopia, or night blindness, is vision that is defective in reduced illumination. It generally implies impairment in function of the rods, particularly in dark adaptation time and perceptual threshold. Stationary congenital night blindness may occur as an autosomal dominant, autosomal recessive, or X-linked recessive condition. It may be associated with myopia and nystagmus. Children may have excessive problems going to sleep in a dark room, which may be mistaken for a behavioral problem. Progressive night blindness usually indicates primary or secondary retinal, choroidal, or vitreoretinal degeneration (see Chapter 670); it occurs also in vitamin A deficiency or as a result of retinotoxic drugs such as quinine.

PSYCHOGENIC DISTURBANCES

Vision problems of psychogenic origin are common in school-age children. Both conversion reactions and willful feigning are encountered. The usual manifestation is a report of reduced visual acuity in one or both eyes. Another common manifestation is constriction of the visual field. In some cases, the symptom is diplopia or polyopia (see Chapters 35 and 38).

Important clues to the diagnosis are inappropriate affect, excessive grimacing, inconsistency in performance, and suggestibility. A thorough ophthalmologic examination is essential to differentiate organic from functional visual disorders.

Affected children usually fare well with reassurance and positive suggestions. In some cases, mental health care is indicated. In all cases, the approach must be supportive and nonpunitive.

DYSLEXIA

This is the inability to develop the capability to read at an expected level despite an otherwise normal intellect (see Chapter 51). The terms *reading disability* and *dyslexia* are often used interchangeably. Most dyslexic individuals also display poor writing ability. Dyslexia is a primary reading disorder and should be differentiated from secondary reading difficulties caused by intellectual disability, environmental or educational deprivation, and systemic physical or other organic brain or eye diseases. Because there is not one standard test for dyslexia, the diagnosis is usually made by comparing reading ability with intelligence and standard reading expectations. Dyslexia is a language-based disorder and is not caused by any defect in the eye or visual acuity per se, nor is it attributable to a defect in ocular motility or binocular alignment. Although ophthalmologic evaluation of children with a reading problem is recommended to diagnose and correct any concurrent ocular problems such as a refractive error, amblyopia, or strabismus, treatment directed to the eyes themselves cannot be expected to correct developmental dyslexia (see Chapter 51).

Visit Elsevier eBooks+ at eBooks.Health.Elsevier.com for Bibliography.

Chapter 662

Abnormalities of Pupil and Iris

Scott E. Olitsky and Justin D. Marsh

ANIRIDIA

The term *aniridia* is a misnomer because some iris tissue is usually present, although it is hypoplastic (Fig. 662.1). Two-thirds of the cases are dominantly transmitted with a high degree of penetrance. The other third of cases are sporadic and are considered new pathologic genetic variants. The condition is bilateral in 98% of all patients, regardless of the means of transmission, and is found in approximately 1/50,000 persons. Pathologic variants in *PAX6* on 11p13 are typically implicated, and aniridia may be associated with other ocular findings.

Aniridia is a panocular disorder and should not be thought of as an isolated iris defect. Macular and optic nerve hypoplasia are commonly present and lead to decreased vision and sensory nystagmus. The visual acuity is approximately 20/200 in most patients, although the vision may occasionally be better. Other ocular deformities are common and may involve the lens and cornea. The cornea may be small, and a cellular infiltrate (pannus) occasionally develops in the superficial layers of the peripheral cornea (keratopathy). Clinically this appears as a gray opacification. Lens abnormalities include cataract formation and partial or total lens dislocation. **Glaucoma** develops in as many as 75% of individuals with aniridia.

One-fifth of sporadic aniridic patients may develop **Wilms tumor** (see Chapter 548.1). Because of their proximity in location, large deletions may include both *PAX6* and *WT1*, leading to this association. Although it has traditionally been taught that only patients with sporadic aniridia are at risk for developing Wilms tumor, it has also been reported in individuals with familial aniridia. Additionally, genitourinary abnormalities and intellectual disability, when present with aniridia, are strongly associated with Wilms tumor (WAGR syndrome). Wilms tumor usually presents before the fifth year, and these children should be screened using renal ultrasonography every 3-6 months until approximately 5 years of age if there is an 11p13 region deletion placing the child at risk for Wilms tumor.

COLOBOMA OF THE IRIS

A **coloboma** is the defect formed when the embryonic fissure fails to close completely. This unilateral or bilateral developmental defect may present as a defect in a sector of the iris, a hole in the substance of the iris, or a notch in the pupillary margin (Fig. 662.2). Simple (isolated) colobomas may be sporadic but are frequently transmitted as an autosomal dominant trait and may occur alone or in association with other anomalies and syndromes (syndromic) (Table 662.1). Because of the anatomic location of the embryonic fissure, an iris coloboma is always located inferiorly, giving the iris a keyhole appearance. An iris coloboma may be the only externally visible part of a more extensive coloboma that also involves the choroid, retina, and optic nerve. When this occurs, vision is likely to be severely affected. Complications include retinal detachment, cataract formation, and choroidal neovascularization. All children with an iris coloboma should undergo a full ophthalmologic examination.

MICROCORIA

Microcoria (congenital miosis) appears as a small pupil that does not react to light or accommodation and that dilates poorly, if at all, with medication. The condition may be unilateral or bilateral. In bilateral cases, the degree of miosis may be different in each eye. The eye may be otherwise normal or may demonstrate other abnormalities of the

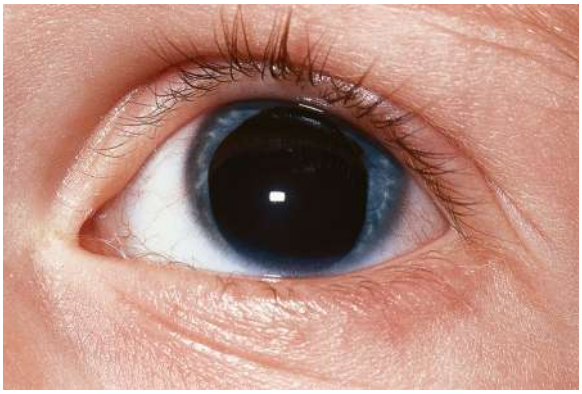

Fig. 662.1 Partial aniridia in a member of an autosomal dominant pedigree. *(From Hoyt CS, Taylor D, eds. Pediatric Ophthalmology and strabismus. 4th ed. Elsevier; 2013; Fig. 32.22, p. 304.)*

NYCTALOPIA

Nyctalopia, or night blindness, is vision that is defective in reduced illumination. It generally implies impairment in function of the rods, particularly in dark adaptation time and perceptual threshold. Stationary congenital night blindness may occur as an autosomal dominant, autosomal recessive, or X-linked recessive condition. It may be associated with myopia and nystagmus. Children may have excessive problems going to sleep in a dark room, which may be mistaken for a behavioral problem. Progressive night blindness usually indicates primary or secondary retinal, choroidal, or vitreoretinal degeneration (see Chapter 670); it occurs also in vitamin A deficiency or as a result of retinotoxic drugs such as quinine.

PSYCHOGENIC DISTURBANCES

Vision problems of psychogenic origin are common in school-age children. Both conversion reactions and willful feigning are encountered. The usual manifestation is a report of reduced visual acuity in one or both eyes. Another common manifestation is constriction of the visual field. In some cases, the symptom is diplopia or polyopia (see Chapters 35 and 38).

Important clues to the diagnosis are inappropriate affect, excessive grimacing, inconsistency in performance, and suggestibility. A thorough ophthalmologic examination is essential to differentiate organic from functional visual disorders.

Affected children usually fare well with reassurance and positive suggestions. In some cases, mental health care is indicated. In all cases, the approach must be supportive and nonpunitive.

DYSLEXIA

This is the inability to develop the capability to read at an expected level despite an otherwise normal intellect (see Chapter 51). The terms *reading disability* and *dyslexia* are often used interchangeably. Most dyslexic individuals also display poor writing ability. Dyslexia is a primary reading disorder and should be differentiated from secondary reading difficulties caused by intellectual disability, environmental or educational deprivation, and systemic physical or other organic brain or eye diseases. Because there is not one standard test for dyslexia, the diagnosis is usually made by comparing reading ability with intelligence and standard reading expectations. Dyslexia is a language-based disorder and is not caused by any defect in the eye or visual acuity per se, nor is it attributable to a defect in ocular motility or binocular alignment. Although ophthalmologic evaluation of children with a reading problem is recommended to diagnose and correct any concurrent ocular problems such as a refractive error, amblyopia, or strabismus, treatment directed to the eyes themselves cannot be expected to correct developmental dyslexia (see Chapter 51).

Visit Elsevier eBooks+ at eBooks.Health.Elsevier.com for Bibliography.

Chapter 662

Abnormalities of Pupil and Iris

Scott E. Olitsky and Justin D. Marsh

ANIRIDIA

The term *aniridia* is a misnomer because some iris tissue is usually present, although it is hypoplastic (Fig. 662.1). Two-thirds of the cases are dominantly transmitted with a high degree of penetrance. The other third of cases are sporadic and are considered new pathologic genetic variants. The condition is bilateral in 98% of all patients, regardless of the means of transmission, and is found in approximately 1/50,000 persons. Pathologic variants in *PAX6* on 11p13 are typically implicated, and aniridia may be associated with other ocular findings.

Aniridia is a panocular disorder and should not be thought of as an isolated iris defect. Macular and optic nerve hypoplasia are commonly present and lead to decreased vision and sensory nystagmus. The visual acuity is approximately 20/200 in most patients, although the vision may occasionally be better. Other ocular deformities are common and may involve the lens and cornea. The cornea may be small, and a cellular infiltrate (pannus) occasionally develops in the superficial layers of the peripheral cornea (keratopathy). Clinically this appears as a gray opacification. Lens abnormalities include cataract formation and partial or total lens dislocation. **Glaucoma** develops in as many as 75% of individuals with aniridia.

One-fifth of sporadic aniridic patients may develop **Wilms tumor** (see Chapter 548.1). Because of their proximity in location, large deletions may include both *PAX6* and *WT1*, leading to this association. Although it has traditionally been taught that only patients with sporadic aniridia are at risk for developing Wilms tumor, it has also been reported in individuals with familial aniridia. Additionally, genitourinary abnormalities and intellectual disability, when present with aniridia, are strongly associated with Wilms tumor (WAGR syndrome). Wilms tumor usually presents before the fifth year, and these children should be screened using renal ultrasonography every 3-6 months until approximately 5 years of age if there is an 11p13 region deletion placing the child at risk for Wilms tumor.

COLOBOMA OF THE IRIS

A **coloboma** is the defect formed when the embryonic fissure fails to close completely. This unilateral or bilateral developmental defect may present as a defect in a sector of the iris, a hole in the substance of the iris, or a notch in the pupillary margin (Fig. 662.2). Simple (isolated) colobomas may be sporadic but are frequently transmitted as an autosomal dominant trait and may occur alone or in association with other anomalies and syndromes (syndromic) (Table 662.1). Because of the anatomic location of the embryonic fissure, an iris coloboma is always located inferiorly, giving the iris a keyhole appearance. An iris coloboma may be the only externally visible part of a more extensive coloboma that also involves the choroid, retina, and optic nerve. When this occurs, vision is likely to be severely affected. Complications include retinal detachment, cataract formation, and choroidal neovascularization. All children with an iris coloboma should undergo a full ophthalmologic examination.

MICROCORIA

Microcoria (congenital miosis) appears as a small pupil that does not react to light or accommodation and that dilates poorly, if at all, with medication. The condition may be unilateral or bilateral. In bilateral cases, the degree of miosis may be different in each eye. The eye may be otherwise normal or may demonstrate other abnormalities of the

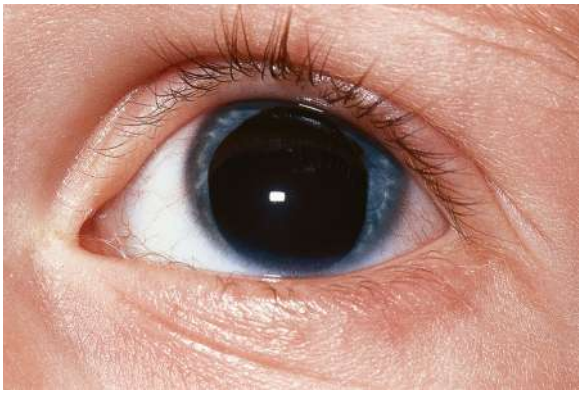

Fig. 662.1 Partial aniridia in a member of an autosomal dominant pedigree. *(From Hoyt CS, Taylor D, eds. Pediatric Ophthalmology and strabismus. 4th ed. Elsevier; 2013; Fig. 32.22, p. 304.)*

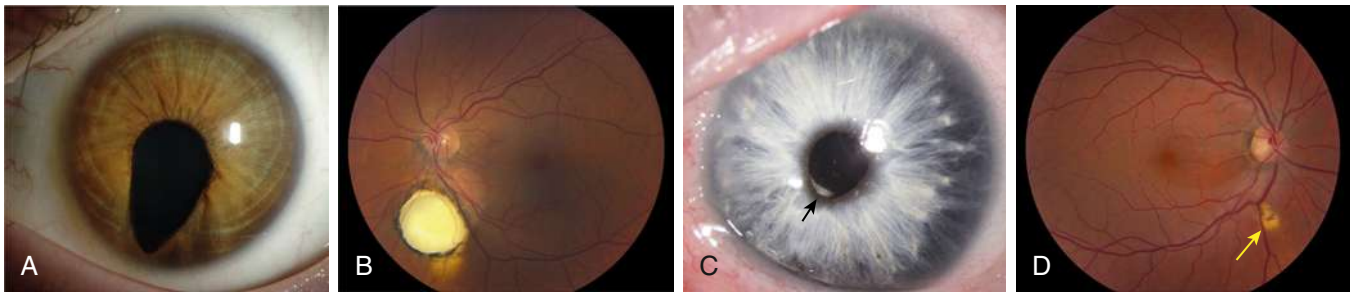

Fig. 662.2 Clinical presentations of uveal coloboma. **A,** Typical iris coloboma of a left eye. Note the inferonasal positioning of the coloboma, corresponding to the position of the optic fissure. **B,** Typical chorioretinal coloboma inferior to the optic nerve in a patient with excellent visual acuity. **C,** Microform of iris coloboma in a patient with Waardenburg syndrome, type 2A. Note slight peaking of the pupil of the inferonasal quadrant *(arrow).* **D,** Microform of a chorioretinal coloboma in the asymptomatic mother of a patient with bilateral nonsyndromic coloboma. *(From George A, Cogliati T, Brooks BP. Genetics of syndromic ocular coloboma: CHARGE and COACH syndromes. Exp Eye Res. 2020;193:107940; Fig. 2).*

Table 662.1 Syndromes Associated with Coloboma

Cat eye syndrome
CHARGE association
COACH
Coloboma with agenesis of corpus callosum
Congenital colobomatous microphthalmia iris coloboma and anal atresia
Congenital disorder of glycosylation type IV
Deletion 4p, 7p, 13q, 2q31.1, 14q24.3, 15q24
Glotz
Goldenhar
Jacobsen
Joubert
Klippel Feil 1,3
Meckel Gruber
Morning glory anomaly
Noonan
Renpenning
Rieger
Rubinstein-Taybi
SOX2-related eye disorders
Temtamy
Trisomy 13, 18, 22
Warburg

Plus >40 single gene pathologic variants.
COACH, Cerebral vermis hypoplasia, oligophrenia, ataxia, coloboma, hepatic fibrosis; CHARGE, coloboma, heart defect, atresia choanae, retarded growth and development, genital hypoplasia, ear anomalies, deafness.

anterior segment. Congenital microcoria is usually transmitted as an autosomal dominant trait, although it may occur sporadically.

CONGENITAL MYDRIASIS

In this disorder, the pupils appear dilated, do not constrict significantly to light or near gaze, and respond minimally to miotic agents. The iris is otherwise normal, and affected children are usually healthy. Trauma, pharmacologic mydriasis, and neurologic disorders should be considered. Congenital mydriasis is one component of the **multisystemic smooth muscle dysfunction syndrome**; associated features include a patent ductus arteriosus and dilation of the aorta. Many apparent cases of congenital mydriasis show abnormalities of the central iris structures and may be considered a form of aniridia.

DYSCORIA AND CORECTOPIA

Dyscoria is abnormal shape of the pupil, and corectopia is abnormal pupillary position. They may occur together or independently as congenital or acquired anomalies.

Congenital corectopia is usually bilateral and symmetric and rarely occurs as an isolated anomaly; it is often accompanied by dislocation of the lens (ectopia lentis et pupillae), and the lens and pupil are commonly dislocated in opposite directions. **Ectopia lentis et pupillae** is transmitted as an autosomal recessive disorder; consanguinity is common. It is associated with pathologic variants in *ADAMTSL4*, which encodes a secreted glycoprotein widely distributed in the eye, which binds fibrillin-1 microfibrils and accelerates microfibril biogenesis.

When acquired, distortion and displacement of the pupil are frequently a result of trauma or intraocular inflammation. Prolapse of the iris after perforating injuries of the eye leads to peaking of the pupil in the direction of the perforation. Posterior synechiae (adhesions of the iris to the lens) are commonly seen when inflammation from any cause occurs in the anterior segment.

ANISOCORIA

Anisocoria occurs when the pupils are of different sizes. This may be a result of local or neurologic disorders. As a rule, if the inequality is more pronounced in the *presence of bright focal illumination* or on near gaze, there is a defect in pupillary constriction and the larger pupil is abnormal. If the anisocoria is worse in *reduced illumination*, a defect in dilation exists and the smaller pupil is abnormal (Figs. 662.3 and 662.4). Neurologic causes of anisocoria (parasympathetic or sympathetic lesions) must be differentiated from local causes such as synechiae (adhesions), congenital iris defects (colobomas, aniridia), and pharmacologic effects. **Horner syndrome** is an important cause of anisocoria (see later). Simple central anisocoria may occur in otherwise healthy individuals.

DILATED FIXED PUPIL

A dilated, unreactive pupil may be caused by internal ophthalmoplegia, Hutchinson pupil of transtentorial herniation, tonic pupil, pharmacologic blockade, and iridoplegia secondary to ocular trauma (see Fig. 662.3).

The most common cause of a dilated unreactive pupil is purposeful or accidental instillation of a cycloplegic agent, particularly atropine and related substances. Central nervous system lesions, such as a pinealoma, may cause internal ophthalmoplegia in children. Because the external surface of the oculomotor nerve carries the fibers responsible for pupillary constriction, compression of the nerve along its intracranial course may be associated with internal ophthalmoplegia, even before the development of ptosis or an ocular motility deficit. Although ophthalmoplegic migraine is a common cause of a third nerve palsy with pupillary involvement in children, an intracranial aneurysm must also be considered in the differential diagnosis. The blown pupil of transtentorial herniation, occurring with increasing intracranial pressure, is generally unilateral, and patients usually are obviously ill. The **pilocarpine test** can help differentiate neurologic iridoplegia from pharmacologic blockade. In the case of neurologic iridoplegia, the dilated pupil constricts within minutes after instillation of 1 or 2 drops of 0.5–1% pilocarpine; if the pupil has been dilated with atropine, pilocarpine has no effect. Because pilocarpine is a long-acting drug, this test is not to be used in acute situations in which pupillary signs must be carefully monitored. Because of the consensual pupil response to light, even complete uniocular blindness does not cause a unilaterally dilated pupil.

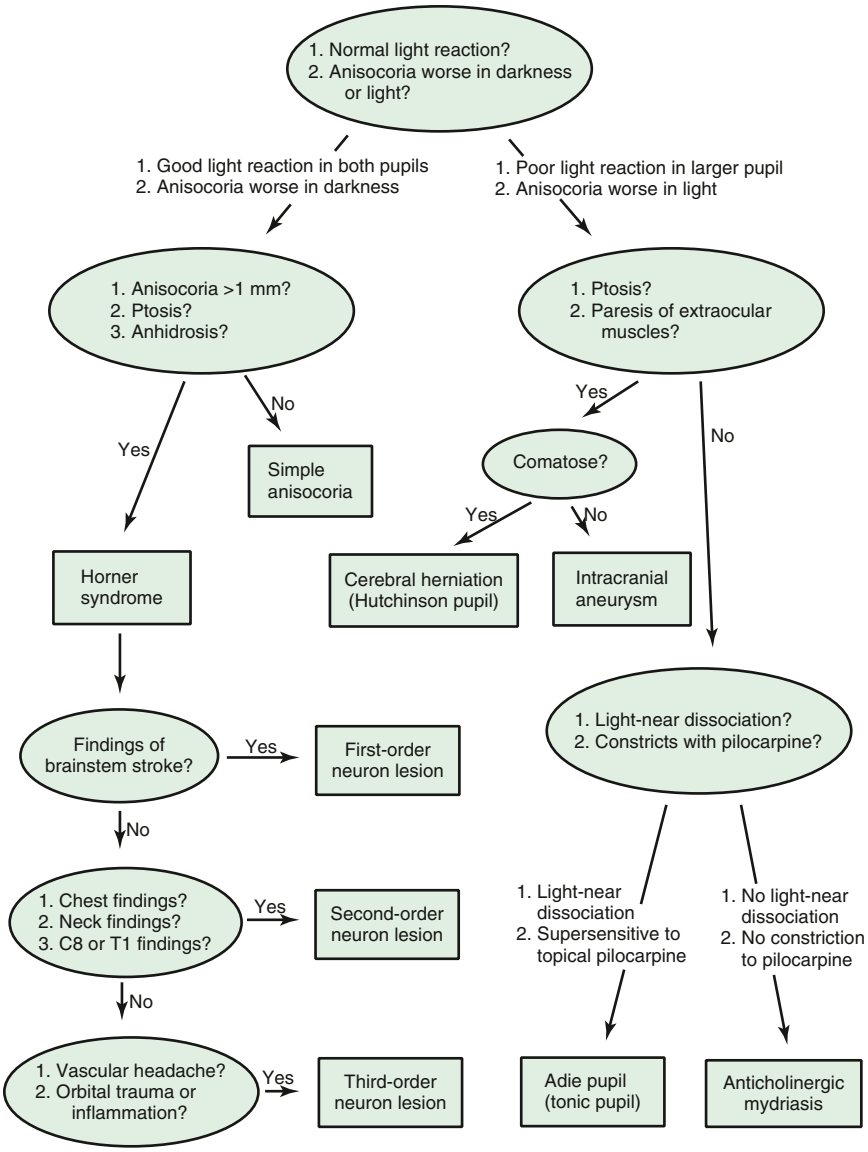

Fig. 662.3 Approach to anisocoria. The first two questions (Is there normal light reaction? And is anisocoria worse in darkness or light?) distinguish problems with the pupillary dilator muscle (i.e., Horner syndrome, simple anisocoria; *left side of figure*) from problems with the pupillary constrictor muscle (i.e., third cranial nerve, iris; *right side of figure*). Two other tests distinguish Horner syndrome from simple anisocoria: the cocaine test and pupillary dilator lag (i.e., the pupil dilates slowly in darkness, as documented in photographs). *(From Czarnecki JSC, Pilley SFJ, Thompson HS. The analysis of anisocoria: the use of photography in the clinical evaluation of unequal pupils. Can J Ophthalmol. 1979;14:297-302; and Thompson HS, Pilley SFJ. Unequal pupils: a flow chart for sorting out the anisocorias. Surv Ophthalmol. 1976;21[1]:45-48.)*

TONIC PUPIL

This is typically a large pupil that reacts poorly to light (the reaction may be very slow or even absent), reacts poorly and slowly to accommodation, and redilates in a slow, tonic manner. The features of tonic pupil are explained by cholinergic supersensitivity of the sphincter after peripheral (postganglionic) denervation and imperfect reinnervation. A distinctive feature of a tonic pupil is its sensitivity to dilute cholinergic agents. Instillation of 0.125% pilocarpine causes significant constriction of the involved pupil and has little or no effect on the unaffected side. The condition is usually unilateral.

Tonic pupil may develop after the acute stage of a partial or complete iridoplegia. It can be seen after trauma to the eye or orbit and may occur in association with toxic or infectious conditions. For those in the pediatric age group, tonic pupil is uncommon. Infectious processes (primarily viral syndromes) and trauma are the primary causes. Features of tonic pupil may also be seen in infants and children with familial dysautonomia (Riley-Day syndrome), although the significance of these findings has been questioned. Tonic pupil has also been reported in young children with Charcot-Marie-Tooth disease. Tonic pupil and other pupillary abnormalities may be noted in ROHHAD syndrome (rapid onset obesity, hypoventilation, hypothalamic dysfunction, and autonomic dysregulation). The occurrence of tonic pupil in association with decreased deep tendon reflexes in young women is referred to as **Adie syndrome.**

Ross syndrome is similar to Adie syndrome and includes decreased deep tendon reflexes and hypohidrosis.

MARCUS GUNN PUPIL

A **relative afferent pupillary defect** (Marcus Gunn pupil) indicates an asymmetric, *prechiasmatic*, afferent conduction defect. It is best demonstrated by the swinging flashlight test, which allows comparison of the direct and consensual pupillary responses in both eyes (Fig. 662.5). With patients fixing on a distant target (to control accommodation), a bright focal light is directed alternately into each eye in turn. In the presence of an afferent lesion, both the direct response to light in the affected eye and the consensual response in the other eye are subnormal. Swinging the light to the better or normal eye causes both pupils to react (constrict) normally. Swinging the light back to the affected eye causes both pupils to redilate to some degree, reflecting the defective conduction. This is a very sensitive and useful test for detecting and confirming optic nerve and retinal disease. This test is only abnormal if there is a "relative" difference in the conduction properties of the optic nerves. Therefore patients with bilateral and symmetric optic nerve

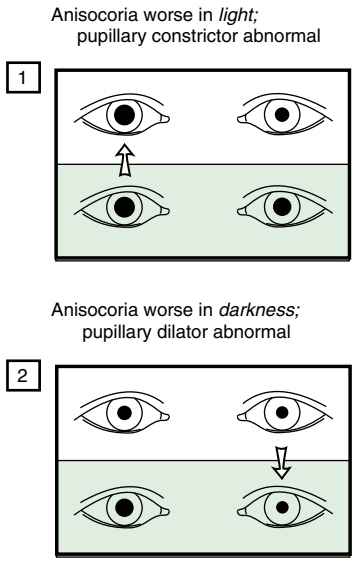

Fig. 662.4 Patient 1 *(top)* has more prominent anisocoria in light than darkness, indicating that the pupillary constrictor of the larger pupil is abnormal (i.e., it fails to constrict in light, *arrow*). Patient 2 has more prominent anisocoria in darkness than light, indicating that the pupillary dilator of the smaller pupil is abnormal (i.e., it fails to dilate in darkness, *arrow*). The diagnosis in patient 1 (abnormal pupillary constrictor) could be a third nerve palsy, tonic pupil, pharmacologic mydriasis, or a disorder of the iris. The diagnosis in patient 2 (abnormal pupillary dilator) could be Horner syndrome or simple anisocoria. In patient 2, both pupils will react to light, whereas the larger pupil of patient 1 does not react well to light. *(From McGee S. Evidence-Based Physical Diagnosis. 3rd ed. Elsevier; 2012; Fig. 20.4, p. 170.)*

disease will not demonstrate an afferent pupillary defect. A subtle relative afferent defect may be found in some children with amblyopia.

HORNER SYNDROME

The principal signs of oculosympathetic paresis (Horner syndrome) are homolateral miosis, mild ptosis, and apparent enophthalmos with slight elevation of the lower lid as a result of the ptosis. Patients may also have decreased facial sweating, increased amplitude of accommodation, and transient decrease in intraocular pressure. If paralysis of the ocular sympathetic fibers occurs before the age of 2 years, heterochromia iridis with hypopigmentation of the iris may occur on the affected side (Fig. 662.6).

Oculosympathetic paralysis may be caused by a lesion (tumor, trauma, infarction) in the midbrain, brainstem, upper spinal cord, neck, middle fossa, or orbit (Table 662.2). Congenital oculosympathetic paresis, often as part of **Klumpke brachial palsy**, is common, although the ocular signs, particularly the anisocoria, may pass undetected for years. Horner syndrome is also seen in some children after thoracic surgery. *Congenital* Horner syndrome may occur in association with vertebral anomalies and with enterogenous cysts. In some infants and children, Horner syndrome is the presenting sign of tumor in the mediastinal or cervical region—specifically neuroblastoma. Rare causes of Horner syndrome, such as vascular lesions or ectopic thymus tissue, also occur in the pediatric age group. In many cases, no cause of congenital Horner syndrome can be identified. Occasionally the condition is familial.

When the cause of Horner syndrome is in question, investigative procedures should be implemented and may include imaging of the head, neck, and chest, as well as 24-hour urinary catecholamine assay. Examining old photographs and old records can sometimes be helpful in establishing the age at onset of Horner syndrome.

The cocaine test is useful in diagnosing oculosympathetic paralysis; a normal pupil dilates within 20-45 minutes after instillation of one or two drops of 4% cocaine, whereas the miotic pupil of an oculosympathetic paresis dilates poorly, if at all, with cocaine. In some cases, there is also denervation supersensitivity of the affected eye to dilute

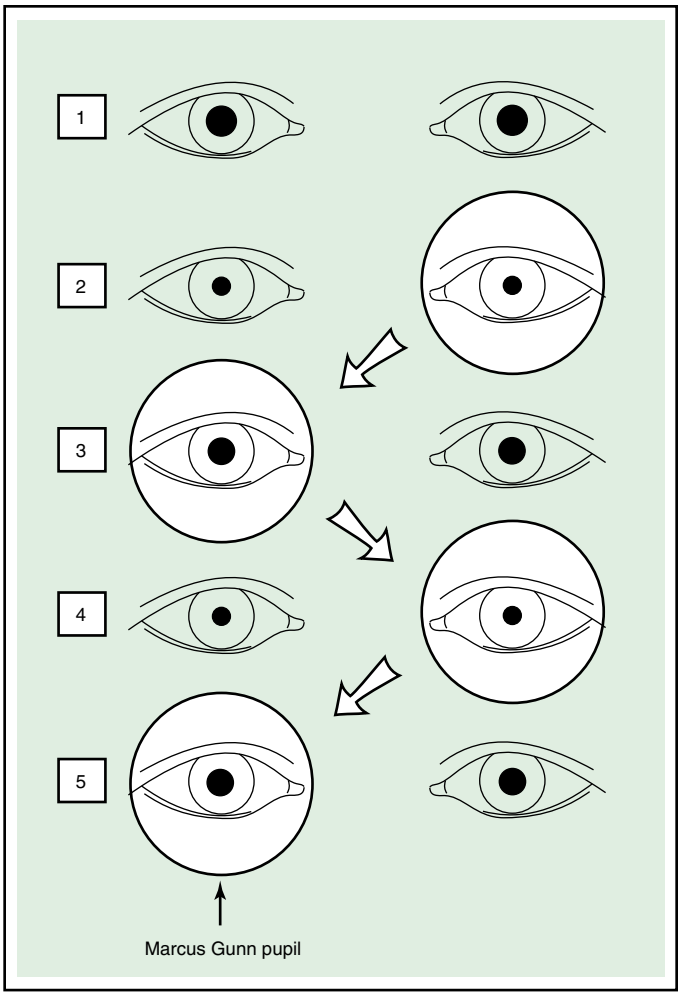

Fig. 662.5 The relative afferent pupillary defect (Marcus Gunn pupil). The figure depicts a patient with an abnormal right optic nerve. Under normal room light illumination (row 1), the pupils are symmetrical. During the swinging flashlight test, the pupils constrict when the normal eye is illuminated (rows 2 and 4) but dilate when the abnormal eye is illuminated (rows 3 and 5). Although both pupils constrict or dilate simultaneously, the clinician is usually focused on just the illuminated pupil. The pupil that dilates during the swinging flashlight test has the "relative afferent pupillary defect" and is labeled the Marcus Gunn pupil. *(From McGee S. Evidence-Based Physical Diagnosis. 3rd ed. Elsevier; 2012; Fig. 20.2, p. 165.)*

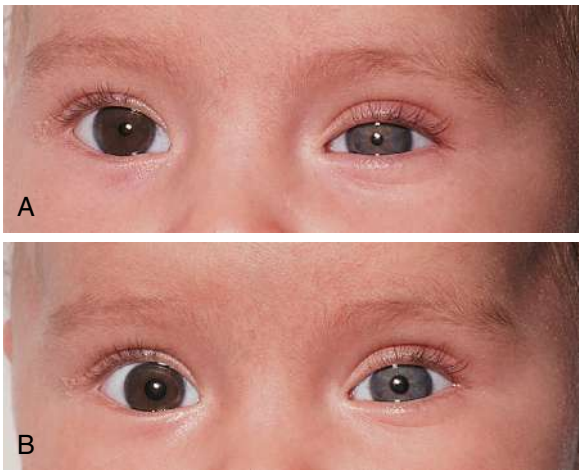

Fig. 662.6 Left congenital Horner syndrome showing upper- and lower-lid ptosis and an iris heterochromia, with the lighter eye being the affected eye. In bright light (**A**) and in the dark (**B**). *(From Hoyt CS, Taylor D, eds. Pediatric Ophthalmology and strabismus. 4th ed. Elsevier; 2013; Fig. 63.9, p. 661.)*

Table 662.2	Causes of Horner Syndrome
CENTRAL (FIRST-ORDER NEURON)	
Brainstem disease – commonly stroke (e.g. lateral medullary infarction), but also tumor, demyelination	
Syringomyelia	
Lateral medullary (Wallenberg) syndrome	
Cervical spinal cord lesion	
Diabetic autonomic neuropathy	
PREGANGLIONIC (SECOND-ORDER NEURON)	
Pancoast tumor	
Carotid and aortic aneurysm and dissection	
Thoracic spinal cord lesion	
Miscellaneous neck lesions (thyroid tumour, enlarged lymph nodes, trauma, postsurgical)	
POSTGANGLIONIC (THIRD-ORDER NEURON)	
Internal carotid artery dissection	
Nasopharyngeal tumour	
Cavernous sinus mass	
Otitis media	
CLUSTER HEADACHE (MIGRAINOUS NEURALGIA)	

From Salman JF: Kanski's Clinical Ophthalmology, 9th ed. London: Elsevier, 2020. Table 19.4

phenylephrine or similar agents. When present, the topical administration of a weak alpha$_1$ agonist may dilate only the affected pupil, leading to a "reversal" of the apparent miosis. Furthermore, instillation of 1% hydroxyamphetamine hydrobromide can help determine the location of sympathetic lesion because it only dilates the pupil if the postganglionic sympathetic neuron is intact.

PARADOXICAL PUPIL REACTION

Some children exhibit paradoxical constriction of the pupils to darkness. An initial brisk constriction of the pupils occurs when the light is turned off, followed by slow redilation of the pupils. The response to direct light stimulation and the near response are normal. The mechanism is not clear, but paradoxical constriction of the pupils in reduced light can be a sign of retinal or optic nerve abnormalities. The phenomenon has been observed in children with congenital stationary night blindness, albinism, retinitis pigmentosa, Leber congenital retinal amaurosis, and Best disease. It has also been observed in those with optic nerve anomalies, optic neuritis, optic atrophy, and possibly amblyopia. Thus children with paradoxical pupillary constriction to darkness should have a thorough ophthalmologic examination.

PERSISTENT PUPILLARY MEMBRANE

Involution of the pupillary membrane and anterior vascular capsule of the lens is usually completed during months 5-6 of fetal development. It is common to see some remnants of the pupillary membrane in newborns, particularly in premature infants. These membranes are nonpigmented strands of obliterated vessels that cross the pupil and may secondarily attach to the lens or cornea. The remnants tend to atrophy in time and usually present no problem. In some cases, however, significant remnants that remain obscure the pupil and interfere with vision. In rare cases, there is patency of the vascular elements; hyphema may result from rupture of persistent vessels.

Intervention must be considered to minimize amblyopia in infants with extensive persistent pupillary membrane of sufficient degree to interfere with vision in the early months of life. In some cases, mydriatics and occlusion therapy may be effective, but in others, surgery may be needed to provide an adequate pupillary aperture.

HETEROCHROMIA

In heterochromia, the two irises are of different color (heterochromia iridium) or a portion of an iris differs in color from the remainder (heterochromia iridis). Simple heterochromia may occur as an autosomal dominant characteristic. Congenital heterochromia is also a feature of Waardenburg syndrome, an autosomal dominant condition characterized principally by lateral displacement of the inner canthi and puncta, pigmentary disturbances (usually a median white forelock and patches of hypopigmentation of the skin), and defective hearing. Change in the color of the iris may occur as a result of trauma, hemorrhage, intraocular inflammation (iridocyclitis, uveitis), intraocular tumor (especially retinoblastoma), intraocular foreign body, glaucoma, iris atrophy, or oculosympathetic palsy (Horner syndrome), which may be associated with a cervical neuroblastoma, melanosis oculi, previous intraocular surgery, and some glaucoma medications.

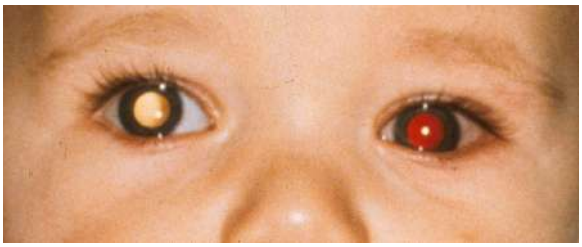

Fig. 662.7 Red reflex. Normal red reflex in the left eye and white reflex in the right eye. This patient was later diagnosed with retinoblastoma in the right eye. *(From Martin RJ, Fanaroff AA, Walsch MC eds. Fanaroff & Martin's Neonatal-Perinatal Medicine. 10th ed. Vol 2, Elsevier; 2015; Fig. 103.7, p. 1739.)*

OTHER IRIS LESIONS

Discrete nodules of the iris, referred to as **Lisch nodules**, are commonly seen in patients with neurofibromatosis (see Chapter 636.1). Lisch nodules represent melanocytic hamartomas of the iris and vary from slightly elevated pigmented areas to distinct ball-like excrescences. The nodules cause no visual disturbance. Lisch nodules are found in 92–100% of individuals older than 5 years of age who have neurofibromatosis but are rare in infancy. Slit-lamp identification of these nodules may help fulfill the criteria required to confirm the diagnosis of neurofibromatosis.

In leukemia (see Chapter 544), there may be infiltration of the iris, sometimes with **hypopyon**, an accumulation of white blood cells in the anterior chamber, which may herald relapse or involvement of the central nervous system.

The lesion of **juvenile xanthogranuloma** (nevoxanthoendothelioma; see Chapter 711) may occur in the eye as a yellowish fleshy mass or plaque of the iris. Spontaneous **hyphema** (blood in the anterior chamber), glaucoma, or a red eye with signs of uveitis may be associated. A search for the skin lesions of xanthogranuloma should be made in any infant or young child with spontaneous hyphema, although the iris lesions may be present without cutaneous manifestations. In many cases, the ocular lesion responds to topical corticosteroid therapy.

LEUKOCORIA

This includes any white pupillary reflex, or so-called *cat's-eye reflex*. Primary diagnostic considerations in any child with leukocoria are cataract, persistent hyperplastic primary vitreous, cicatricial retinopathy of prematurity, retinal detachment, retinoschisis, larval granulomatosis, and retinoblastoma (Fig. 662.7). Also to be considered are endophthalmitis, organized vitreous hemorrhage, leukemic ophthalmopathy, exudative retinopathy (as in Coats disease), and less-common conditions such as medulloepithelioma, massive retinal gliosis, the retinal pseudotumor of Norrie disease, the so-called *pseudoglioma of the Bloch-Sulzberger syndrome*, retinal dysplasia, and the retinal lesions of the phakomatoses. A white reflex may also be seen with fundus coloboma, large atrophic chorioretinal scars, and ectopic medullation of retinal nerve fibers. *Leukocoria is an indication for prompt and thorough evaluation.*

The diagnosis can often be made by direct examination of the eye by ophthalmoscopy and biomicroscopy. Ultrasonographic and radiologic examinations are often helpful. In some cases, the final diagnosis rests with a pathologist.

Visit Elsevier eBooks+ at eBooks.Health.Elsevier.com for Bibliography.

Chapter 663

Disorders of Eye Movement and Alignment

Scott E. Olitsky and Justin D. Marsh

STRABISMUS

Strabismus, or misalignment of the eyes, is one of the most common eye problems encountered in children, affecting approximately 4% of children younger than 6 years of age. Strabismus can result in vision loss (amblyopia) and can have significant psychologic effects. Early detection and treatment of strabismus are essential to prevent permanent visual impairment. Of children with strabismus, 30–50% develop amblyopia. Restoration of proper alignment of the visual axis must occur at an early stage of visual development to allow these children a chance to develop normal binocular vision. The word strabismus means "to squint or to look obliquely." Many terms are used in discussing and characterizing strabismus (Table 663.1).

Orthophoria is the ideal condition of exact ocular balance. It implies that the oculomotor apparatus is in perfect equilibrium so that the eyes remain coordinated and aligned in all positions of gaze and at all distances. Even when binocular vision is interrupted, as by occlusion of one eye, truly orthophoric individuals maintain perfect alignment. Orthophoria is seldom encountered because the majority of individuals have a small latent deviation (heterophoria).

Heterophoria is a latent tendency for the eyes to deviate. This latent deviation is normally controlled by fusional mechanisms that provide binocular vision or avoid diplopia (double vision). The eye deviates only under certain conditions, such as fatigue, illness, or stress, or during tests that interfere with maintenance of these normal fusional abilities (such as covering one eye). If the amount of heterophoria is large, it may give rise to bothersome symptoms, such as transient diplopia (double vision), headaches, or asthenopia (eyestrain). Some degree of heterophoria is found in normal individuals; it is usually asymptomatic.

Heterotropia is a misalignment of the eyes that is constant. It occurs because of an inability of the fusional mechanism to control the deviation. Tropias may be unilateral or may alternate between either eye, depending on the patient. In an alternating tropia, there is no preference for fixation of either eye, and both eyes drift with equal frequency. Because each eye is used periodically, vision usually develops normally. A unilateral tropia is a more serious situation because only one eye is constantly misaligned. The undeviated eye becomes the preferred eye, resulting in loss of vision or amblyopia of the deviated eye.

It is common in ocular misalignments to describe the type of deviation. This helps to make decisions on the cause and treatment of the strabismus. The prefixes *eso-*, *exo-*, *hyper-*, and *hypo-* are added to the terms *phoria* and *tropia* to further delineate the type of strabismus. Esophorias and esotropias are inward or convergent deviations of the eyes, commonly known as *crossed eyes*. Exophorias and exotropias are divergent or outward-facing eye deviations, *walleyed* being the lay term. Hyperdeviations and hypodeviations designate upward or downward, respectively, deviations of an eye. In cases of unilateral strabismus, the deviating eye is often part of the description of the misalignment (left esotropia).

Diagnosis

Many techniques are used to assess ocular alignment and movement of the eyes to aid in diagnosing strabismic disorders. In a child with strabismus or any other ocular disorder, assessment of visual acuity is mandatory. Decreased vision in one eye requires evaluation for a strabismus or other ocular abnormalities, which may be difficult to discern on a brief screening evaluation. Even strabismic deviations of only a few degrees in magnitude, too small to be evident by gross inspection, may lead to amblyopia and significant vision loss.

Corneal light reflex tests are perhaps the most rapid and easily performed diagnostic tests for strabismus. They are particularly useful in children who are uncooperative and in those who have poor ocular fixation. To perform the **Hirschberg corneal reflex test,** the examiner projects a light source onto the cornea of both eyes simultaneously as a child looks directly at the light. Comparison should then be made of the placement of the corneal light reflex in each eye. In straight eyes, the light reflection appears symmetric and, because of the relationship between the cornea and the macula, slightly nasal to the center of each pupil. If strabismus is present, the reflected light is asymmetric and appears displaced in one eye. The Krimsky method of the corneal reflex test uses prisms placed over one or both eyes to align the light reflections. The amount of prism needed to align the reflections is used to measure the degree of deviation. Although it is a useful screening test, corneal light reflex testing may not detect a small angle or an intermittent strabismus.

Cover tests for strabismus require a child's attention and cooperation, good eye movement capability, and reasonably good vision in each eye (Fig. 663.1). If any of these are lacking, the results of these tests may not be valid. These tests consist of the cover-uncover test and the alternate cover test. In the cover-uncover test, a child looks at an object in the distance, preferably 6 m away. An eye chart is commonly used for fixation in children older than 3 years of age. For younger children, a noise-making toy or movie helps hold their attention for the test. As the child looks at the distant object, the examiner covers one eye and watches for movement of the uncovered eye. If no movement occurs, there is no apparent misalignment of that eye. After one eye is tested, the same procedure is repeated on the other eye. When performing the alternate cover test, the examiner rapidly covers and uncovers each eye, shifting back and forth from one eye to the other. If the child has an ocular deviation, the eye rapidly moves as the cover is shifted to the other eye. Both the cover-uncover test and the alternate cover test should be performed at both distance and near fixation. The cover-uncover test differentiates tropias, or manifest deviations, from latent deviations, called **phorias**.

Clinical Manifestations and Treatment

The etiologic classification of strabismus is complex, and the causative types must be distinguished; there are comitant and noncomitant forms of strabismus.

Comitant Strabismus

Comitant strabismus is the most common type of strabismus. The individual extraocular muscles usually have no defect, and extraocular motility is full in all positions of gaze. The amount of deviation is constant, or relatively constant, in the various directions of gaze.

Pseudostrabismus is one of the most common reasons a pediatric ophthalmologist is asked to evaluate an infant. This condition is characterized by the false appearance of strabismus when the visual axes are aligned accurately. This appearance may be caused by a flat, broad nasal bridge, prominent epicanthal folds, or a narrow interpupillary distance, giving the appearance of esotropia despite the eyes being aligned (pseudoesotropia). The observer may see less white sclera nasally than would be expected, and the impression is that the eye is turned in toward the nose, especially when the child gazes to either side. Parents frequently comment that when their child looks to the side, the eye almost disappears from view. Pseudoesotropia can be differentiated from a true misalignment of the eyes when the corneal light reflex is centered in both eyes and when the cover-uncover test shows no refixation movement. Once pseudoesotropia has been confirmed, parents can be reassured that the child will outgrow the appearance of esotropia. As the child grows, the bridge of the nose becomes more prominent and displaces the epicanthal folds, and the medial sclera becomes proportional to the amount visible on the lateral aspect. It is the appearance of crossing that the child will outgrow. Because true esotropia can develop later in children with pseudoesotropia, parents and pediatricians should

be cautioned that reassessment is required if the apparent deviation does not improve.

Esodeviations are the most common type of ocular misalignment in children and represent >50% of all ocular deviations. *Congenital esotropia* is a confusing term. Few children who are diagnosed with this disorder are actually born with an esotropia. For this reason, infants with confirmed onset earlier than 6 months are typically considered to have what was previously classified as congenital esotropia, although the term **infantile esotropia** is perhaps a more accurate description.

Between 2-4 months of age, many infants will exhibit strabismus, including esotropia, which typically resolve spontaneously. Esotropia that resolves without treatment do so before 10-12 weeks of age and have intermittent or variable deviations. Those most likely to benefit from active treatment have persistent esotropia (10 weeks-6 months of age) and constant esotropia (40 PD), in combination with a refractive error ≤ +3.00 D, and the absence of prematurity, developmental delay, meningitis, nystagmus, eye anomalies, and incomitant or paralytic strabismus. The evaluation is noted in Figure 663.2.

Table 663.1 Description of Alignment and Movement

NORMAL OCULAR ALIGNMENT: ORTHOPHORIA
LATENCY
phoria: development of abnormality only during certain conditions (fatigue, illness, cover test)
tropia: abnormality present during normal conditions; deviation may be constant or intermittent
DIRECTION OF DEVIATION
Eso-: inward, horizontal deviation ("crossing")
Exo-: outward, horizontal deviation ("wall eye")
Hyper-: upward, vertical deviation
Hypo-: downward, vertical deviation
Incyclo-: nasal torsional deviation of the superior pole of the cornea
Excyclo-: temporal torsional deviation of the superior pole of the cornea
EQUALITY OF DEVIATION
Concomitant: misalignment is equal in all positions of gaze
Noncomitant: misalignment varies significantly in different positions of gaze
NEUROMUSCULAR DYSFUNCTION
Paralytic: misalignment secondary to a cranial nerve palsy, muscle weakness, or mechanical restriction (usually noncomitant)
Nonparalytic: no underlying neuromuscular dysfunction; usually concomitant but can be noncomitant
TANDEM MOVEMENTS OF BOTH EYES
version: both eyes move in same direction (conjugate); direction of movement: levo- (left), dextro- (right), supra- (up), infra- (down)
vergence: eyes move in opposite directions (disconjugate); convergence (inward movement), divergence (outward movement)

From Costakos D. Eye disorders. In: Kliegman RM, Bordini BJ, Toth H, Basel D, eds. *Nelson Pediatric Symptom-Based Diagnosis.* 2nd ed, Philadelphia: Elsevier; 2022: Table 43.2, p. 787.

The characteristic angle of infantile esodeviations is large and constant (Fig. 663.3). Because of the large deviation, cross-fixation is frequently encountered. This is a condition in which the child looks to the right with the left eye and to the left with the right eye. With cross-fixation, there is no need for the eye to turn away from the nose (abduction) as the adducting eye is used in side gaze; this condition simulates a sixth nerve palsy. Abduction can be demonstrated by the doll's-head maneuver or by patching one eye for a short time. Children with infantile esotropia tend to have refractive errors similar to those of normal children of the same age. This contrasts with the characteristic high level of farsightedness associated with accommodative esotropia. **Amblyopia** is common in children with infantile esotropia.

The primary goal of **treatment** in infantile esotropia is to eliminate or reduce the deviation as much as possible. Ideally this results in normal sight in each eye, in straight-looking eyes, and in the development of binocular vision. Early treatment (before age 2 years) is more likely to lead to the development of binocular vision, which helps maintain long-term ocular alignment. Once any associated amblyopia is treated, surgery is performed to align the eyes. Even with successful surgical alignment, it is common for vertical deviations to develop in children with a history of infantile esotropia. The two most common forms of vertical deviations to develop are inferior oblique muscle overaction and dissociated vertical deviation. In inferior oblique muscle overaction, the overactive inferior oblique muscle produces an upshoot of the eye closest to the nose when the patient looks to the side (Fig. 663.4). In dissociated vertical deviation, one eye drifts up slowly with no movement of the other eye. Surgery may be necessary to treat either or both of these conditions.

It is important that parents realize that early successful surgical alignment is only the beginning of the treatment process. Because many children may redevelop strabismus or amblyopia, they need to be monitored closely during the visually immature period of life.

Accommodative esotropia is defined as a "convergent deviation of the eyes associated with activation of the accommodative (focusing) reflex." It usually occurs in a child who is between 2-3 years of age and who has a history of acquired intermittent or constant crossing. Amblyopia occurs in the majority of cases.

The mechanism of accommodative esotropia involves uncorrected hyperopia, accommodation, and accommodative convergence. The image entering a hyperopic (farsighted) eye is blurred. If the amount of hyperopia is not significant, the blurred image can be sharpened by accommodating (focusing of the lens of the eye). Accommodation is closely linked with convergence (eyes turning inward) because both are required to view an object at near. If a child's hyperopic refractive error

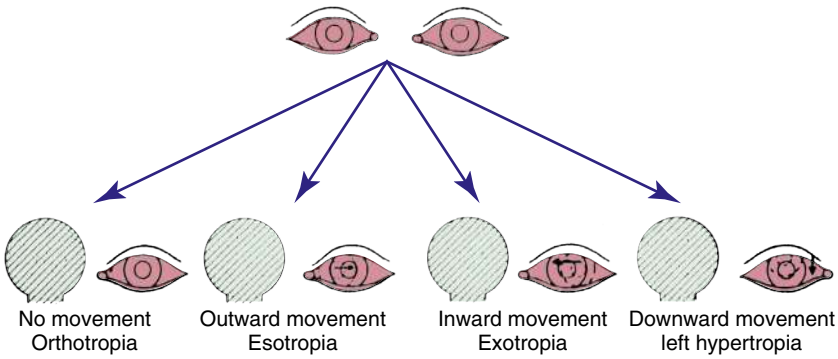

Fig. 663.1 The cover test. In each instance, the occluder is placed over the right eye while the patient is viewing a fixation target and the examiner is watching for movement of the patient's left eye. If the left eye is not aligned, it will need to move to look at the fixation target. If there is no movement of the left eye, the test needs to be repeated by occluding the left eye and watching for movement of the right eye. *(From Kliegman RM, Lye PS, Bordini BJ, Toth H, Basel D, eds. Nelson Pediatric Symptom-Based Diagnosis. Elsevier; 2018: Fig. 32.6, p. 567).*

is large or if the amount of convergence that occurs in response to each unit of accommodative effort is great, esotropia may develop.

The **treatment** for accommodative esotropia is to prescribe the full hyperopic (farsighted) correction. These glasses eliminate a child's need to accommodate and therefore correct the esotropia (Fig. 663.5). Although many parents are initially concerned that their child will not want to wear glasses, the benefits of binocular vision and the decrease in the focusing effort required to see clearly provide a strong stimulus to wear glasses, and they are generally accepted well. The full hyperopic correction sometimes straightens the eye position at distance fixation but leaves a residual deviation at near fixation. This may be observed, treated with bifocal lenses, or treated with surgery.

It is important to warn parents of children with accommodative esotropia that the esodeviation may appear to increase without glasses after the initial correction is worn. Parents frequently state that before wearing glasses, their child had a small esodeviation, whereas after removal of the glasses, the esodeviation becomes quite large. Parents often blame the increased esodeviation on the glasses. This apparent increase is a result of the child using the appropriate amount of accommodative effort after the glasses have been worn. When these children remove their glasses, they continue to use an accommodative effort to bring objects into proper focus and increase the esodeviation.

Most children maintain straight eyes once initially treated. Because hyperopia generally decreases with age, patients may outgrow the need to wear glasses to maintain alignment. In some patients, a residual esodeviation persists even when wearing their glasses. This condition commonly occurs when there is a delay between the onset of accommodative esotropia and treatment. In others, the esotropia may initially be eliminated with glasses, but crossing redevelops and is not correctable with glasses. Any residual component of esotropia that is not fully correctable with glasses is typically referred to as "nonaccommodative," and a child with both accommodative and nonaccommodative components of esotropia is often referred to as having "partially accommodative" esotropia. Surgery for the nonaccommodative portion of the crossing may be indicated to restore binocular vision.

Exodeviations are the second most common type of misalignment. The divergent deviation may be intermittent or constant. Intermittent exotropia is the most common exodeviation in childhood. It is characterized by outward drifting of one eye, which usually occurs when a child is fixating at distance. The deviation is generally more frequent with fatigue or illness. Exposure to bright light may cause reflex closure of the exotropic eye. Because the eyes initially can be kept straight most of the time, visual acuity tends to be good in both eyes and binocular vision is initially normal.

The age at onset of intermittent exotropia varies but is often between age 6 months and 4 years. The decision to perform eye muscle surgery is based on the amount and frequency of the deviation. If the deviation is small and infrequent, it is reasonable to observe the child. If the exotropia is large or increasing in frequency, surgery is indicated to maintain normal binocular vision.

Constant exotropia may rarely be congenital. Congenital exotropia may be associated with neurologic disease or abnormalities of the bony orbit, as in Crouzon syndrome. Exotropia that occurs later in life may represent a deterioration of an intermittent exotropia that was present in childhood. Surgery can restore binocular vision even in long-standing cases.

Noncomitant Strabismus

When an eye muscle is paretic, palsied, or restricted, a muscle imbalance occurs in which the deviation of the eye varies according to the direction of gaze. Recent onset of a paretic muscle can be suggested by the symptom of double vision that increases in one direction, the findings of an ocular deviation that increases in the field of action of the paretic muscle, and an increase in the deviation when the child fixates with the paretic eye. It is important to differentiate a noncomitant strabismus from a comitant deviation because noncomitant forms

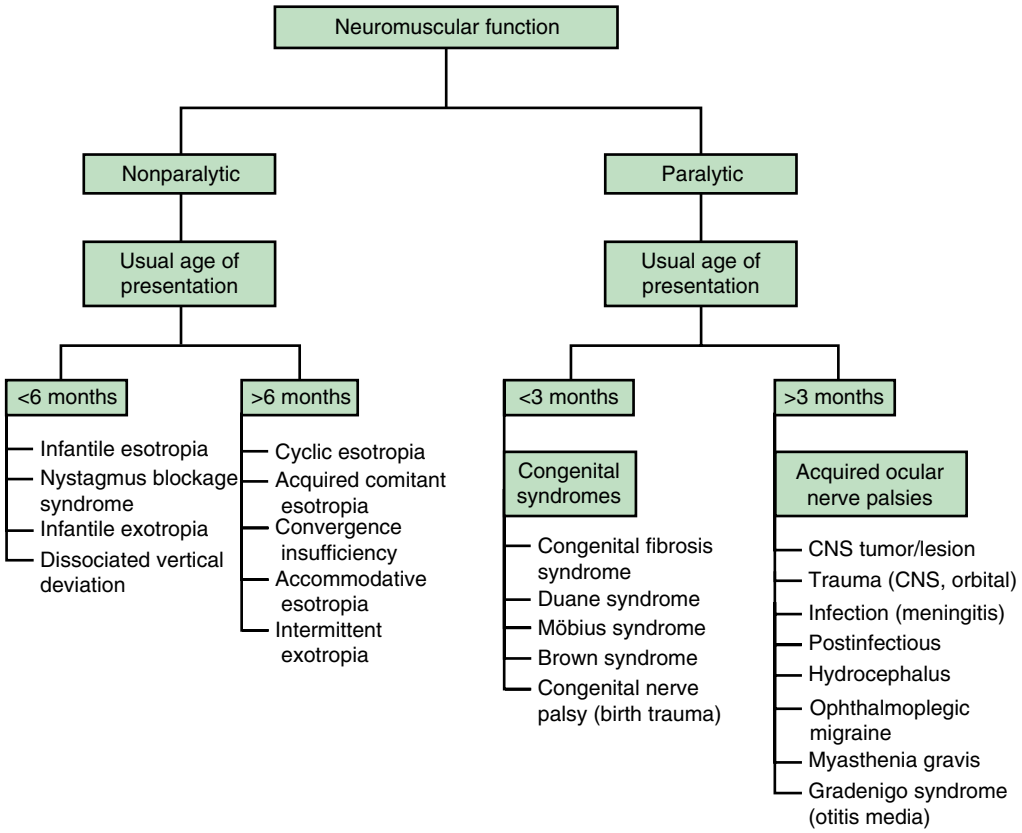

Fig. 663.2 Evaluation of strabismus. CNS, Central nervous system. *(From Costakos D. Eye disorders. In: Kliegman RM, Bordini BJ, Toth H, Basel D, eds. Nelson Pediatric Symptom-Based Diagnosis. 2nd ed. Philadelphia: Elsevier; 2022: Fig. 43.9, p. 789).*

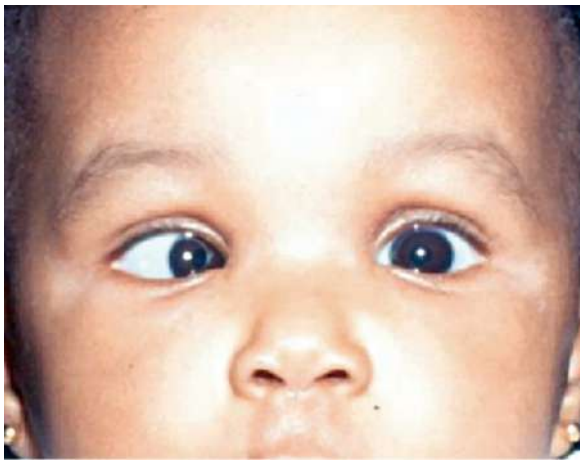

Fig. 663.3 Congenital esotropia. Note the large angle of crossing.

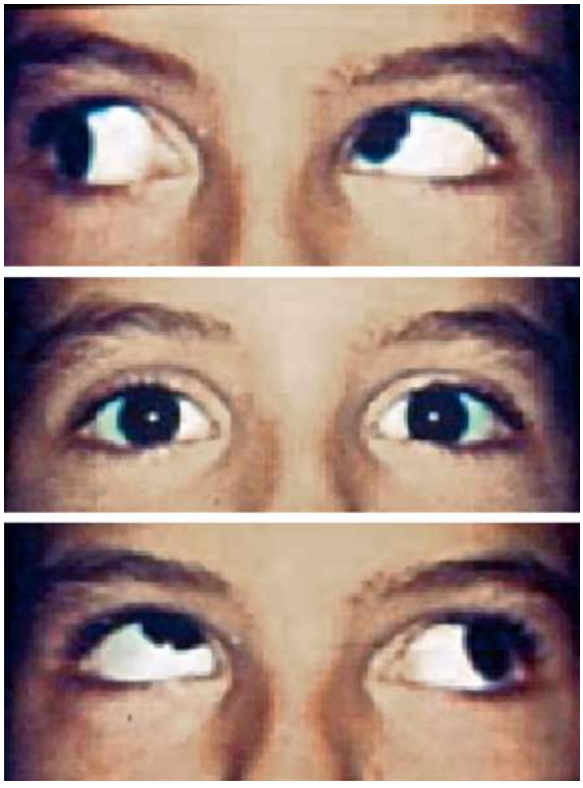

Fig. 663.4 Inferior oblique muscle overaction.

of strabismus are often associated with trauma, systemic disorders, or neurologic abnormalities (Table 663.2).

Third Nerve Palsy

In the pediatric population, third nerve palsies are usually congenital. The congenital form is often associated with a developmental anomaly or birth trauma. Acquired third nerve palsies in children can be an ominous sign and may indicate a neurologic abnormality such as increased intracranial pressure (ICP) and an intracranial neoplasm or aneurysm. Other, less serious causes include an inflammatory or infectious lesion, head trauma, postviral syndromes, and migraines.

A third nerve palsy, whether congenital or acquired, usually results in an exotropia and a hypotropia, or downward deviation of the affected eye, as well as complete or partial ptosis of the upper lid. This characteristic strabismus results from the action of the normal, unopposed muscles, the lateral rectus muscle, and the superior oblique muscle. If

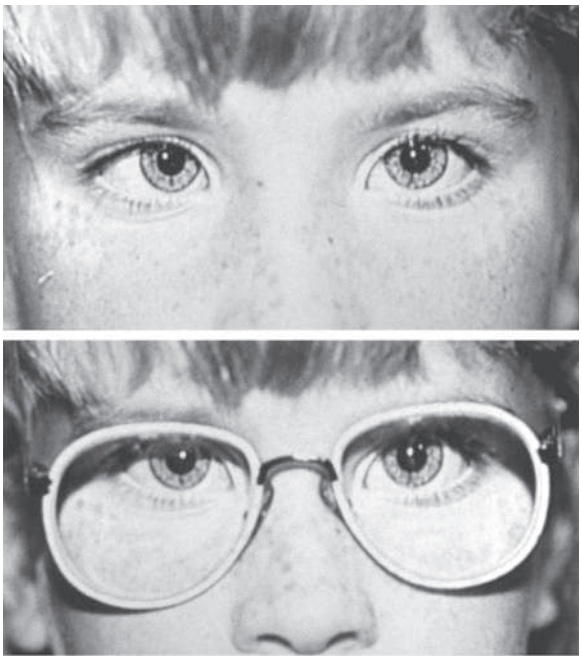

Fig. 663.5 Accommodative esotropia. Control of deviation with corrective lenses.

the internal branch of the third nerve is involved, pupillary dilation may be noted as well. Eye movements are usually limited nasally, in elevation, and in depression. In addition, clinical findings and treatment may be complicated in congenital and traumatic cases of third nerve palsy, owing to misdirection of regenerating nerve fibers, referred to as *aberrant regeneration*. This results in anomalous and paradoxical eyelid, eye, and pupil movement such as elevation of the eyelid, constriction of the pupil, or depression of the globe on attempted medial gaze.

Fourth Nerve Palsy

These palsies can be congenital or acquired. Because the fourth nerve has a long intracranial course, it is susceptible to damage resulting from head trauma. In children, however, fourth nerve palsies are more frequently congenital than traumatic. A palsied fourth nerve results in weakness in the superior oblique muscle, which causes an upward deviation of the affected eye, a hypertropia. Because the antagonist muscle, the inferior oblique, is relatively unopposed, the affected eye demonstrates an upshoot when looking toward the nose. Children typically present with a head tilt to the shoulder opposite the affected eye and may also position their chin down and face turned away from the affected side. This head position places the eye away from the area of greatest action of the affected muscle and therefore minimizes the deviation and the associated double vision. Because the abnormal head posture maintains the child's ocular alignment, amblyopia is uncommon. Because no abnormality exists in the neck muscles, attempts to correct the head tilt by exercises and neck muscle surgery are ineffective. Recognition of a superior oblique paresis can be difficult because deviation of the head and the eye may be minimal. **Treatment** may include eye muscle surgery to improve the ocular alignment and eliminate the abnormal head posture.

Sixth Nerve Palsy

These palsies produce markedly crossed eyes with limited ability to move the afflicted eye laterally. Children frequently present with their head turned toward the palsied muscle, a position that helps preserve binocular vision. The esotropia is largest when the eye is moved toward the affected muscle.

Congenital sixth nerve palsies are rare. Decreased lateral gaze in infants is often associated with other disorders, such as infantile esotropia or Duane retraction syndrome. In neonates, a transient sixth nerve paresis can occur; it usually clears spontaneously by 6 weeks. It

Table 663.2 Less Common Forms of Strabismus

TYPE OF STRABISMUS	PRESENTING SYMPTOMS AND SIGNS	CAUSE	TREATMENT
Duane syndrome	Esotropia with deficient abduction or exotropia with deficient adduction of one eye; head turn	Absence of sixth nerve nucleus and aberrant innervation of lateral rectus muscle from third cranial nerve	Strabismus surgery for correction of large deviations or abnormal head position
Dissociated vertical deviation	One eye turns up intermittently, especially with fatigue	Eye movement abnormality related most commonly to congenital esotropia	Eye muscle surgery on superior rectus and inferior oblique muscles
Brown syndrome	Head tilt; inability to elevate eye in adduction	Restriction of free passage of superior oblique tendon through trochlea	Observation if not severe; superior oblique tendon surgery if severe
Möbius syndrome	Masklike facies; inability to abduct both eyes; difficulty closing eyes	Bilateral sixth and seventh nerve palsies	Protect corneas from exposure; strabismus surgery
Congenital fibrosis syndrome	Chin-up head position; inability to elevate eyes; ptosis	Autosomal dominant gene on chromosome 16 in some patients; superior division of third nerve in others	Surgical release of tight extraocular muscles
Third nerve palsy	Exotropia and hypertropia; ptosis; dilated, nonreactive pupil	Congenital absence of third nerve; trauma; tumor	Ptosis and strabismus surgery
Double elevator palsy	Chin-up head posture; inability to elevate one eye	Paresis of superior rectus muscle	Transposition strabismus surgery
Orbital floor fracture	Vertical diplopia; chin-up head position	Entrapment of orbital tissues in fracture	Repair of floor fracture; release of inferior rectus muscle restriction
Myasthenia: congenital or acquired	Variable ptosis and eye movement abnormalities	Blockage of acetylcholine receptor sites by immune complexes	Treatment of systemic myasthenia; strabismus surgery if patient is stable
Mitochondrial disorders	Ptosis, progressive external ophthalmoplegia, optic neuropathy, cardiomyopathy, peripheral myopathy	Various mitochondrial variants	Supportive

From Costakos D. Eye disorders. In: Kliegman RM, Bordini BJ, Toth H, Basel D, eds. *Nelson Pediatric Symptom-Based Diagnosis.* 2nd ed. Philadelphia: Elsevier; 2022: Table 43.3, p. 790.

is believed that increased ICP associated with labor and delivery is the contributing factor.

Acquired sixth nerve palsies in childhood are often an ominous sign because the sixth nerve is susceptible to increased ICP associated with hydrocephalous and intracranial tumors. Other causes of sixth nerve defects in children include trauma, vascular malformations, meningitis, and Gradenigo syndrome. A benign sixth nerve palsy, which is painless and acquired, can be noted in infants and older children. This is frequently preceded by a febrile illness or upper respiratory tract infection and may be recurrent. Complete resolution of the palsy is common in this scenario, although other causes of an acute sixth nerve palsy should be eliminated before this diagnosis is made.

Strabismus Syndromes

Special types of strabismus have unusual clinical features. Most of these disorders are caused by structural anomalies of the extraocular muscles or adjacent tissues. Most strabismus syndromes produce noncomitant misalignments.

Monocular Elevation Deficiency

A monocular elevation deficit in both abduction and adduction is referred to as *monocular elevation deficiency* (previously called *double-elevator palsy*). It may represent a paresis of both elevators, the superior rectus and inferior oblique muscles, or a possible restriction to elevation from a fibrotic inferior rectus muscle. When an affected child fixates with the nonparetic eye, the paretic eye is hypotropic and the ipsilateral upper eyelid may appear ptotic. Fixation with the paretic eye causes a hypertropia of the nonparetic eye and a disappearance of the ptosis (Fig. 663.6). Because the apparent ptosis is actually secondary to the strabismus, correction of the hypotropia treats the pseudoptosis.

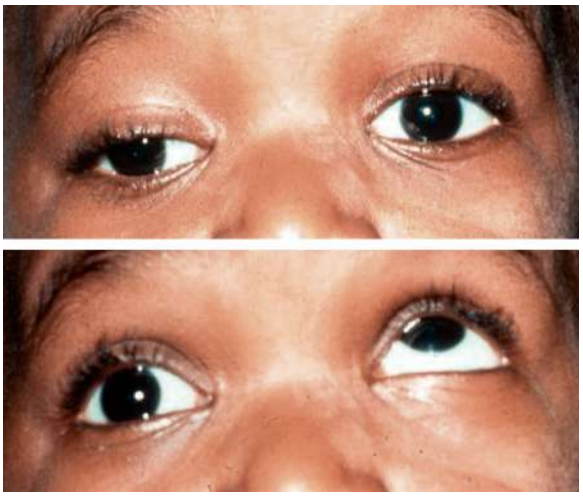

Fig. 663.6 Double-elevator palsy of the right eye. Note the disappearance of the apparent ptosis when fixating with the involved eye.

Duane Syndrome

This congenital disorder of ocular motility is characterized by retraction of the globe on adduction. Duane syndrome occurs more frequently in females and involves the left eye more commonly than the right eye. It is caused by the absence of the sixth nerve nucleus and subsequent anomalous innervation of the lateral rectus muscle, which results in co-contraction of the medial and lateral rectus muscles on attempted adduction of the affected eye. Within the spectrum of Duane syndrome, patients may exhibit impairment of abduction, impairment

of adduction, or upshoot or downshoot of the involved eye on adduction. They may have esotropia, exotropia, or relatively straight eyes. Many children exhibit a compensatory head posture to maintain single vision. Some develop amblyopia. Surgery to improve alignment or to reduce a noticeable face turn can be helpful in selected cases. Duane syndrome usually occurs sporadically, but it can be inherited as an autosomal dominant trait. While typically occurring as an isolated condition, some patients may have various associated ocular and systemic anomalies.

Möbius Syndrome

The distinctive features of Möbius syndrome are congenital facial paresis and abduction weakness. The facial palsy is commonly bilateral, frequently asymmetric, and often incomplete, tending to spare the lower face and platysma. Ectropion, epiphora, and exposure keratopathy may develop. The abduction defect may be unilateral or bilateral. Esotropia is common. The cause is unknown. Whether the primary defect is maldevelopment of cranial nerve nuclei, hypoplasia of the muscles, or a combination of central and peripheral factors is unclear. Some familial cases have been reported. Associated developmental defects may include ptosis, palatal and lingual palsy, hearing loss, pectoral and lingual muscle defects, micrognathia, syndactyly, supernumerary digits, and the absence of hands, feet, fingers, or toes. Surgical correction of the esotropia is indicated and any attendant amblyopia should be treated.

Brown Syndrome

In this syndrome, elevation of the eye in the adducted position is restricted (Fig. 663.7). An associated downward deviation of the affected eye in adduction may also occur. A compensatory head posture may be evident. Brown syndrome occurs as a result of restriction of the superior oblique tendon as it moves through the trochlea. Cases may be congenital or acquired. Acquired Brown syndrome may follow trauma to the orbit involving the region of the trochlea or sinus surgery. It may also occur with inflammatory processes, particularly sinusitis and juvenile idiopathic arthritis.

Acquired inflammatory Brown syndrome may respond to treatment with either nonsteroidal medications or corticosteroids. Surgery may be helpful for selected cases of Brown syndrome.

Parinaud Syndrome

This eponym designates a palsy of vertical gaze, isolated or associated with pupillary or nuclear oculomotor (third cranial nerve) paresis. It indicates a lesion affecting the mesencephalic tegmentum. The ophthalmic signs of midbrain disease include vertical gaze palsy, dissociation of the pupillary responses to light and to near focus, general pupillomotor paralysis, corectopia, dyscoria, accommodative disturbances, pathologic lid retraction, ptosis, extraocular muscle paresis, and convergence paralysis. Some cases have associated spasms of convergence, convergent retraction nystagmus, and vertical nystagmus, particularly on attempted vertical gaze. Combinations of these signs are referred to as the **sylvian aqueduct syndrome**.

A principal cause of vertical gaze palsy and associated mesencephalic signs in children is tumor of the pineal gland or third ventricle. Differential diagnosis includes trauma and demyelinating disease. In children with hydrocephalus, impairment of vertical gaze and pathologic lid retraction are referred to as the *setting-sun sign*. A transient supranuclear disorder of gaze is sometimes seen in healthy neonates.

CONGENITAL OCULAR MOTOR APRAXIA

This congenital disorder of conjugate gaze is characterized by a defect in voluntary horizontal gaze, compensatory jerking movement of the head, and retention of slow pursuit and reflexive eye movements. Additional features are absence of the fast (refixation) phase of optokinetic nystagmus and obligate contraversive deviation of the eyes on rotation of the body. Affected children typically are unable to look quickly to either side voluntarily in response to a command or in response to an eccentrically presented object but may be able to follow a slowly moving target to either side. To compensate for the defect in purposive lateral eye movements, children jerk their head to bring the eyes into the desired position and may also blink repetitively in an attempt to change fixation. The signs tend to become less conspicuous with age.

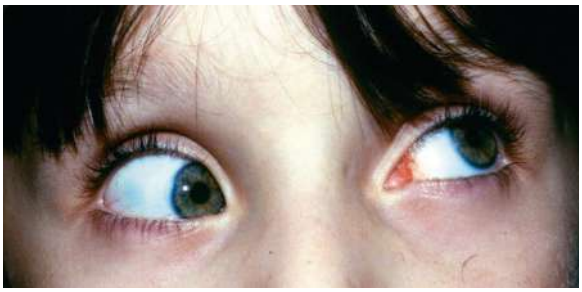

Fig. 663.7 Brown syndrome of the right eye.

The pathogenesis of congenital ocular motor apraxia is unknown. It may be a result of delayed myelination of the ocular motor pathways. Structural abnormalities of the central nervous system (CNS) have been found in a few patients, including agenesis of the corpus callosum and cerebellar vermis, porencephaly, hamartoma of the foramen of Monro, and macrocephaly. Many children with congenital ocular motor apraxia show delayed motor and cognitive development.

NYSTAGMUS

Nystagmus (rhythmic oscillations of one or both eyes) may be caused by an abnormality in any one of the three basic mechanisms that regulate position and movement of the eyes: the fixation, conjugate gaze, or vestibular mechanism. In addition, physiologic nystagmus may be elicited by appropriate stimuli (Table 663.3).

Congenital sensory nystagmus is generally associated with ocular abnormalities that lead to decreased visual acuity; common disorders that lead to early-onset nystagmus include albinism, aniridia, achromatopsia, congenital cataracts, congenital macular lesions, congenital optic atrophy, and congenital optic nerve hypoplasia. In some instances, nystagmus occurs as a dominant or X-linked characteristic without obvious ocular abnormalities.

Congenital idiopathic motor nystagmus is characterized by horizontal jerky oscillations, often with gaze preponderance. There are no ocular anatomic defects that cause the nystagmus, and the visual acuity is generally near normal. There may be a null point in which the nystagmus damps and the vision improves; a compensatory head posture will develop that places the eyes into the position of least nystagmus. The cause of congenital idiopathic motor nystagmus is unknown; in some instances, this is familial. Eye muscle surgery may be performed to eliminate an abnormal head posture by bringing the point of best vision into straight-ahead gaze.

Acquired nystagmus requires prompt and thorough evaluation. Spontaneous nystagmus is often associated with either peripheral or central vestibular disorders. Peripheral disorders are often acute and benign, but the severity of symptoms is often problematic to the patient (room spinning, unsteady gait, tinnitus, diaphoresis). Central vestibular lesions are more concerning for CNS disorders (vestibular nuclei, brainstem, cerebellum, cortex); symptoms are more chronic and less severe. Worrisome pathologic types are the gaze-paretic or gaze-evoked oscillations of cerebellar, brainstem, or cerebral disease.

Nystagmus retractorius or **convergent nystagmus** is repetitive jerking of the eyes into the orbit or toward each other. It is usually seen with vertical gaze palsy as a feature of Parinaud (sylvian aqueduct) syndrome. The causal condition may be neoplastic, vascular, or inflammatory. In children, nystagmus retractorius suggests particularly the presence of pinealoma or hydrocephalus.

A diagnostic approach to nystagmus is noted in Figures 663.8 and 663.9 and Table 663.4.

Table 663.3 Specific Patterns of Nystagmus

PATTERN	DESCRIPTION	ASSOCIATED CONDITIONS
Latent nystagmus	Conjugate jerk nystagmus toward viewing eye	Congenital vision defects, occurs with occlusion of eye
Manifest latent nystagmus	Fast jerk to viewing eye	Strabismus, congenital idiopathic nystagmus
Periodic alternating	Cycles of horizontal or horizontal-rotary that change direction	Caused by both visual and neurologic conditions
Seesaw nystagmus	One eye rises and intorts as other eye falls and extorts	Usually associated with optic chiasm defects
Nystagmus retractorius	Eyes jerk back into orbit or toward each other	Caused by pressure on mesencephalic tegmentum (Parinaud syndrome)
Gaze-evoked nystagmus	Jerk nystagmus in direction of gaze	Caused by medications, brainstem lesion, or labyrinthine dysfunction
Gaze-paretic nystagmus	Eyes jerk back to maintain eccentric gaze	Cerebellar disease
Downbeat nystagmus	Fast phase beating downward	Posterior fossa disease, drugs
Upbeat nystagmus	Fast phase beating upward	Brainstem and cerebellar disease; some visual conditions
Vestibular nystagmus	Horizontal-torsional or horizontal jerks	Vestibular system dysfunction
Asymmetric or monocular nystagmus	Pendular vertical nystagmus	Disease of retina and visual pathways
Spasmus nutans	Fine, rapid, pendular nystagmus	Torticollis, head nodding; idiopathic or gliomas of visual pathways

From Kliegman R. *Practical Strategies in Pediatric Diagnosis and Therapy.* Philadelphia: WB Saunders;1996.

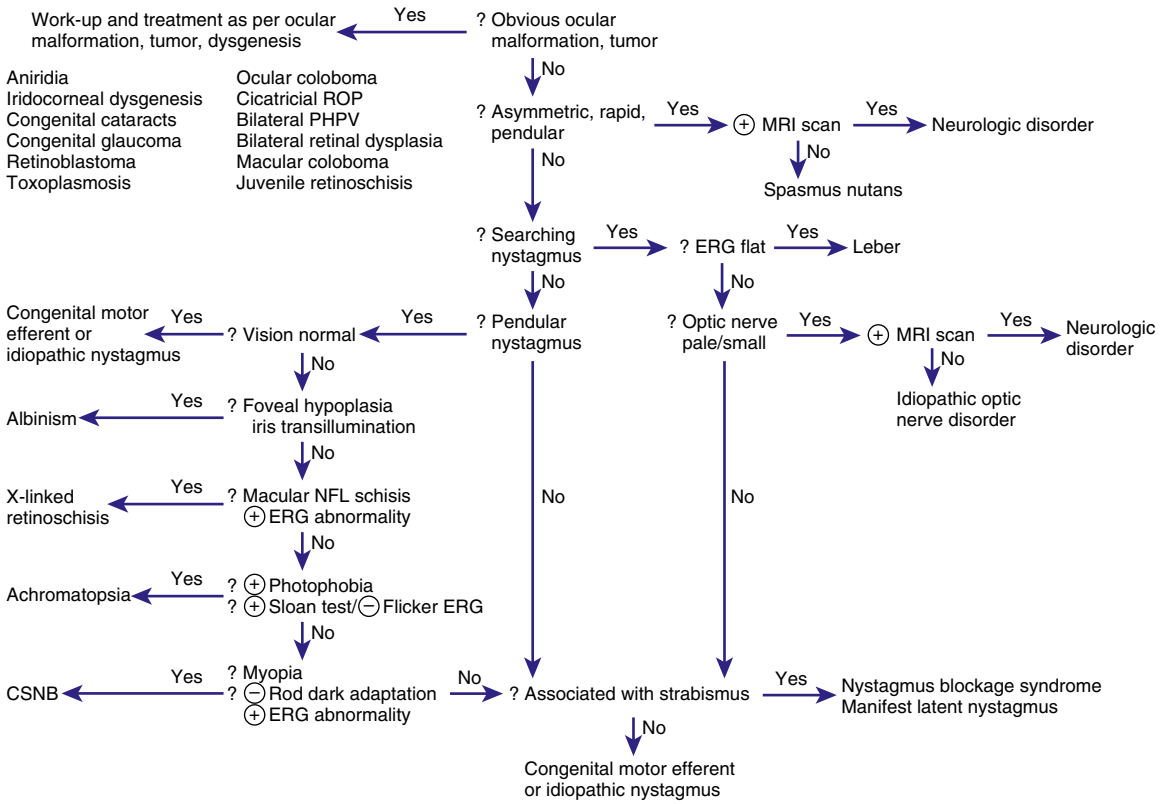

Fig. 663.8 Algorithm for the work-up of an infant with nystagmus. ⊕, Positive; ⊖, negative; CSNB, congenital stationary night blindness; ERG, electroretinogram; NFL, nerve fiber layer; PHPV, persistent hyperplastic primary vitreous; ROP, retinopathy of prematurity. *(From Nelson LB. Harley's Pediatric Ophthalmology. 4th ed. Philadelphia: Saunders; 1998: p. 470.)*

Spasmus nutans is a special type of acquired nystagmus in childhood (see also Chapter 637). In its complete form, it is characterized by the **triad** of pendular nystagmus, head nodding, and torticollis. The nystagmus is characteristically very fine, very rapid, horizontal, and pendular; it is often asymmetric, sometimes unilateral. Signs usually develop within the first year or two of life. Components of the triad may develop at various times. In many cases, the condition is benign and self-limited, usually lasting a few months, sometimes years. The cause of this classic type of spasmus nutans, which usually resolves spontaneously, is unknown. Some children exhibiting signs resembling

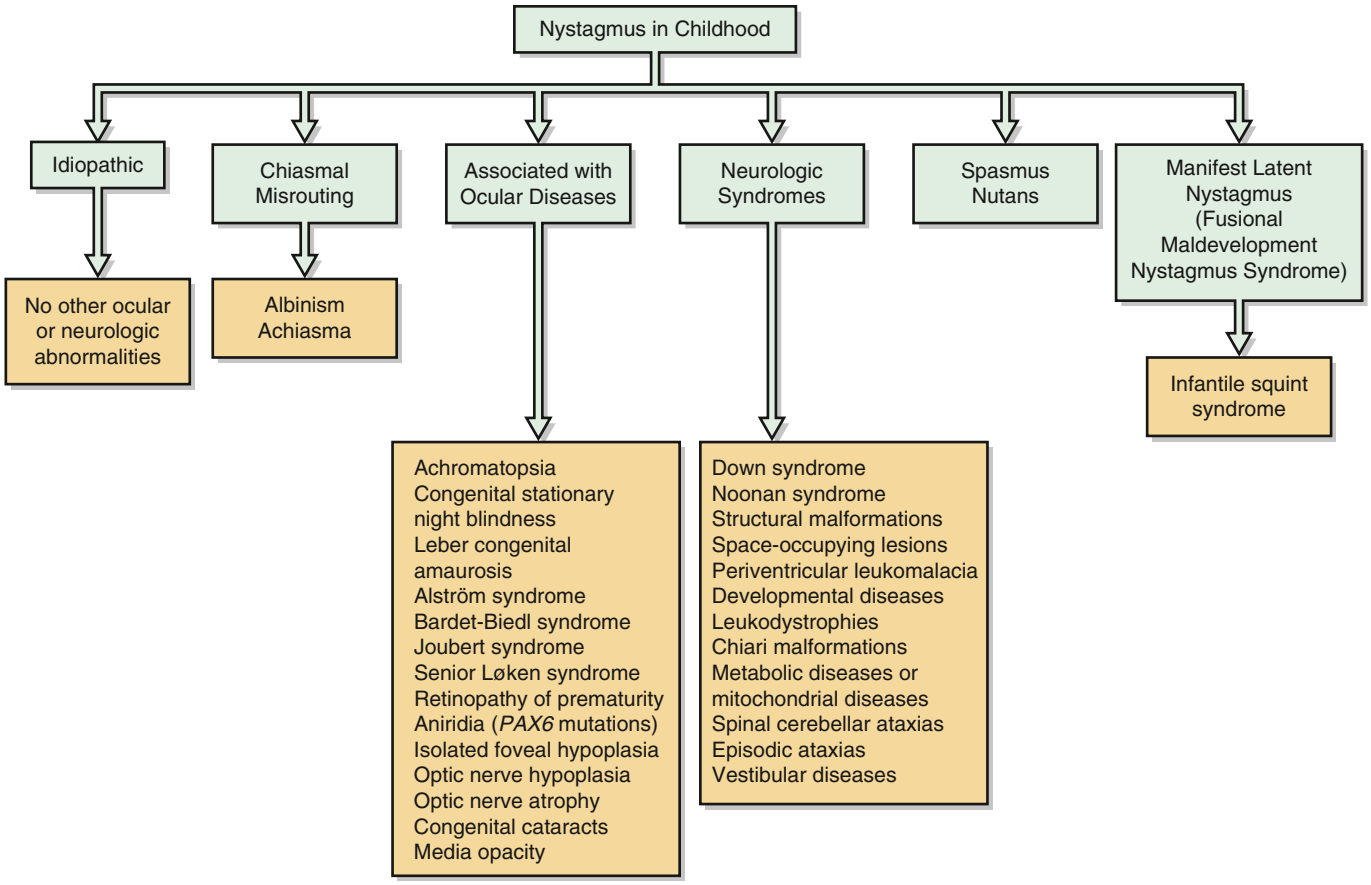

Fig. 663.9 Classification of nystagmus based on associated diseases. *(From Hoyt CS, Taylor D, eds. Pediatric ophthalmology and strabismus. 4th ed. Philadelphia: Elsevier; 2013: Fig. 89.2, p. 910.)*

Table 663.4 Key Distinguishing Features of Peripheral and Central Types of Spontaneous and Positional Nystagmus

TYPE OF NYSTAGMUS	PERIPHERAL (END ORGAN AND NERVE)	CENTRAL (BRAINSTEM AND CEREBELLUM)
Spontaneous	Unidirectional, fast phase away from the lesion, combined horizontal torsional, inhibited with fixation	Bidirectional or unidirectional; often pure horizontal, vertical, or torsional; *not* inhibited with fixation
Static positional	Fixed or changing direction, inhibited with fixation	Fixed or changing direction, *not* inhibited with fixation
Paroxysmal positional	Vertical-torsional, occasionally horizontal-torsional, vertigo prominent, fatigability, latency	Often pure vertical, vertigo less prominent, no latency, nonfatigable

From Goldman L, Schafer AI, eds. *Goldman-Cecil Medicine*. 25 ed. Philadelphia: Elsevier; 2016: Table 424.5, p. 2579.

those of spasmus nutans have underlying brain tumors, particularly hypothalamic and chiasmal optic gliomas. Appropriate neurologic and neuroradiologic evaluation and careful monitoring of infants and children with nystagmus are therefore recommended.

OTHER ABNORMAL EYE MOVEMENTS

To be differentiated from true nystagmus are certain special types of abnormal eye movements, particularly opsoclonus, ocular dysmetria, and flutter (Table 663.5).

Opsoclonus

Opsoclonus and ataxic conjugate movements are spontaneous, nonrhythmic, multidirectional, chaotic movements of the eyes. The eyes appear to be in agitation, with bursts of conjugate movement of varying amplitude in varying directions. Opsoclonus is most often associated with infectious or autoimmune encephalitis. It may be the first sign of neuroblastoma or other tumors producing a paraneoplastic syndrome.

Ocular Motor Dysmetria

This is analogous to dysmetria of the limbs. Affected individuals show a lack of precision in performing movements of refixation, characterized by an overshoot (or undershoot) of the eyes with several corrective to-and-fro oscillations on looking from one point to another. Ocular motor dysmetria is a sign of cerebellar or cerebellar pathway disease.

Table 663.5 Specific Patterns of Nonnystagmus Eye Movements

PATTERN	DESCRIPTION	ASSOCIATED CONDITIONS
Opsoclonus	Multidirectional conjugate movements of varying rate and amplitude	Hydrocephalus, diseases of brainstem and cerebellum, neuroblastoma, paraneoplasia syndrome
Ocular dysmetria	Overshoot of eyes on rapid fixation	Cerebellar dysfunction
Ocular flutter	Horizontal oscillations with forward gaze and sometimes with blinking	Cerebellar disease, hydrocephalus, or central nervous system neoplasm
Ocular bobbing	Downward jerk from primary gaze, remains for a few seconds, then drifts back	Pontine disease
Ocular myoclonus	Rhythmic to-and-fro pendular oscillations of the eyes, with synchronous nonocular muscle movement	Damage to red nucleus, inferior olivary nucleus, and ipsilateral dentate nucleus

From Kliegman R. *Practical Strategies in Pediatric Diagnosis and Therapy.* Philadelphia: Saunders; 1996.

Flutter-Like Oscillations

These intermittent to-and-fro horizontal oscillations of the eyes may occur spontaneously or on change of fixation. They are characteristic of cerebellar disease.

Visit Elsevier eBooks+ at eBooks.Health.Elsevier.com for Bibliography.

Chapter 664

Abnormalities of the Lids

Scott E. Olitsky and Justin D. Marsh

PTOSIS

In blepharoptosis, the upper eyelid droops below its normal level. **Congenital ptosis** is usually a result of a localized dystrophy of the levator muscle in which the striated muscle fibers are replaced with fibrous tissue. The condition may be unilateral or bilateral and can be familial, transmitted as a dominant trait (Figs. 664.1 and 664.2).

Parents often comment that the eye looks smaller because of the drooping eyelid. The lid crease is decreased or absent where the levator muscle would normally insert below the skin surface. Because the levator is replaced by fibrous tissue, the lid does not move downward fully in downgaze (lid lag). If the ptosis is severe, affected children often attempt to raise the lid by lifting their brow or adapting a chin-up head posture to maintain binocular vision.

Marcus Gunn jaw-winking ptosis (maxillopalpebral synkinesis) accounts for 5% of ptosis in children. In this syndrome, an abnormal synkinesis exists between the fifth and third cranial nerves; this causes the eyelid to elevate with movement of the jaw. The wink is produced by chewing or sucking and may be more noticeable than the ptosis itself (Fig. 664.3).

Although ptosis in children is often an isolated finding, it may also be acquired and occur in association with other ocular or systemic disorders (Fig. 664.4). Systemic disorders include myasthenia gravis, muscular dystrophy, Miller Fisher variant of Guillain Barré syndrome, and botulism. Ocular disorders include mechanical ptosis secondary to lid tumors, blepharophimosis syndrome, congenital fibrosis syndrome, combined levator/superior rectus maldevelopment, and congenital or acquired third nerve palsy. Ptosis may be a sign of cerebral herniation. A small degree of ptosis is seen in Horner syndrome (see Chapter 662). A complete ophthalmic and systemic examination is therefore important in the evaluation of a child with ptosis.

Amblyopia may occur in children with ptosis. The amblyopia may be secondary to the lid covering the visual axis (deprivation) or induced astigmatism (anisometropia). When amblyopia occurs, it should generally be treated before treating the ptosis.

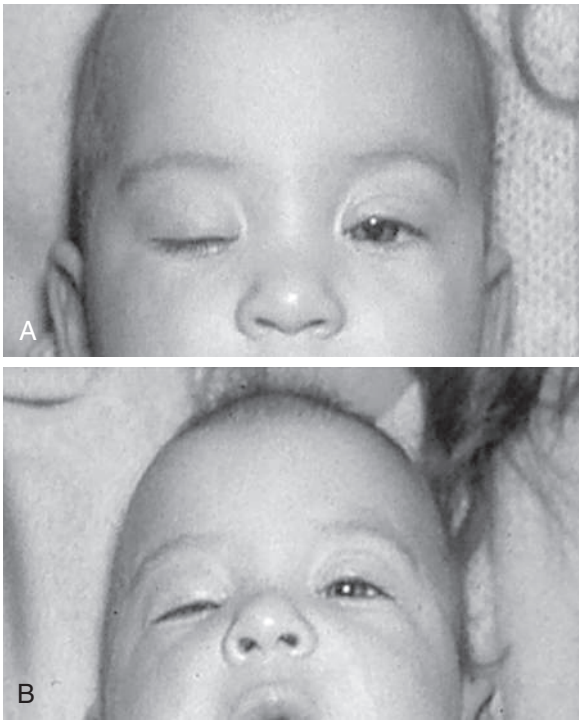

Fig. 664.1 A, Congenital ptosis of the right upper eyelid. B, The child adopted a compensatory chin-up head posture to allow use of both eyes together and did not have amblyopia. *(From Costakos DM. Eye disorders In Kliegman RM, Bordini BJ, Toth H, Basel D, eds. Nelson Pediatric Symptom-Based Diagnosis. 2nd ed. Philadelphia: Elsevier; 2022: Fig. 43.20, p. 805.)*

Treatment of ptosis in a child is indicated for elimination of an abnormal head posture, improvement in the visual field, prevention of amblyopia, and restoration of a normal eyelid appearance. The timing of surgery depends on the degree of ptosis, its cosmetic and functional severity, the presence or absence of compensatory posturing, the wishes of the parents, and the discretion of the surgeon. Surgical treatment is determined by the amount of levator function that is present. A levator resection may be used in children with moderate to good function. In patients with poor or absent function, a frontalis suspension procedure may be necessary. This technique requires that a suspension material be placed between the frontalis muscle and the tarsus of the eyelid. It allows patients to use their brow and frontalis muscle more effectively to raise their eyelid. Amblyopia may still exist even after surgical correction and should be treated if present.

Table 663.5 Specific Patterns of Nonnystagmus Eye Movements

PATTERN	DESCRIPTION	ASSOCIATED CONDITIONS
Opsoclonus	Multidirectional conjugate movements of varying rate and amplitude	Hydrocephalus, diseases of brainstem and cerebellum, neuroblastoma, paraneoplasia syndrome
Ocular dysmetria	Overshoot of eyes on rapid fixation	Cerebellar dysfunction
Ocular flutter	Horizontal oscillations with forward gaze and sometimes with blinking	Cerebellar disease, hydrocephalus, or central nervous system neoplasm
Ocular bobbing	Downward jerk from primary gaze, remains for a few seconds, then drifts back	Pontine disease
Ocular myoclonus	Rhythmic to-and-fro pendular oscillations of the eyes, with synchronous nonocular muscle movement	Damage to red nucleus, inferior olivary nucleus, and ipsilateral dentate nucleus

From Kliegman R. *Practical Strategies in Pediatric Diagnosis and Therapy.* Philadelphia: Saunders; 1996.

Flutter-Like Oscillations

These intermittent to-and-fro horizontal oscillations of the eyes may occur spontaneously or on change of fixation. They are characteristic of cerebellar disease.

Visit Elsevier eBooks+ at eBooks.Health.Elsevier.com for Bibliography.

Chapter 664

Abnormalities of the Lids

Scott E. Olitsky and Justin D. Marsh

PTOSIS

In blepharoptosis, the upper eyelid droops below its normal level. **Congenital ptosis** is usually a result of a localized dystrophy of the levator muscle in which the striated muscle fibers are replaced with fibrous tissue. The condition may be unilateral or bilateral and can be familial, transmitted as a dominant trait (Figs. 664.1 and 664.2).

Parents often comment that the eye looks smaller because of the drooping eyelid. The lid crease is decreased or absent where the levator muscle would normally insert below the skin surface. Because the levator is replaced by fibrous tissue, the lid does not move downward fully in downgaze (lid lag). If the ptosis is severe, affected children often attempt to raise the lid by lifting their brow or adapting a chin-up head posture to maintain binocular vision.

Marcus Gunn jaw-winking ptosis (maxillopalpebral synkinesis) accounts for 5% of ptosis in children. In this syndrome, an abnormal synkinesis exists between the fifth and third cranial nerves; this causes the eyelid to elevate with movement of the jaw. The wink is produced by chewing or sucking and may be more noticeable than the ptosis itself (Fig. 664.3).

Although ptosis in children is often an isolated finding, it may also be acquired and occur in association with other ocular or systemic disorders (Fig. 664.4). Systemic disorders include myasthenia gravis, muscular dystrophy, Miller Fisher variant of Guillain Barré syndrome, and botulism. Ocular disorders include mechanical ptosis secondary to lid tumors, blepharophimosis syndrome, congenital fibrosis syndrome, combined levator/superior rectus maldevelopment, and congenital or acquired third nerve palsy. Ptosis may be a sign of cerebral herniation. A small degree of ptosis is seen in Horner syndrome (see Chapter 662). A complete ophthalmic and systemic examination is therefore important in the evaluation of a child with ptosis.

Amblyopia may occur in children with ptosis. The amblyopia may be secondary to the lid covering the visual axis (deprivation) or induced astigmatism (anisometropia). When amblyopia occurs, it should generally be treated before treating the ptosis.

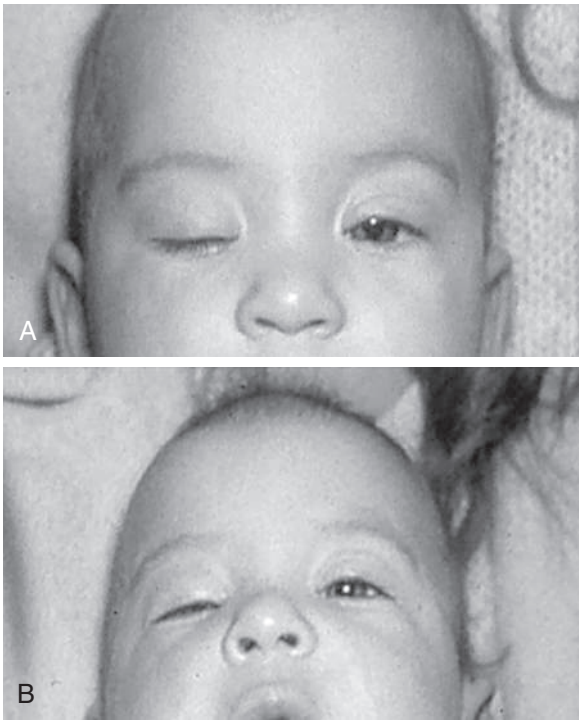

Fig. 664.1 A, Congenital ptosis of the right upper eyelid. B, The child adopted a compensatory chin-up head posture to allow use of both eyes together and did not have amblyopia. *(From Costakos DM. Eye disorders In Kliegman RM, Bordini BJ, Toth H, Basel D, eds. Nelson Pediatric Symptom-Based Diagnosis. 2nd ed. Philadelphia: Elsevier; 2022: Fig. 43.20, p. 805.)*

Treatment of ptosis in a child is indicated for elimination of an abnormal head posture, improvement in the visual field, prevention of amblyopia, and restoration of a normal eyelid appearance. The timing of surgery depends on the degree of ptosis, its cosmetic and functional severity, the presence or absence of compensatory posturing, the wishes of the parents, and the discretion of the surgeon. Surgical treatment is determined by the amount of levator function that is present. A levator resection may be used in children with moderate to good function. In patients with poor or absent function, a frontalis suspension procedure may be necessary. This technique requires that a suspension material be placed between the frontalis muscle and the tarsus of the eyelid. It allows patients to use their brow and frontalis muscle more effectively to raise their eyelid. Amblyopia may still exist even after surgical correction and should be treated if present.

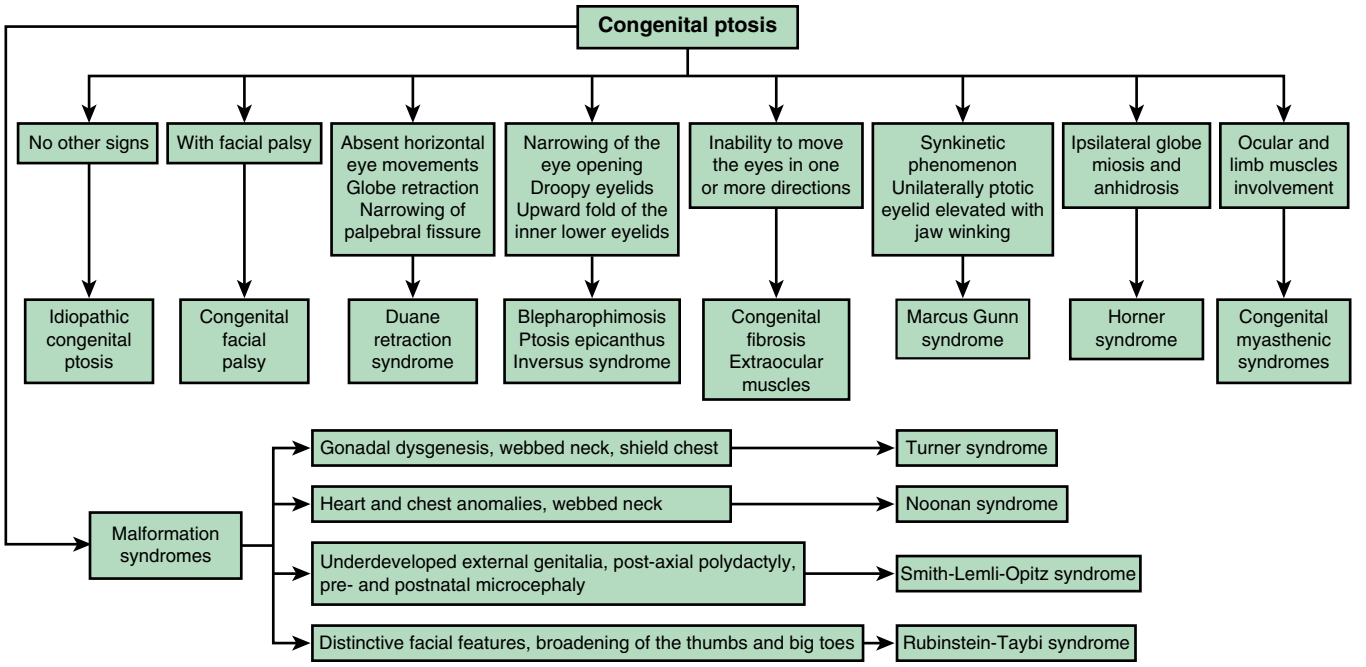

Fig. 664.2 Flow chart outlining congenital types of ptosis. *(From Pavone P, Cho YC, Pratico AD, et al. Ptosis in childhood: A clinical sign of several disorders. Medicine. 2018 Sep;97[36]:e12124, Fig. 8A.)*

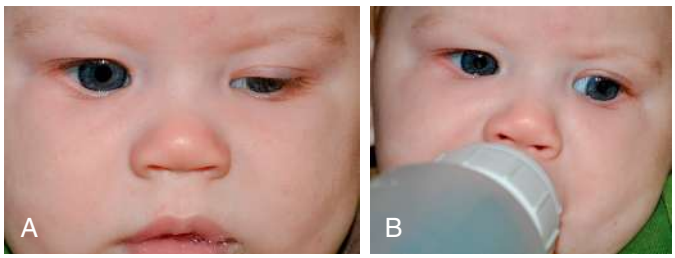

Fig. 664.3 Marcus Gunn jaw-winking phenomenon. A, Left upper lid ptosis. B, The left lid raises up while the patient sucks from the bottle. *(From Martin RJ, Fanaroff AA, Walsch MC, eds. Fanaroff & Martin's Neonatal-Perinatal Medicine. 10th ed. Philadelphia: Elsevier; 2015: Fig. 103.2.)*

EPICANTHAL FOLDS

These vertical or oblique folds of skin extend on either side of the bridge of the nose from the brow or lid area, covering the inner canthal region. They are present to some degree in most young children and become less apparent with age. The folds may be sufficiently broad to cover the medial aspect of the eye, making the eyes appear crossed (pseudoesotropia). Epicanthal folds are a common feature of many syndromes, including chromosomal aberrations (trisomies) and disorders of single genes.

LAGOPHTHALMOS

This is a condition in which complete closure of the lids over the globe is difficult or impossible. It may be paralytic because of a facial palsy involving the orbicularis muscle, or spastic, as in thyrotoxicosis. It may be structural when retraction or shortening of the lids results from scarring or atrophy consequent to injury (burns) or disease. Children with various craniosynostosis syndromes can have problematic lagophthalmos. Infants with congenital ichthyosis may have lagophthalmos caused by the restrictive effect of the lids. Lagophthalmos may accompany proptosis or **buphthalmos** (enlarged cornea because of elevated intraocular pressure) when the lids, although normal, cannot effectively cover the enlarged or protuberant eye. A degree of physiologic lagophthalmos may occur normally during sleep, but functional lagophthalmos in an unconscious or debilitated patient can be a problem.

In patients with lagophthalmos, exposure of the eye may lead to drying, infection, corneal ulceration, or perforation of the cornea; the result may be loss of vision, even loss of the eye. In lagophthalmos, protection of the eye by artificial tear preparations, ophthalmic ointment, or moisture chambers is essential. Gauze pads are to be avoided because the gauze may abrade the cornea. In some cases, surgical closure of the lids (tarsorrhaphy) may be necessary for long-term protection of the eye.

LID RETRACTION

Pathologic retraction of the lid may be myogenic or neurogenic. Myogenic retraction of the upper lid occurs in **thyrotoxicosis**, in which it is associated with three classic signs: a staring appearance (Dalrymple sign), infrequent blinking (Stellwag sign), and lag of the upper lid on downward gaze (von Graefe sign).

Neurogenic retraction of the lids may occur in conditions affecting the anterior mesencephalon. Lid retraction is a feature of the **syndrome of the sylvian aqueduct**. In children, it is commonly a sign of hydrocephalus. It may occur with meningitis. Paradoxical retraction of the lid is seen in the Marcus Gunn jaw-winking syndrome. It may also be seen with attempted eye movement after recovery from a third nerve palsy if aberrant regeneration of the oculomotor nerve fibers has occurred.

Simple staring and the physiologic or reflexive lid retraction ("eye popping"), in contrast to pathologic lid retractions, occur in infants in response to a sudden reduction in illumination or as a startle reaction.

ECTROPION, ENTROPION, AND EPIBLEPHARON

Ectropion is eversion of the lid margin; it may lead to overflow of tears (epiphora) and subsequent maceration of the skin of the lid, inflammation of exposed conjunctiva, or superficial exposure keratopathy. Common causes are scarring consequent to inflammation, burns, or trauma and weakness of the orbicularis muscle as a result of facial palsy; these forms may be corrected surgically. Protection of the cornea is essential. Ectropion is also seen in certain children who have faulty development of the lateral canthal ligament; this may occur in Down syndrome.

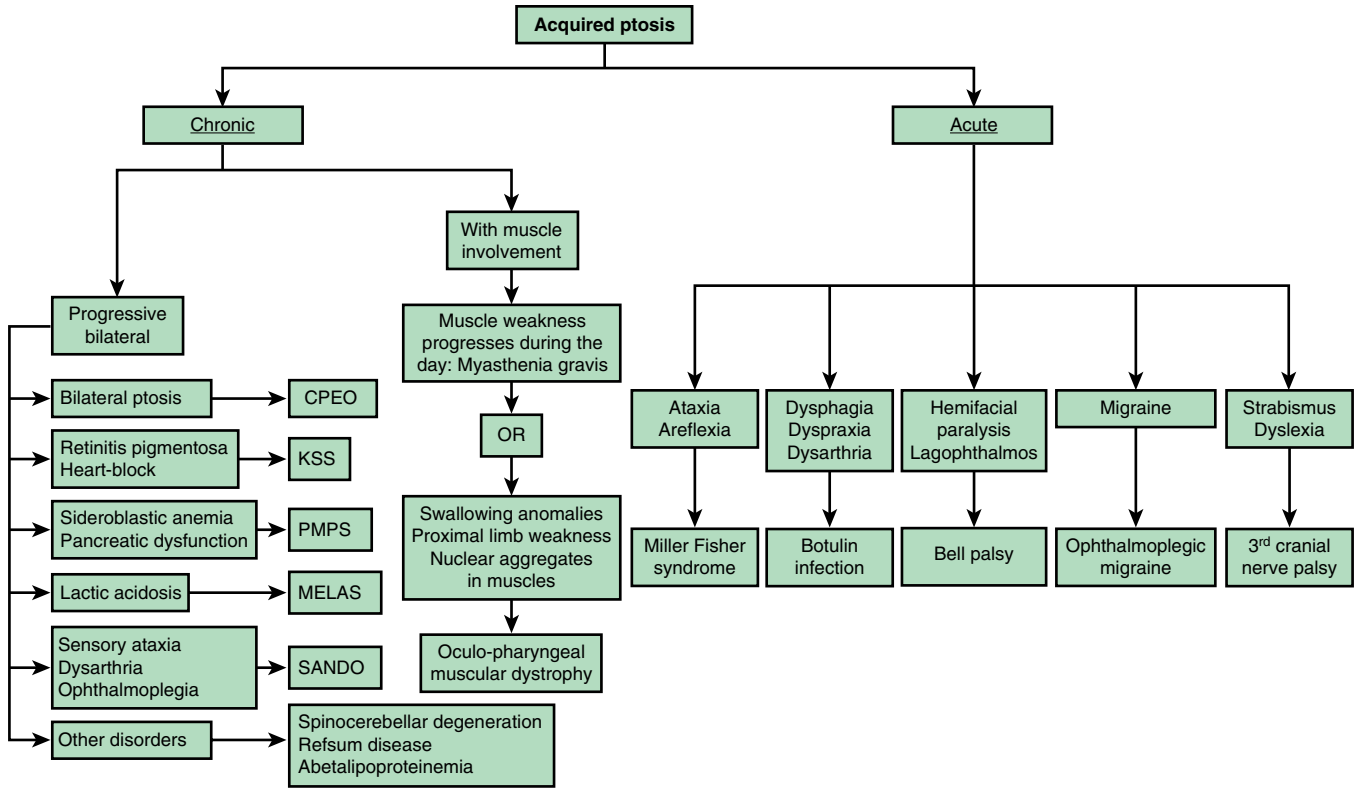

Fig. 664.4 Flow chart outlining acquired types of ptosis. CPEO, Chronic progressive external ophthalmoplegia; KSS, Kearns-Sayre syndrome; MELAS, mitochondrial encephalopathy, lactic acidosis, and strokelike episodes; PMPS, Pearson marrow pancreas syndrome; SANDO, sensory ataxic neuropathy, dysarthria, and ophthalmoparesis. *(From Pavone P, Cho YC, Pratico AD, et al. Ptosis in childhood: A clinical sign of several disorders. Medicine. 2018 Sep;97[36]:e12124, Fig. 8B.)*

Entropion is inversion of the lid margin, which may cause discomfort and corneal damage because of the inward turning of the lashes (trichiasis). A principal cause is scarring secondary to inflammation, such as occurs in trachoma or as a sequela of Stevens-Johnson syndrome. There is also a rare congenital form. Surgical correction is effective in many cases.

Epiblepharon is commonly seen in childhood and may be confused with entropion. In epiblepharon, a roll of skin beneath the lower eyelid lashes causes the lashes to be directed vertically and to touch the cornea (Fig. 664.5). Unlike entropion, the eyelid margin itself is not rotated toward the cornea. Epiblepharon usually resolves spontaneously. When mild symptoms are present, such as mild ocular irritation, lubrication is typically recommended. Rarely, corneal scarring may occur, and surgery may be necessary.

BLEPHAROSPASM

This spastic or repetitive closure of the lids may be caused by irritative disease of the cornea, conjunctiva, or facial nerve; fatigue or uncorrected refractive error; or common tic. Thorough ophthalmic examination for pathologic causes, such as trichiasis, keratitis, conjunctivitis, or foreign body, is indicated. Local injection of botulinum toxin may give relief but frequently must be repeated.

BLEPHARITIS

This inflammation of the lid margins is characterized by erythema and crusting or scaling; the usual symptoms are irritation, burning, and itching. The condition is commonly bilateral and chronic or recurrent. The two main types are **staphylococcal** and **seborrheic.** In staphylococcal blepharitis, ulceration of the lid margin is common, the lashes tend to fall out, and conjunctivitis and superficial keratitis are often associated. In seborrheic blepharitis, the scales tend to be greasy, the lid margins are less red, and ulceration usually does not occur. Commonly blepharitis presents as a combination of the two.

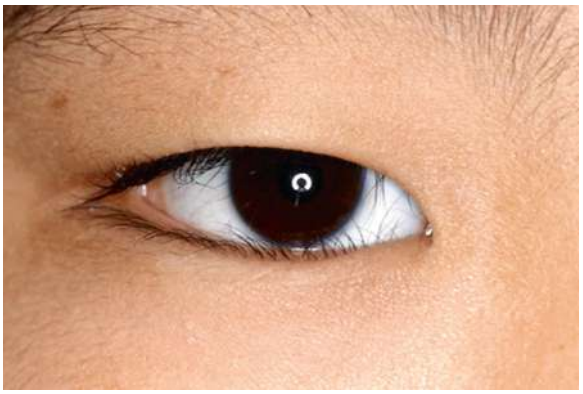

Fig. 664.5 Epiblepharon.

Thorough daily cleansing of the lid margins with a cloth or moistened cotton applicator to remove scales and crusts is important in the **treatment** of both forms. Staphylococcal blepharitis is treated with an antistaphylococcal antibiotic applied directly to the lid margins. When a child also has seborrhea, concurrent treatment of the scalp is important.

Pediculosis of the eyelashes may produce a clinical picture of blepharitis. The lice can be smothered with ophthalmic-grade petrolatum ointment applied to the lid margin and lashes. Nits should be mechanically removed from the lashes. It should be remembered that pediculosis can represent a sexually transmitted disease.

Mites (*Demodex* spp.) are an increasingly recognized cause of blepharitis, including in children and adolescents. Close inspection of the eyelashes often reveals sheathing of the lash at its base. Tea tree oil or products containing tea tree oil may be helpful, in addition to diligent lid hygiene.

HORDEOLUM (STYE)

Infection of the glands of the lid may be acute or subacute; tender focal swelling and redness are noted. The usual agent is *Staphylococcus aureus.* When the meibomian glands are involved, the lesion is referred to as an internal hordeolum; the abscess tends to be large and may point through either the skin or the conjunctival surface. When the infection involves the glands of Zeis or Moll, the abscess tends to be smaller and more superficial and points at the lid margin; it is then referred to as an *external hordeolum* or *stye*.

Treatment is frequent warm compresses and, if necessary, surgical incision and drainage. In addition, topical antibiotic preparations are often used. Untreated, the infection may progress to cellulitis of the lid or orbit, requiring the use of systemic antibiotics.

CHALAZION

A chalazion is a granulomatous inflammation of a meibomian gland characterized by a firm, nontender nodule in the upper or lower lid. This lesion tends to be chronic and differs from internal hordeolum in the absence of acute inflammatory signs. Although many chalazia subside spontaneously, incision and drainage may be necessary if they become large enough to distort vision (by inducing astigmatism by exerting pressure on the globe) or become cosmetically unacceptable. Patients who experience frequent chalazia formation, or those who have significant corneal changes secondary to the underlying blepharitis, may benefit from systemic, low-dose erythromycin or azithromycin treatment.

COLOBOMA OF THE EYELID

This cleftlike deformity may vary from a small indentation or notch of the free margin of the lid to a large defect involving almost the entire lid. If the gap is extensive, ulceration and corneal opacities may result from exposure. Early surgical correction of the lid defect is recommended. Other deformities frequently associated with lid colobomas include dermoid cysts or dermolipomas on the globe; they often occur in a position corresponding to the site of the lid defect. Lid colobomas may also be associated with extensive facial malformation, as in mandibulofacial dysostosis (Franceschetti or Treacher Collins syndrome).

TUMORS OF THE LID

A number of lid tumors arise from surface structures (the epithelium and sebaceous glands). Nevi may appear in early childhood; most are junctional. Compound nevi tend to develop in the prepubertal years and dermal nevi at puberty. Malignant epithelial tumors (basal cell carcinoma, squamous cell carcinoma) are rare in children, but the basal cell nevus syndrome and the malignant lesions of xeroderma pigmentosum and of Rothmund-Thomson syndrome may develop in childhood.

Other lid tumors arise from deeper structures (the neural, vascular, and connective tissues). **Capillary hemangiomas** are especially common in children (Fig. 664.6). Many tend to regress spontaneously, although they may show alarmingly rapid growth in infancy. In many cases, the best management of such hemangiomas is patient observation, allowing spontaneous regression to occur (see Chapter 691). In the case of a rapidly expanding lesion, which may cause amblyopia by obstructing the visual axis or inducing astigmatism, **treatment** should be considered. Systemic propranolol is an effective treatment without the risks associated with corticosteroid use. Other treatment options include topical timolol, corticosteroids (systemically or by direct injection), and surgical excision. Cutaneous capillary malformations (e.g., port-wine stain) can occur as an isolated lesion or in association with other signs of Sturge-Weber syndrome. Affected patients should be monitored for the development of glaucoma. **Lymphangiomas** (lymphatic malformations) of the lid appear as firm masses at or soon after birth and tend to enlarge slowly during the growing years. Associated conjunctival involvement, appearing as a clear, cystic, sinuous conjunctival mass, may provide a clue to the diagnosis. In some cases, there is also orbital involvement. The **treatment** may include sclerosant therapy, percutaneous drainage, or surgical excision.

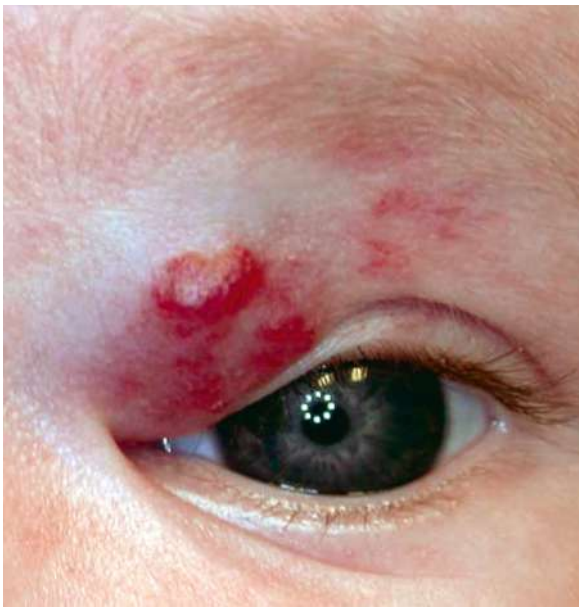

Fig. 664.6 Capillary hemangioma of the eyelid. *(Courtesy Amy Nopper, MD, and Brandon Newell, MD.)*

Plexiform neuromas of the lids occur in children with neurofibromatosis, often with ptosis as the first sign. The lid may take on an S-shaped configuration. The lids may also be involved by other tumors, such as retinoblastoma, neuroblastoma, and rhabdomyosarcoma of the orbit; these conditions are discussed elsewhere.

Visit Elsevier eBooks+ at eBooks.Health.Elsevier.com for Bibliography.

Chapter 665

Disorders of the Lacrimal System

Scott E. Olitsky and Justin D. Marsh

THE TEAR FILM

The tear film, which bathes the eye, is a complex structure composed of three layers. The innermost mucin layer is secreted by the goblet and epithelial cells of the conjunctiva and the acinar cells of the lacrimal gland. It adds stability and provides an attachment for the tear film to the conjunctiva and cornea. The middle aqueous layer constitutes 98% of the tear film and is produced by the main lacrimal gland and accessory lacrimal glands. It contains various electrolytes and proteins as well as antibodies. The outermost lipid layer is produced largely from the sebaceous meibomian glands of the eyelid and retards evaporation of the tear film. Tears drain medially into the punctal openings of the lid margin and flow through the canaliculi into the lacrimal sac and then through the nasolacrimal duct into

the nose (Fig. 665.1). Preterm infants have reduced tear secretion. This may mask the diagnosis of a nasolacrimal duct obstruction and concentrate topically applied medications. Tear production reaches adult levels at 1-3 months.

DACRYOSTENOSIS

Congenital nasolacrimal duct obstruction (CNLDO), or dacryostenosis, is the most common disorder of the lacrimal system, occurring in up to 20% of newborn infants. It is usually caused by a failure of canalization of the epithelial cells (resulting in membrane formation) that form the nasolacrimal duct as it enters the nose beneath the inferior turbinate (valve of Hasner). Signs of CNLDO may be present at the time of birth, although the condition may not become evident until normal tear production develops. Signs of CNLDO include an excessive tear lake, overflow of tears onto the lid and cheek, and reflux of mucoid material that is produced in the lacrimal sac. Erythema or maceration of the skin may result from irritation and rubbing produced by dripping of tears and discharge. If the blockage is complete, these signs may be severe and continuous. If obstruction is only partial, the nasolacrimal duct may be capable of draining the basal tear film that is produced. However, under periods of increased tear production (exposure to cold, wind, sunlight) or increased closure of the distal end of the nasolacrimal duct (nasal mucosal edema), tear overflow may become evident or may increase.

Infants at increased risk for CNLDO include those with trisomy 21, EEC (ectrodactyly, ectodermal dysplasia, clefting) syndrome, branchiooculofacial syndrome, craniometaphyseal or craniodiaphyseal dysplasias, LADD (lacrimo-auriculo-dento-digital) syndrome, CHARGE (coloboma, heart anomaly, choanal atresia, retardation, genital, and ear anomalies) syndrome, and Goldenhar syndrome (Table 665.1).

Infants with CNLDO may develop acute infection and inflammation of the nasolacrimal sac **(dacryocystitis)**, inflammation of the surrounding tissues **(pericystitis)**, or, rarely, periorbital cellulitis. With dacryocystitis, the sac area is swollen, red, and tender, and patients may have systemic signs of infection such as fever and irritability.

The primary **treatment** of uncomplicated nasolacrimal duct obstruction is a regimen of nasolacrimal massage, usually two or three times daily, accompanied by cleansing of the lids with warm water. Topical antibiotics are used for control of mucopurulent drainage. A bland ophthalmic ointment may be used on eyelids if the skin is macerated. Most cases of CNLDO resolve spontaneously; 96% resolve before 1 year of age. For cases that do not resolve by 1 year, the nasolacrimal duct may be probed, with a cure rate of approximately 80%. Some ophthalmologists intubate the nasolacrimal system at the same time because this may improve the outcome of the procedure.

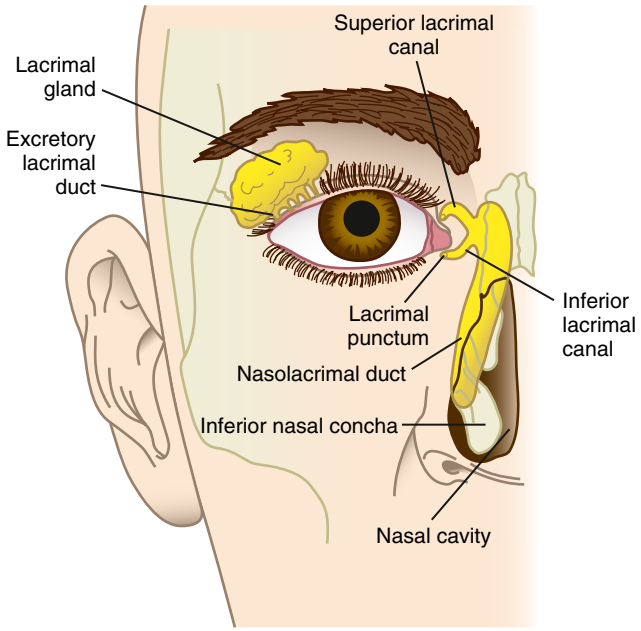

Fig. 665.1 The lacrimal apparatus.

Acute dacryocystitis (Fig. 665.2) requires prompt treatment with systemic antibiotics. In such cases, some form of definitive surgical intervention is usually indicated.

A **dacryocystocele** (mucocele) is an unusual presentation of a nonpatent nasolacrimal sac that is obstructed both proximally and distally. Dacryocystoceles can be seen at birth or shortly after birth as a bluish subcutaneous mass just below the medial canthal tendon (Figs. 665.3 and 665.4). Initial **treatment** of dacryocystocele is usually conservative, involving massage/digital decompression of the lacrimal sac. If resolution of the dacryocystocele is not achieved with conservative management, surgical probing may be beneficial. At times, the intranasal portion of the nasolacrimal duct becomes distended, causing respiratory compromise. In one study, 9.5% of infants with dacryocystocele had related respiratory compromise, and this may be more common when dacryocystoceles are present bilaterally. These infants benefit from early probing. When left untreated, dacryocystocele may progress to dacryocystitis/cellulitis, requiring systemic antibiotics and often hospitalization. Once the cellulitis has improved, the nasolacrimal system should be probed if spontaneous resolution has not occurred.

Not all tearing in infants and children is caused by nasolacrimal obstruction. Tearing may also be a sign of glaucoma, intraocular inflammation, or external irritation, such as that from a corneal abrasion or foreign body.

ALACRIMA AND "DRY EYE"

Alacrima refers to a wide spectrum of disorders with reduced or absent tear secretion. Occasionally normal basal tearing occurs with an absence of emotional tearing. Etiologies can be divided into syndromes that have a pathologic association or are inherited. Associated syndromes include familial dysautonomia (Riley-Day syndrome), anhidrotic ectodermal dysplasia, and triple-A syndrome (Allgrove syndrome: achalasia, alacrima, adrenal insufficiency). Examples of pathologic association include aplasia of cranial nerve nuclei and lacrimal gland aplasia/hypoplasia. Both autosomal recessive and autosomal dominant inheritance have been reported in isolated congenital alacrima. In addition, medications with anticholinergic side effects can decrease tear production. The patients with alacrima have variable presentation, including no symptoms, photophobia, foreign body sensation, eye pain, and decreased vision. The symptoms, if present, often occur early in life. Because the dryness can be severe, damage to the cornea and subsequent loss of vision may occur. The goal of treatment is to minimize corneal irritation, corneal scarring, and loss of vision. Aggressive ocular lubrication is used to prevent these sequelae.

An **acquired abnormality** of any layer of the tear film may produce a dry eye. Commonly acquired disorders that may lead to a decreased or unstable tear film include Sjögren syndrome, Stevens-Johnson syndrome, toxic epidermal necrolysis, vitamin A deficiency, viral infections of the lacrimal gland, ocular pemphigoid, trachoma, chemical burns, irradiation, isotretinoin treatment of acne, graft-versus-host disease, and meibomian gland dysfunction. Corneal exposure as a consequence of poor lid closure or other pathologic states can quickly lead to pathologically dry eyes. Examples of conditions leading to such exposure include ichthyosis, xeroderma pigmentosum, and certain

Table 665.1 Syndromes Associated with Congenital Lacrimal Drainage Anomalies

Down syndrome	Branchio-oto-renal syndrome
Ectrodactyly-ectodermal dysplasia clefting (EEC) syndrome	Crouzon syndrome
Treacher Collins syndrome	Klinefelter syndrome
Rubinstein-Taybi syndrome	Fraser syndrome
Lacrimo-auriculo-dento-digital (LADD) or Levy-Hollister syndrome	Goltz-Gorlin syndrome
	Wolf-Hirschhorn or 4p-syndrome
Hay-Wells syndrome	Congenital rubella syndrome
ADULT syndrome	Turner syndrome
Limb-mammary syndrome	Fetal alcohol syndrome
Rapp-Hodgkin syndrome	Hallermann-Streiff syndrome
Split-hand/split-foot syndrome	Fetal valproate syndrome
Aplasia of the lacrimal and salivary glands (ALSG) syndrome	HPPD syndrome (hypertelorism, preauricular sinus, punctal pits, deafness)
Apert syndrome	
Saethre-Chotzen syndrome	Velocardiofacial (VCFS) syndrome
CHARGE syndrome	Poland-Möbius syndrome
Branchio-oculo-facial (BOF) syndrome	Robinow syndrome
Goldenhar syndrome	Angelman syndrome
Cornelia de Lange syndrome	Waardenburg-Klein syndrome
Congenital arhinia-microphthalmia syndrome	PHACE syndrome
Johanson Blizzard syndrome	Williams-Beuren syndrome
Pashayan syndrome	Peter's plus syndrome
Millers syndrome	Kabuki syndrome
Kallmann syndrome	Angora hair nevus syndrome
Nager syndrome	TARP syndrome
Blepharophimosis syndrome	11q trisomy syndrome
VACTERL association	Barber-Say syndrome

ADULT, acro-dermato-ungual-lacrimal-tooth; CHARGE, coloboma, heart, atresia choanae, growth retardation, genital ear; PHACE, posterior fossa, hemangioma, arterial, cardiac, eye or endocrine; TARP, talipes equinovarus, atrial septal defects, Robin syndrome, persistent left superior vena cava; VACTERL, vertebral, anal atresia, cardiac, tracheo-esophageal atresia, renal, limb.

Modified from Ali MJ. Updates on congenital lacrimal drainage anomalies and their association with syndromes and systemic disorders: A major review. *Ann Anatomy.* 2021;233:151613: Table 665.1.

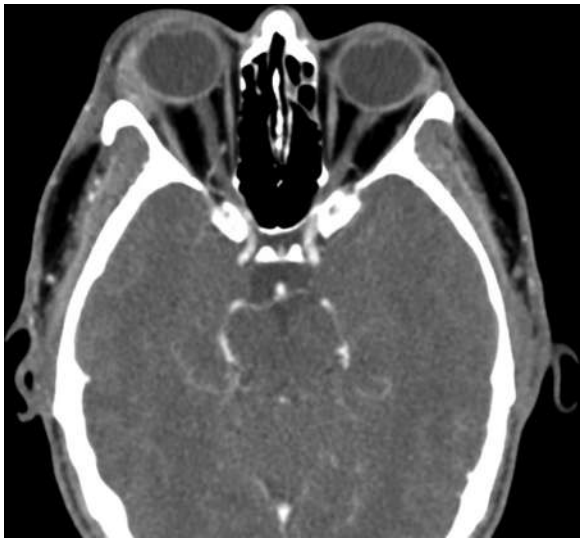

Fig. 665.2 Noncontrast axial CT study exhibiting right acute dacryoadenitis with inflammation adjacent to the lateral orbital wall and lateral rectus muscle. *(From Maamari RN, Couch SM. Nonspecific orbital inflammation. Adv Ophthalmol Optom. 2018;3[1]:315-335, Fig. 3.)*

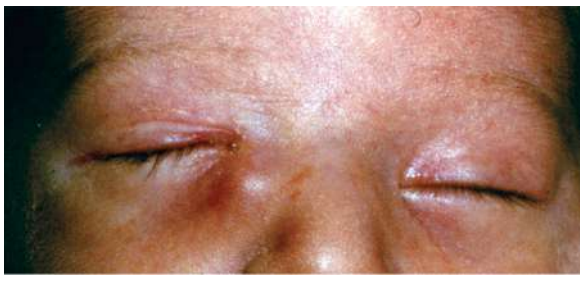

Fig. 665.3 Dacryocystocele below inner canthus of the right eye.

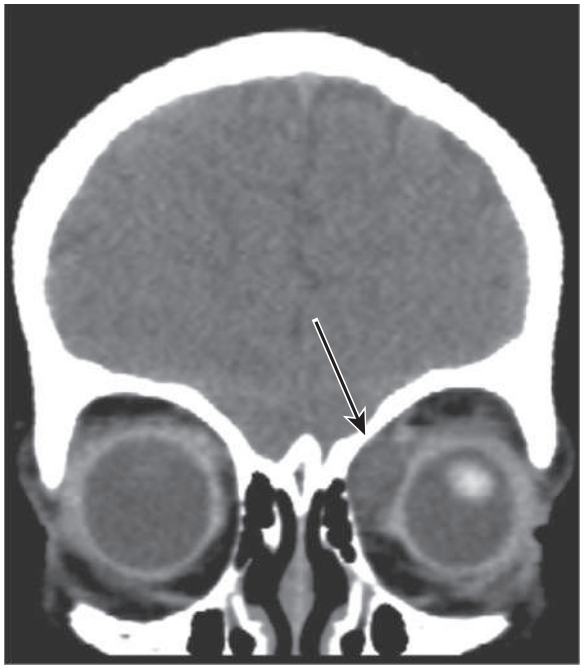

Fig. 665.4 Coronal CT shows a left dacryocystocele *(arrow)*. *(Modified from Coley BD, ed. Caffey's Pediatric Diagnostic Imaging, 13th ed. Philadelphia: Elsevier; 2019: Fig. 5.23, p. 36.)*

craniosynostoses syndromes, such as Crouzon, Apert, or Pfeiffer. Any tear deficiency can lead to corneal ulceration, scarring, or infection. **Treatment** includes correction of the underlying disorder when possible and frequent instillation of an ocular lubricant. In some cases, occlusion of the lacrimal puncta is helpful. In severe cases, tarsorrhaphy may be necessary to protect the cornea.

Visit Elsevier eBooks+ at eBooks.Health.Elsevier.com for Bibliography.

Chapter 666

Disorders of the Conjunctiva

Scott E. Olitsky and Justin D. Marsh

CONJUNCTIVITIS

The conjunctiva reacts to a wide range of bacterial and viral agents, allergens, irritants, toxins, and systemic diseases. Conjunctivitis is common in childhood and may be infectious or noninfectious. The differential diagnosis of a red-appearing eye includes conjunctival disease, as well as other ocular sites (Table 666.1).

Ophthalmia Neonatorum

This form of conjunctivitis, occurring in infants younger than 4 weeks of age, is the most common eye disease of newborns. Its many different causal agents vary greatly in their virulence and outcome. Silver nitrate instillation may result in a mild self-limited chemical conjunctivitis, whereas *Neisseria gonorrhoeae* and *Pseudomonas* are capable of causing corneal perforation, blindness, and death. The risk of conjunctivitis in newborns depends on frequencies of maternal infections, prophylactic measures, circumstances during labor and delivery, and postdelivery exposure to microorganisms.

Epidemiology

Conjunctivitis during the neonatal period is usually acquired during vaginal delivery and reflects the sexually transmitted infections prevalent in the community. The incidence of gonococcal ophthalmia neonatorum can be reduced by widespread use of topical silver nitrate or erythromycin prophylaxis, prenatal screening, and treatment of maternal gonorrhea. Gonococcal ophthalmia neonatorum has an incidence of 0.3/1,000 live births in the United States. In comparison, *Chlamydia trachomatis* is the most common organism causing ophthalmia neonatorum in the United States, with an incidence of 8.2/1,000 births.

Clinical Manifestations

The clinical manifestations of the various forms of ophthalmia neonatorum are not specific enough to allow an accurate diagnosis. Although the timing and character of the signs are somewhat typical for each cause of this condition, there is considerable overlap, and physicians should not rely solely on clinical findings. Regardless of its cause, ophthalmia neonatorum is characterized by redness and chemosis (swelling) of the conjunctiva, edema of the eyelids, and discharge, which may be purulent.

Neonatal conjunctivitis is a potentially blinding condition. The infection may also have associated systemic manifestations that require treatment. Any newborn infant who develops signs of conjunctivitis needs a prompt and comprehensive systemic and ocular evaluation to determine the agent causing the infection and the appropriate treatment.

The onset of inflammation caused by silver nitrate drops usually occurs within 6-12 hours after birth, with clearing by 24-48 hours. The usual incubation period for conjunctivitis caused by *N. gonorrhoeae* is 2-5 days, and for that caused by *C. trachomatis*, 5-14 days. Gonococcal infection may be present at birth owing to prolonged rupture of amniotic membranes or be delayed beyond 5 days of life because of partial suppression by ocular prophylaxis. Gonococcal conjunctivitis may also begin in infancy after inoculation by the contaminated fingers of adults. The time of onset of disease with other bacteria is highly variable.

Gonococcal conjunctivitis begins with mild inflammation and a serosanguineous discharge. Within 24 hours, the discharge becomes thick and purulent, and tense edema of the eyelids with marked chemosis occurs. If proper treatment is delayed, the infection may spread to involve the deeper layers of the conjunctivae and the cornea. Complications include corneal ulceration and perforation, iridocyclitis, anterior synechiae, and, rarely, panophthalmitis. Conjunctivitis caused by *C. trachomatis* (inclusion blennorrhea) may vary from mild inflammation to severe swelling of the eyelids with copious purulent discharge. The process involves mainly the tarsal conjunctivae; the corneas are rarely affected. Conjunctivitis caused by *Staphylococcus aureus* or other organisms is similar to that produced by *C. trachomatis.* Conjunctivitis caused by *Pseudomonas aeruginosa* is uncommon, acquired in the nursery, and a potentially serious process. It is characterized by the appearance on days 5-18 of edema, erythema of the lids, purulent discharge, pannus formation, endophthalmitis, sepsis, shock, and death.

Diagnosis

Conjunctivitis appearing after 48 hours should be evaluated for a possibly infectious cause. Gram stain of the purulent discharge should be performed and tested by polymerase chain reaction (PCR) for gonococcus. If a viral cause is suspected, a swab should be submitted for PCR testing. In chlamydial conjunctivitis, the diagnosis is made by tests for chlamydial antigen or DNA. The differential diagnosis of ophthalmia neonatorum includes dacryocystitis caused by congenital nasolacrimal duct obstruction with lacrimal sac distention (dacryocystocele; see Chapter 665).

Treatment

Treatment of infants in whom gonococcal ophthalmia is suspected where the Gram stain shows the characteristic intracellular Gram-negative diplococci should be initiated immediately with ceftriaxone, 25-50 mg/kg/24 hr for one dose IV or IM, not to exceed 125 mg. The eye should also be irrigated initially with saline every 10-30 minutes, gradually increasing to 2-hour intervals until the purulent discharge has cleared. Treatment (ceftriaxone 25-50 mg/kg/day, IM or IV in a single daily dose for 7 days, with cefotaxime 25 mg/kg q 12 hr substituted if the patient has hyperbilirubinemia) is extended if sepsis or other extraocular sites are involved. Associated meningitis is treated for 10-14 days. Neonatal conjunctivitis secondary to chlamydial infections is treated with oral erythromycin (50 mg/kg/24 hr in four divided doses) for 2 weeks. This cures conjunctivitis and may prevent subsequent chlamydial pneumonia. *Pseudomonas* neonatal conjunctivitis is treated with systemic antibiotics, including an aminoglycoside, plus local saline irrigation and gentamicin ophthalmic ointment. Staphylococcal conjunctivitis is treated with parenteral methicillin and local saline irrigation.

Prognosis and Prevention

Before the institution of topical ophthalmic prophylaxis at birth, gonococcal ophthalmia was a common cause of blindness or permanent eye damage. If properly applied, this form of prophylaxis is highly effective unless infection is present at birth. Drops of 0.5% erythromycin or 1% silver nitrate are instilled directly into the open eyes at birth using wax or plastic single-dose containers. Saline irrigation after silver nitrate application is unnecessary. Silver nitrate is ineffective against active infection and may have limited use against *Chlamydia*. Povidone-iodine (2% solution) may also be an effective prophylactic agent, especially in developing countries.

Identification of maternal gonococcal infection and appropriate treatment has become a standard element of routine prenatal care. An infant born to a woman who has untreated gonococcal infection should receive a single dose of ceftriaxone, 50 mg/kg (maximum 125 mg) IV or IM, in addition to topical prophylaxis. The dose should be reduced for premature infants. Penicillin (50,000 units) should be used if the mother's gonococcal isolate is known to be penicillin sensitive.

Neither topical prophylaxis nor topical treatment prevents the afebrile pneumonia that occurs in 10–20% of infants exposed to *C. trachomatis.* Although chlamydial conjunctivitis is often a self-limiting disease, chlamydial pneumonia may have serious consequences. It is important that infants with chlamydial disease receive systemic treatment. Treatment of colonized pregnant people with erythromycin may prevent neonatal disease.

Table 666.1 The Red Eye

CONDITION	CAUSE	SIGNS/SYMPTOMS	TREATMENT
Bacterial conjunctivitis	*Haemophilus influenzae*, *H. influenzae aegyptius*, *Streptococcus pneumoniae*, *Neisseria gonorrhoeae*, *Staphylococcus aureus*, *Yersinia* species, cat-scratch bacillus less common	Mucopurulent unilateral or bilateral discharge, normal vision, photophobia usually absent Conjunctival injection and edema (chemosis); gritty sensation	Topical antibiotics: systemic ceftriaxone for gonococcus, *H. influenzae*
Viral conjunctivitis	Adenovirus, ECHO virus, coxsackievirus, herpes simplex virus, coronavirus	As above; may be hemorrhagic, unilateral enlarged preauricular lymph nodes	Self-limited
Neonatal conjunctivitis	*Chlamydia trachomatis*, gonococcus, chemical (silver nitrate), *S. aureus*	Palpebral conjunctival follicle or papillae; as above	Ceftriaxone for gonococcus and oral erythromycin for *C. trachomatis*
Allergic conjunctivitis	Seasonal pollens or allergen exposure	Itching, incidence of bilateral chemosis (edema) greater than that of erythema, tarsal papillae	Antihistamines, steroids, cromolyn
Keratitis	Herpes simplex, adenovirus, *S. pneumoniae*, *S. aureus*, *Pseudomonas* species, *Acanthamoeba* species, chemicals	Severe pain, corneal swelling, clouding, limbus erythema, hypopyon, cataracts; contact lens history with amebic infection	Specific antibiotics for bacterial/fungal infections; keratoplasty, acyclovir for herpes
Endophthalmitis	*S. aureus*, *S. pneumoniae*, *Candida albicans*, associated surgery or trauma	Acute onset, pain, loss of vision, swelling, chemosis, redness; hypopyon and vitreous haze	Antibiotics
Anterior uveitis (iridocyclitis)	JIA, reactive arthritis, sarcoidosis, Behçet disease, Kawasaki disease, inflammatory bowel disease	Unilateral/bilateral; erythema, ciliary flush (in circumcorneal area), irregular pupil, iris adhesions; pain, marked photophobia, small pupil, poor vision, no discharge	Topical steroids, plus therapy for primary disease
Posterior uveitis (choroiditis)	Toxoplasmosis, histoplasmosis, *Toxocara canis*	No sign of erythema, decreased vision, no discharge	Specific therapy for pathogen
Episcleritis/ scleritis	Idiopathic autoimmune disease (e.g., SLE, Henoch-Schönlein purpura)	Localized pain, intense erythema, unilateral; blood vessels bigger than in conjunctivitis; scleritis may cause globe perforation, no discharge	Episcleritis is self-limiting; topical steroids for fast relief
Foreign body	Occupational exposure	Unilateral, red, gritty feeling; visible or microscopic size	Irrigation, removal; check for ulceration
Blepharitis	*S. aureus*, *S. epidermidis*, seborrheic, blocked lacrimal duct: rarely, molluscum contagiosum, *Pthirus pubis*, *Pediculosis capitis*	Bilateral, irritation, itching, hyperemia, crusting, affecting lid margins	Topical antibiotics, warm compresses
Dacryocystitis	Obstructed lacrimal sac: *S. aureus*, *H. influenzae*, pneumococcus	Pain, tenderness, erythema, and exudate in area of lacrimal sac (inferomedial to inner canthus); tearing (epiphora); possible orbital cellulitis	Systemic, topical antibiotics; surgical drainage
Dacryoadenitis	*S. aureus*, *Streptococcus* species, CMV, measles, EBV, enteroviruses, trauma, sarcoidosis, leukemia	Pain, tenderness, edema, erythema over gland area (upper temporal lid); fever, leukocytosis	Systemic antibiotics; drainage of orbital abscesses
Orbital cellulitis	Paranasal sinusitis: *H. influenzae*, *S. aureus*, *S. pneumoniae*, other *Streptococcus* species Trauma: *S. aureus* Fungi: *Aspergillus*, *Mucor* species if immunodeficient	Rhinorrhea, chemosis, vision loss, painful extraocular motion, proptosis, ophthalmoplegia, fever, lid edema, leukocytosis	Systemic antibiotics (postseptal cellulitis), drainage of orbital abscesses
Periorbital cellulitis	Trauma: *S. aureus*, *Streptococcus* species Bacteremia: *H. influenzae*, pneumococci, *S. pyogenes*, *S. aureus*	Cutaneous erythema, warmth, normal vision, minimal involvement of orbit, fever, leukocytosis, toxic appearance	Systemic antibiotics (preseptal cellulitis)

CMV, Cytomegalovirus; EBV, Epstein-Barr virus; ECHO, enteric cytopathogenic human orphan; JIA, juvenile idiopathic arthritis; SLE, systemic lupus erythematosus.
Modified from Behrman RE, Kliegman RM. *Nelson Essentials of Pediatrics*. 3rd ed. Philadelphia: WB Saunders; 1998; with data from Rosenbaum JT, Nozik RA. Uveitis: many diseases, one diagnosis. *Am J Med*. 1985;79:545–547; Elkington AR, Khaw PT. The red eye. *BMJ*. 1988;296:1720–1724; Wilhemus KR. The red eye. Infectious conjunctivitis, keratitis, endophthalmitis, and periocular cellulitis. *Infect Dis Clin North Am*. 1988;2:99–116; Forrester JV. Uveitis: pathogenesis. *Lancet*. 1991;338:1498–1501; Gioliotti F. Acute conjunctivitis of childhood. *Pediatr Ann*. 1993;22:353–356.

Acute Purulent Conjunctivitis

This is characterized by more or less generalized (bilateral in 50–75%) conjunctival hyperemia, edema, mucopurulent exudate, glued eyes (lids stuck together after sleeping), and various degrees of ocular pain and discomfort. It is usually a result of bacterial infection. In addition, there is usually little or no pruritus or periauricular lymph node enlargement; the peak season is between December and April. Bacterial conjunctivitis is more common in young children (<5 years), whereas viral conjunctivitis is more common among adolescents and adults. The most frequent causes are nontypeable *Haemophilus influenzae* (60–80%; associated with ipsilateral otitis media), pneumococci (20%), and staphylococci (5–10%). Bacterial purulent conjunctivitis, especially that caused by

pneumococcus or *H. influenzae,* may occur in epidemics. Conjunctival smear and culture are helpful in differentiating specific types. These common forms of acute purulent conjunctivitis usually respond well to warm compresses and topical instillation of antibiotic drops, which shortens the duration of illness and hastens return to school. Topical antibiotics include aminoglycosides (gentamicin, tobramycin), quinolones (ciprofloxacin, ofloxacin, moxifloxacin), and combinations of antibiotics and chloramphenicol (Table 666.2). Brazilian purpuric fever caused by *Haemophilus aegyptius* manifests as conjunctivitis and sepsis. **Hyperacute bacterial conjunctivitis** is caused by gonococcal or meningococcal infection and requires systemic, not topical, antimicrobial therapies. Concerning symptoms that should require an ophthalmology referral include vision loss, severe purulent discharge, corneal involvement, conjunctival scarring, cutaneous-conjunctival involvement (Stevens-Johnson syndrome), recurrent symptoms, severe pain, herpes simplex virus infection, severe photophobia, and involvement with a contact (cosmetic or prescription) lens.

Viral Conjunctivitis

This is generally characterized by a watery discharge. Follicular changes (small aggregates of lymphocytes) are often found in the palpebral conjunctiva. Involvement is often unilateral and associated with periauricular nodes. Viral conjunctivitis occurs more often in the summer and in older children (>5 years). Conjunctivitis resulting from adenovirus infection is relatively common, sometimes with corneal involvement as well as pharyngitis or pneumonia. Outbreaks of conjunctivitis caused by enterovirus are also encountered; this type may be hemorrhagic (Fig. 666.1). Acute hemorrhagic conjunctivitis may be epidemic because of enterovirus CA24 or 70 and is characterized by red, swollen, and painful eyes with a hemorrhagic watery discharge. Conjunctivitis is commonly associated with such systemic viral infections as childhood exanthems, particularly measles. Viral conjunctivitis is usually self-limited.

Epidemic Keratoconjunctivitis

This is caused by adenovirus serotypes 8, 19, or 37, and is transmitted by direct contact. It initially presents as a sensation of a foreign body beneath the lids, with itching and burning. Edema (chemosis) and photophobia develop rapidly, and large oval follicles appear within the conjunctiva. Preauricular adenopathy and a pseudomembrane on the conjunctival surface occur frequently. Subepithelial corneal infiltrates may develop and may cause blurring of vision; these usually disappear but may permanently reduce visual acuity. Corneal complications are less common in children than in adults. Children may have associated upper respiratory tract infection and pharyngitis. No specific medical therapy is available to decrease the symptoms or shorten the course of the disease. Emphasis must be placed on prevention of spread of the disease. A replicating virus is present in 95% of patients 10 days after the appearance of symptoms.

Pharyngoconjunctival fever presents with high fever, pharyngitis, bilateral conjunctivitis, and periauricular lymphadenopathy. It is highly contagious.

Membranous and Pseudomembranous Conjunctivitis

These types of conjunctivitis can be encountered in a number of diseases. The classic membranous conjunctivitis is that of diphtheria, accompanied by a fibrin-rich exudate that forms on the conjunctival surface and permeates the epithelium; the membrane is removed with difficulty and leaves raw bleeding areas. In pseudomembranous conjunctivitis, the layer of fibrin-rich exudate is superficial and can often be stripped easily, leaving the surface smooth. This type occurs with

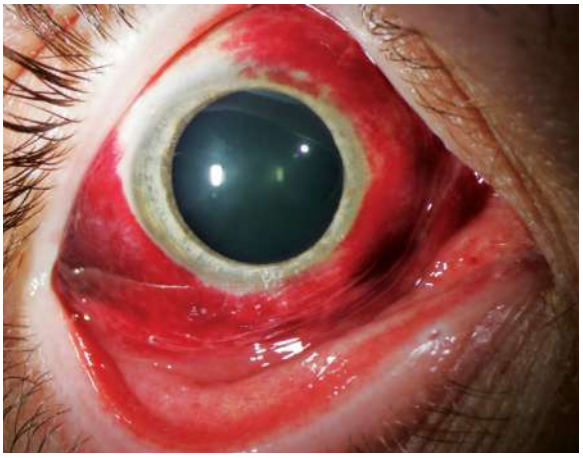

Fig. 666.1 Acute hemorrhagic conjunctivitis (AHC) is a highly contagious conjunctivitis that presents with symptoms of pain, redness, and tearing. Ocular findings include extensive subconjunctival hemorrhages, follicles, and chemosis. Causative agents include coxsackie group A24 (CA24) and enterovirus E70 (EV70). *(From Krachmer JH, Palay DA. Cornea Atlas. 3rd ed. London: Elsevier, 2014: Fig 7-23))*

Table 666.2 Topical Antibiotics Used to Treat Bacterial Conjunctivitis: Adult Dosages

DRUG	DOSAGE
Bacitracin (AK-Tracin, Bacticin) ointment	Apply 0.5 inch in eye q3-4hr
Ciprofloxacin (Ciloxan) 0.3% ophthalmic solution	1-2 gtt in eye q15min × 6 hr, then q30min × 18h, then q1hr × 1 day, then q4hr × 12 days*
Gatifloxacin (Zymar) 0.3% ophthalmic solution	1 gt in eye q2h up to 8 × per day × 2 days, then 1 gt qid × 5 days
Gentamicin (Gentak, Gentasol) 0.3% ophthalmic solution or ointment	Ointment: 0.5 inch applied to eye 2-3 × per day Solution: 1-2 gtt in eye q4hr
Levofloxacin (Quixin) 0.5% ophthalmic solution	1-2 gtt in eye q2hr × 2 days while awake, then q4hr × 5 days while awake
Moxifloxacin (Vigamox) 0.5% ophthalmic solution	1 gt in eye tid × 7 days
Neomycin/polymyxin B/gramicidin (Neosporin) ophthalmic solution	1-2 gtt in eye q4hr × 7-10 days
Ofloxacin (Ocuflox) 0.3% ophthalmic solution	1-2 gtt in eye q2-4hr × 2 days, then 1-2 gtt in eye qid × 5 days
Polymyxin B and trimethoprim (Polytrim) ophthalmic solution	1 gt in eye q3hr × 7-10 days
Sulfacetamide (Isopto Cetamide, Ocusulf-10, Sodium Sulamyd, Sulf-10, AK-Sulf) 10% ophthalmic solution, ointment	Ointment: 0.5-inch ribbon in eye q3-4hr and qhr × 7 days Solution: 1-2 gtt in eye q2-3hr × 7-10 days
Tobramycin (AK-Tob, Tobrex) 0.3% ophthalmic solution	1-2 gtt in eye q4hr

*Exceeds dosage recommended by the manufacturer.
From Bope ET, Kellerman RD, eds. *Conn's Current Therapy.* Philadelphia: Elsevier; 2014: Table 2, p. 321.

many bacterial and viral infections, including staphylococcal, pneumococcal, streptococcal, or chlamydial conjunctivitis, and in epidemic keratoconjunctivitis. It is also found in vernal conjunctivitis and in Stevens-Johnson disease.

Allergic Conjunctivitis

This is usually accompanied by intense itching, clear watery discharge, and conjunctival edema (chemosis) (see Chapter 188). It is commonly seasonal (spring-summer). Cold compresses and topical antihistamine drops give symptomatic relief. Topical mast cell stabilizers or prostaglandin inhibitors may also help. In selected cases, topical corticosteroids are used under an ophthalmologist's supervision but should not be used routinely or for a long time.

Vernal Conjunctivitis

This usually begins in the prepubertal years and may recur for many years. Atopy appears to have a role in its origin, but the pathogenesis is uncertain. Extreme itching and tearing are the usual complaints. Large, flattened, cobblestone-like papillary lesions of the palpebral conjunctivae are characteristic (Fig. 666.2). A stringy exudate and a milky conjunctival pseudomembrane are frequently present. Small elevated lesions of the bulbar conjunctiva adjacent to the limbus (Horner-Trantas dots) may be found. Smear of the conjunctival exudate reveals many eosinophils. Topical corticosteroid therapy and cold compresses afford some relief. Topical mast cell stabilizers or prostaglandin inhibitors are useful when long-term control is needed. The long-term use of corticosteroids should be avoided.

Parinaud Oculoglandular Syndrome

This represents a form of cat-scratch disease and is caused by *Bartonella henselae,* which is transmitted from cat to cat by fleas (see Chapter 255). Kittens are more likely than adult cats to be infected. Humans can become infected when they are scratched by a cat. In addition, bacteria may pass from a cat's saliva to its fur during grooming. The bacteria can then be deposited on the conjunctiva after rubbing one's eyes after handling the cat. Lymphadenopathy and conjunctivitis are hallmarks of the disease. Conjunctival granulomas may develop (Fig. 666.3). The course is generally self-limited, but antibiotics may be used in some cases.

Chemical Conjunctivitis

This can result when an irritating substance enters the conjunctival sac (as in the acute but benign conjunctivitis caused by silver nitrate in newborns). Other common offenders are household cleaning substances (including detergent pods), sprays, smoke, smog, metal halide bulbs, and industrial pollutants. Alkalis tend to linger in the conjunctival tissues and continue to inflict damage for hours or days. Acids precipitate the proteins in tissues and so produce their effect immediately. In either case, prompt, thorough, and copious irrigation is crucial. Extensive tissue damage, even loss of the eye, can result, especially if the offending agent is an alkali.

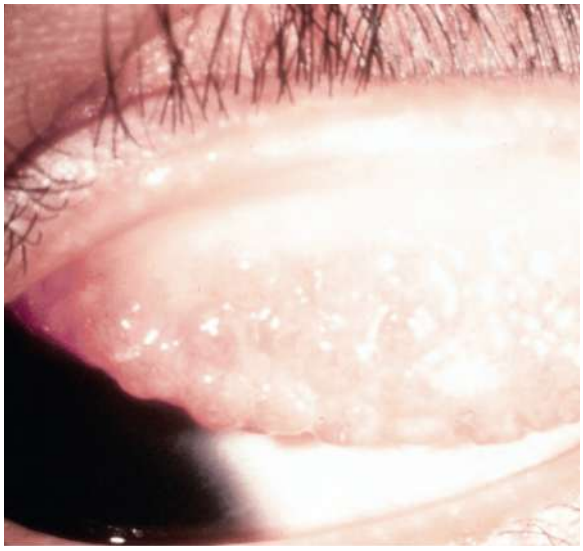

Fig. 666.2 Vernal conjunctivitis.

OTHER CONJUNCTIVAL DISORDERS

Subconjunctival hemorrhage is manifested by bright or dark red patches in the bulbar conjunctiva and may result from injury or inflammation. It commonly occurs spontaneously. It may occasionally result from severe sneezing or coughing. Rarely, it may be a manifestation of a blood dyscrasia. Subconjunctival hemorrhages are self-limiting and require no treatment.

Pinguecula is a yellowish white, slightly elevated mass on the bulbar conjunctiva, usually in the interpalpebral region (Fig. 666.4). It represents elastic and hyaline degenerative changes of the conjunctiva. No treatment is required except for cosmetic reasons, in which case simple excision suffices.

Pterygium is a fleshy triangular conjunctival lesion that may encroach on the cornea. It typically occurs in the nasal interpalpebral region (Fig. 666.5). The pathologic findings are similar to those

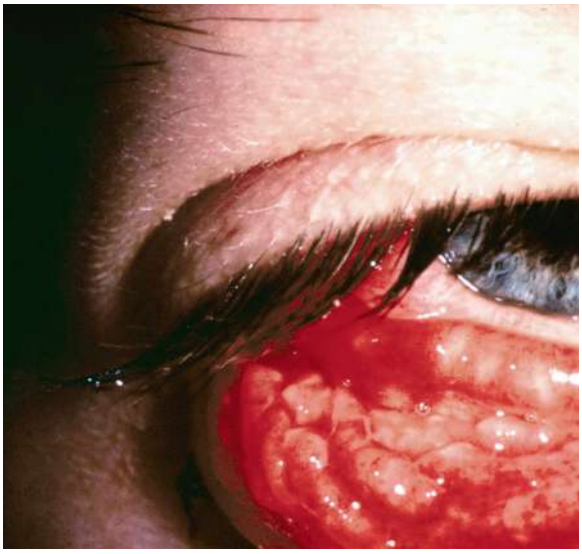

Fig. 666.3 Conjunctival granulomas in Parinaud oculoglandular syndrome.

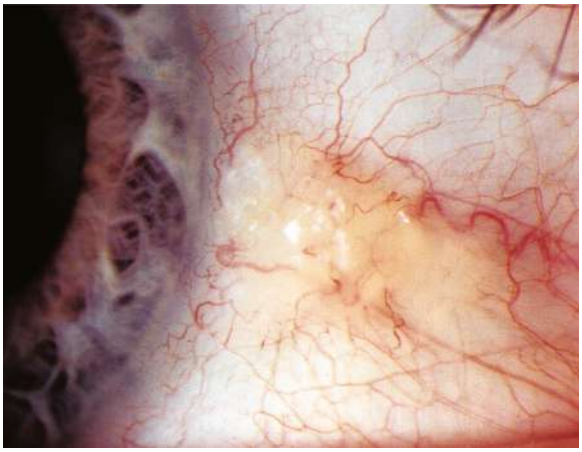

Fig. 666.4 Pinguecula. These lesions are found at the 3 o'clock and 9 o'clock positions and are extremely common, especially in older patients. *(From Palay DA, Krachmer JH. Primary Care Ophthalmology, 2nd ed, Philadelphia: Elsevier Mosby; 2005: Fig. 3.49, p 62.)*

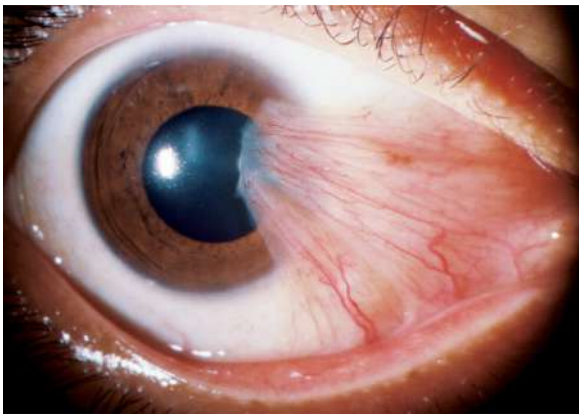

Fig. 666.5 Pterygium. These lesions are found in the horizontal meridian, most common nasally. *(From Palay DA, Krachmer JH. Primary Care Ophthalmology. 2nd ed. Philadelphia: Elsevier Mosby; 2005: Fig. 3.50, p 62.)*

of a pinguecula. The development of pterygia is related to exposure to ultraviolet light, and it therefore is more commonly found among people who live near the equator. Removal is suggested when the lesion encroaches far onto the cornea. Recurrence after removal is common.

Dermoid cyst and **dermolipoma** are benign lesions, clinically similar in appearance. They are smooth, elevated, round to oval lesions of various sizes. The color varies from yellowish white to fleshy pink. The most frequent site is the upper outer quadrant of the globe; they also commonly occur near or straddling the limbus. Dermolipoma is composed of adipose and connective tissue. Dermoid cysts may also contain glandular tissue, hair follicles, and hair shafts. Excision for cosmetic reasons is feasible. Dermolipomas are often connected to the extraocular muscles, making their complete removal impossible without sacrificing ocular motility.

Conjunctival nevus is a small, slightly elevated lesion that may vary in pigmentation from pale salmon to dark brown. It is usually benign, but careful observation for progressive growth or changes suggestive of malignancy is advised.

Symblepharon is a cicatricial adhesion between the conjunctiva of the lid and the globe; the lower lid is usually affected. It follows operation or injuries, especially burns from lye, acids, or molten metals. It is a serious complication of Stevens-Johnson syndrome. It may interfere with motion of the eyeball and may cause diplopia. The adhesions should be separated and the raw surfaces kept from uniting during healing. Grafts of oral mucous membrane may be necessary.

Visit Elsevier eBooks+ at eBooks.Health.Elsevier.com for Bibliography.

Chapter 667

Abnormalities of the Cornea

Scott E. Olitsky and Justin D. Marsh

MEGALOCORNEA

This is a nonprogressive symmetric condition characterized by an enlarged cornea (>12 mm in diameter) and an anterior segment in which there is *no evidence* of previous or concurrent ocular hypertension (glaucoma). High myopia is frequently present and may lead to reduced vision. A frequent complication is the development of lens opacities in adult life. All modes of inheritance have been described, although X-linked recessive is the most common. Systemic abnormalities that may be associated with megalocornea include Marfan syndrome, craniosynostosis, and Alport syndrome. The cause of the enlargement of the cornea and the anterior segment is unknown, but possible explanations include a defect in the growth of the optic cup and an arrest of congenital glaucoma.

Pathologic corneal enlargement caused by glaucoma is to be differentiated from this anomaly. Any progressive increase in the size of the cornea, especially when accompanied by photophobia, lacrimation, or haziness of the cornea, requires prompt ophthalmologic evaluation.

MICROCORNEA

Microcornea, or anterior microphthalmia, is an abnormally small cornea in an otherwise relatively normal eye. It may be familial, with transmission being dominant more often than recessive. More commonly, a small cornea is just one feature of an otherwise developmentally abnormal or microphthalmic eye; associated defects include colobomas, microphakia, congenital cataract, glaucoma, and aniridia.

KERATOCONUS

This is a disease of unclear pathogenesis characterized by progressive thinning and bulging of the central cornea, which becomes cone shaped. Although familial cases are known, most cases are sporadic. It is a common ocular condition with an incidence of 1 in 2,000 adults. Eye rubbing and contact lens wear have been implicated as pathogenic, but the evidence to support this is equivocal. The incidence is increased in individuals with atopy, Down syndrome, Marfan syndrome, and retinitis pigmentosa.

Most cases are bilateral, but involvement may be asymmetric. The disorder usually presents and progresses rapidly during adolescence; progression then slows and stabilizes when patients reach full growth. Descemet's membrane may occasionally be stretched beyond its elastic breaking point, causing an acute rupture in the membrane with resultant sudden and marked corneal edema (acute hydrops, Fig. 667.1) and decrease in vision. The corneal edema resolves as endothelial cells cover the defective area. Some degree of corneal scarring occurs, but the visual acuity is often better than before the initial incident. Signs of keratoconus include Munson sign (bulging of the lower eyelid on looking downward) and the presence of a Fleischer ring (a deposit of iron in the epithelium at the base of the cone). Glasses and contact lenses are the first step in treating the visual distortion caused by keratoconus. Corneal cross-linking is a procedure using riboflavin and UV light and may arrest the progression of keratoconus. If the cornea vaults too severely for the vision to be corrected with contact lenses, then a corneal transplant must be performed to restore vision.

NEONATAL CORNEAL OPACITIES

Loss of the normal transparency of the cornea in neonates may occur secondary to either intrinsic hereditary or extrinsic environmental causes (Table 667.1).

SCLEROCORNEA

In sclerocornea, the normally translucent cornea is replaced by sclera-like tissue. Instead of a clearly demarcated cornea, white, feathery, often ill-defined, and vascularized tissue develops in the peripheral cornea, appearing to blend with and extend from the sclera. The central cornea is usually clearer, but total replacement of the cornea with sclera may occur. The curvature of the cornea is often flatter, similar to the sclera. Potentially coexisting abnormalities include a shallow anterior chamber, iris abnormalities, and microphthalmos. This condition is usually bilateral. In approximately 50% of cases, a dominant or recessive inheritance has been described. Sclerocornea has been reported in association with numerous systemic abnormalities including limb deformities, craniofacial defects, and genitourinary disorders. In generalized sclerocornea, especially if bilateral, early corneal transplantation should be considered in an effort to provide vision.

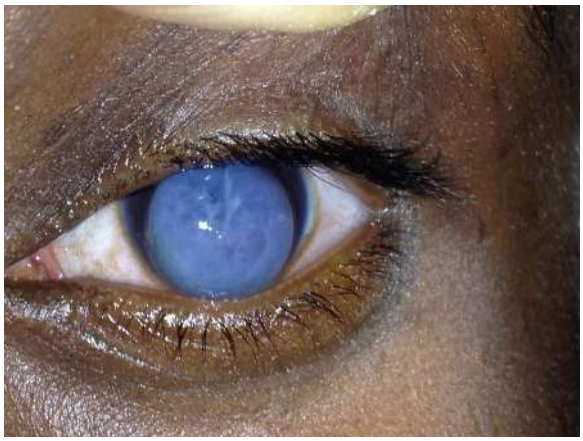

Fig. 667.1 Acute hydrops from keratoconus with significant corneal edema.

Sclerocornea is classified into one of the congenital corneal opacity disorders with cornea plana if it involves peripheral scleralization or a total sclerocornea disorder such as Peters anomaly.

PETERS ANOMALY

Peters anomaly (irido-corneo-trabecular dysgenesis) is a bilateral central corneal opacity (leukoma) that is present at birth (Fig. 667.2). It is often associated with iridocorneal adhesions that extend from the iris collarette to the border of the corneal opacity. Approximately 50% of patients have other ocular abnormalities, which may include cataracts, glaucoma, and microphthalmia. As many as 80% of cases may be bilateral, and 60% are associated with systemic malformations **(Peters plus syndrome)**, which may include short stature, developmental delay, cleft lip and/or palate, dysmorphic facial features, and cardiac, genitourinary, and central nervous system malformations. Peters plus syndrome is an autosomal recessive (*B3GLCT* gene) disorder.

Some investigators have divided Peters anomaly into two types: a mesodermal or neuroectodermal form (type 1), which does not show

Table 667.1 STUMPED: Differential Diagnosis of Neonatal Corneal Opacities

DIAGNOSIS	LATERALITY	OPACITY	OCULAR PRESSURE	OTHER OCULAR ABNORMALITIES	NATURAL HISTORY	INHERITANCE
S—Sclerocornea	Unilateral or bilateral	Vascularized, blends with sclera, clearer centrally	Normal (or elevated)	Cornea plana	Nonprogressive	Sporadic
T—Tears in endothelium and Descemet's membrane						
Birth trauma	Unilateral	Diffuse edema	Normal	Possible hyphema, periorbital ecchymoses	Spontaneous improvement in 1 mo	Sporadic
Infantile glaucoma	Bilateral	Diffuse edema	Elevated	Megalocornea, photophobia and tearing, abnormal angle	Progressive unless treated	Autosomal recessive
U—Ulcers						
Herpes simplex keratitis	Unilateral	Diffuse with geographic epithelial defect	Normal	None	Progressive	Sporadic
Congenital rubella	Bilateral	Disciform or diffuse edema, no frank ulceration	Normal or elevated	Microphthalmos, cataract, pigment epithelial mottling	Stable, may clear	Sporadic
Neurotrophic exposure	Unilateral or bilateral	Central ulcer	Normal	Lid anomalies, congenital sensory neuropathy	Progressive	Sporadic
M—Metabolic (rarely present at birth) (mucopolysaccharidoses IH, IS; mucolipidosis type IV)*	Bilateral	Diffuse haze, denser peripherally	Normal	Few	Progressive	Autosomal dominant
P—Posterior corneal defect	Unilateral or bilateral	Central, diffuse haze or vascularized leukoma	Normal or elevated	Anterior chamber cleavage syndrome	Stable, sometimes early clearing or vascularization	Sporadic, autosomal recessive
E—Endothelial dystrophy						
Congenital hereditary endothelial dystrophy	Bilateral	Diffuse corneal edema, marked corneal thickening	Normal	None	Stable	Autosomal dominant or recessive
Posterior polymorphous dystrophy	Bilateral	Diffuse haze, normal corneal thickness	Normal	Occasional peripheral anterior synechiae	Slowly progressive	Autosomal dominant
Congenital hereditary stromal dystrophy	Bilateral	Flaky, feathery stromal opacities; normal corneal thickness	Normal	None	Stable	Autosomal dominant
D—Dermoid	Unilateral or bilateral	White vascularized mass, hair, lipid arc	Normal	None	Stable	Sporadic

*Mucopolysaccharidosis IH (Hurler syndrome); mucopolysaccharidosis IS (Scheie syndrome).
From Nelson LB, Calhoun JH, Harley RD. *Pediatric Ophthalmology*. 3rd ed. Philadelphia: WB Saunders; 1991, p. 210.

Fig. 667.2 Peters anomaly. Central opacity in a patient with Peters anomaly.

associated lens changes, and a surface ectodermal form (type 2), which does. Histologic findings include a focal absence of Descemet's membrane and corneal endothelium in the region of the opacity. Peters anomaly may be caused by incomplete migration and differentiation of the precursor cells of the central corneal endothelium and Descemet's membrane, or a defective separation between the primitive lens and cornea during embryogenesis. Peters anomaly may be autosomal recessive (*CYP1B1* gene) or autosomal dominant (*FOXC1*, *PAX6*, *PITX2* genes).

CORNEAL DYSTROPHIES

These are rare inherited disorders that may present at birth, during childhood, or during early adulthood with bilateral involvement (although severity may be asymmetric) and that progress with time (Table 667.2). In most, inheritance is autosomal dominant with variable expression; the most common pathogenic variant is in *TGFB1*, which is associated with the granular corneal dystrophy types 1 and 2, as well as lattice corneal dystrophy. Congenital hereditary endothelial dystrophy is both an autosomal recessive and dominant disorder; the recessive form presents at birth and is more severe (Fig. 667.3; see also Table 667.2); three variants are X-linked.

DERMOIDS

Epibulbar dermoids are choristomas. They are often present at birth and may increase in size with age. They occur most frequently in the lower temporal quadrant. They most commonly straddle the limbus and extend into the peripheral cornea (Fig. 667.4). Rarely, they may be confined entirely to the cornea or conjunctiva. Epibulbar (or limbal) dermoids may cause visual disturbance by encroaching on the visual axis or by contributing to the development of astigmatism, which may lead to amblyopia.

A dermoid usually appears as a well-circumscribed, rounded or oval, gray or pinkish-yellow mass with a dry surface from which short hairs may protrude. It may affect only the superficial layers of the cornea, although full-thickness involvement is common. Associated ocular anomalies include eyelid and iris colobomas, microphthalmos, and retinal and choroidal defects. A total of 30% of dermoids are associated with systemic abnormalities. Many of the associated anomalies involve developmental defects of the first branchial arch (vertebral anomalies, dysostosis of the facial bones, ear anomalies and dental anomalies, and Goldenhar syndrome). Epibulbar dermoids are found in 75% of cases of Goldenhar syndrome.

DENDRITIC KERATITIS

Infection of the cornea with the herpes simplex virus produces a characteristic lesion of the corneal epithelium, referred to as a dendrite; it has a branching, treelike pattern that can be demonstrated by fluorescein staining (Fig. 667.5). The acute episode is accompanied by pain, photophobia, tearing, blepharospasm, and conjunctival injection. Specific treatment may include mechanical debridement of the involved corneal epithelium to remove the source of infection and eliminate an antigenic stimulus to inflammation in the adjacent stroma. Medical treatment may include the use of topical trifluridine, topical ganciclovir, or systemic acyclovir/valacyclovir. In addition, a cycloplegic agent is useful to relieve pain from spasm of the ciliary muscle. Overly aggressive topical antiviral treatment itself can be toxic to the cornea and should be avoided. Recurrent infection and deep stromal involvement can lead to corneal scarring and loss of vision.

Topical use of corticosteroids causes exacerbation of superficial herpetic disease of the eye and may lead to corneal perforation; eye drops combining steroids and antibiotics are therefore to be avoided in treatment of red eye, unless there are clear-cut indications for their use and close supervision during therapy.

Infants born to mothers infected with herpes simplex virus should be examined carefully for signs of ocular involvement. Intravenous acyclovir is required for treatment of ocular herpes in newborns.

CORNEAL ULCERS

The usual signs and symptoms are focal or diffuse corneal haze, hyperemia, lid edema, pain, photophobia, tearing, and blepharospasm. It is important to distinguish a corneal ulcer from that of a corneal abrasion. Although a corneal abrasion involves loss of the epithelial layer of the cornea and subsequently stains with topical fluorescein, a corneal ulcer also has underlying stromal infiltration and appears white or hazy on examination. Corneal ulcers can be infectious or noninfectious in origin. **Hypopyon** (pus in the anterior chamber) is common, particularly when the cause is infection. Regardless of cause, corneal ulcers require prompt treatment. Infectious cases result most frequently from contact lens wear and traumatic lesions that become secondarily infected. Although many organisms are capable of infecting the cornea, *Pseudomonas aeruginosa* can be particularly devastating because it can rapidly destroy stromal tissue and lead to corneal perforation. *Neisseria gonorrhoeae* also is particularly damaging to the cornea. Indolent ulcers may be caused by fungi, often in association with the use of contact lenses. In each case, scrapings of the cornea must be studied in an effort to identify the infectious agent and determine the best therapy. Although aggressive local treatment is generally needed to save the eye, systemic treatment may be necessary in some cases as well. Perforation or scarring resulting from corneal ulceration is an important cause of blindness throughout the world and is estimated to be responsible for 10% of blindness in the United States.

Unexplained corneal ulcers in infants and young children should raise the question of a sensory defect, as in Riley-Day or Goldenhar-Gorlin syndrome, or of a metabolic disorder, such as tyrosinemia (Fig. 667.6). Corneal ulceration can also occur as a consequence of severe vitamin deficiencies, such as those seen with malabsorption in cystic fibrosis or restrictive eating disorders. Peripherally located inflammatory ulcers are commonly associated with blepharitis and typically require both topical antibiotic and corticosteroid treatment.

PHLYCTENULES

These are small, yellowish, slightly elevated lesions usually located at the corneal limbus; they may encroach on the cornea and extend centrally. A small corneal ulcer is often found at the head of the advancing lesion, with a fascicle of blood vessels behind the head of the lesion. Although once thought to represent a sign of systemic tuberculin infection, phlyctenular keratoconjunctivitis is a morphologic expression of delayed hypersensitivity to diverse antigens. In children, it commonly occurs as a result of a hypersensitivity reaction to nonpathogenic staphylococcal strains at the eyelid margin. Treatment usually consists of eliminating the underlying disorder, usually staphylococcal blepharitis or meibomianitis, and suppressing the immune response with the use of topical corticosteroid therapy. A superficial stromal pannus and scarring sometimes remain after treatment.

Table 667.2 Corneal Dystrophies Classified According to IC3D, Second Edition

NAME	LOCUS	GENE	INHERITANCE
EPITHELIAL AND SUBEPITHELIAL DYSTROPHIES			
Epithelial basement membrane dystrophy	5q31	*TGFBI*	AD Mostly sporadic
Epithelial recurrent erosion dystrophies	10q25.1	*COL17A1*	AD
Subepithelial mucinous corneal dystrophy	Unknown	Unknown	AD
Meesmann corneal dystrophy	12 q13 17q12	*KRT3* *KRT12*	AD
Lisch epithelial corneal dystrophy	Xp22.3	Unknown	XLD
Gelatinous drop–like corneal dystrophy	1p32	*TACSTD2*	AR
EPITHELIAL—STROMAL *TGFBI* DYSTROPHIES			
Reis-Bückler corneal dystrophy	5q31	*TGFBI*	AD
Thiel-Behnke corneal dystrophy	5q31	*TGFBI*	AD
Lattice corneal dystrophy	5q31	*TGFBI*	AD
Granular corneal dystrophy type 1	5q31	*TGFBI*	AD
Granular corneal dystrophy type 2	5q31	*TGFBI*	AD
STROMAL DYSTROPHIES			
Macular corneal dystrophy	16q22	*CHST6*	AR
Schnyder corneal dystrophy	1p36	*UBIAD1*	AD
Congenital stromal corneal dystrophy	12q21.33	*DCN*	AD
Fleck corneal dystrophy	2q34	*PIKFYVE*	AD
Posterior amorphous corneal dystrophy	12q21.33	*DCN* *KERA* *LUM* *EPYC*	AD
Central cloudy dystrophy of Francois	Unknown	Unknown	AD
Pre-Descemet's corneal dystrophy	Xp22.31 Unknown	*STS* Unknown	XLR (when associated with x-linked ichthyosis) AD (in isolated corneal dystrophy)
ENDOTHELIAL DYSTROPHIES			
Fuchs endothelial corneal dystrophy (FECD)	1p34.3-p32 18q21.2 10p11.22 20p13	*COL8A2* *TCF4* *ZEB1* *SLC4A11*	AD (early-onset FECD)
Posterior polymorphous corneal dystrophy	20p11.2-q11.2 1p34.3-p32.3 10p11.22	Unknown *COL8A2* *ZEB1*	AD
Congenital hereditary endothelial dystrophy	20p13	*SLC4A11*	AR
X-linked endothelial corneal dystrophy	Xq25	Unknown	XLD

IC3D, International Committee for Classification of Corneal Dystrophies; AD, autosomal dominant; AR, autosomal recessive; XLD, X-linked dominant.
From Bitar M, Hara Y, Sethi D, Couser NL. Genetic abnormalities of the cornea. In Couser NL, ed. *Ophthalmic Genetic Diseases*. Elsevier; 2019: Table 5.1, p. 62.

INTERSTITIAL KERATITIS

This denotes nonulcerative inflammation of the corneal stroma. There is a diverse list of causes of interstitial keratitis (IK), including bacterial, viral, parasitic, and inflammatory etiologies (Table 667.3). In the United States, herpesvirus infections and congenital syphilis account for the majority of cases of IK. Although the corneal findings may regress with time, "ghost vessels," which represent the previous vascular changes, and patchy corneal scarring remain and serve as permanent stigmata of the disease.

Cogan syndrome is an autoimmune IK associated with hearing loss and vestibular symptoms. Although its cause is unknown, a systemic vasculitis is suspected. Prompt treatment is required to avoid permanent hearing loss. Both the corneal changes and the auditory involvement may respond to the use of corticosteroids and immunosuppressive agents.

CORNEAL MANIFESTATIONS OF SYSTEMIC DISEASE

Several metabolic diseases produce distinctive corneal changes in childhood. Refractile polychromatic crystals are deposited throughout the cornea in cystinosis (see Chapter 105.4). Corneal deposits producing various degrees of corneal haze also occur in certain types

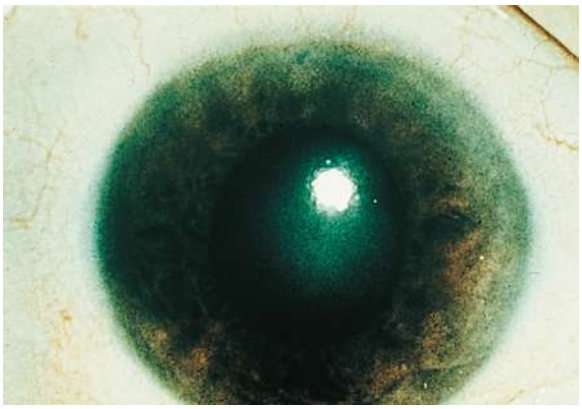

Fig. 667.3 Congenital hereditary endothelial dystrophy. This cornea is markedly edematous but has no enlargement. Intraocular pressure was normal. Patient has since undergone corneal transplantation with excellent results. *(From Stamper RL, Lieberman MF, Drake MV, eds. Becker-Shaffer's Diagnosis and Therapy of the Glaucomas. 8th ed. Philadelphia: Mosby; 2009: Fig. 19-21, p. 30).)*

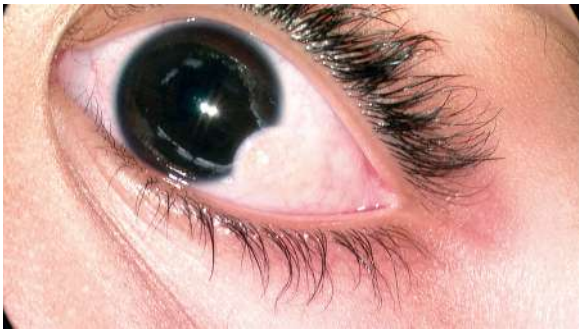

Fig. 667.4 Limbal dermoid. Inferotemporal lesion in a patient with Goldenhar syndrome.

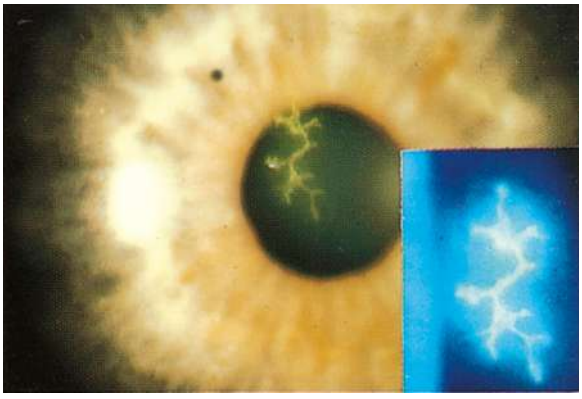

Fig. 667.5 Herpes simplex corneal epithelial keratitis in diffuse light and in light passed through a cobalt blue filter after fluorescein staining *(inset)*. Note the dendritic staining pattern characteristic of herpes simplex. *(From Goldman L, Schafer AI, eds. Goldman-Cecil Medicine. 25th ed. Philadelphia: Elsevier; 2016: Fig. 423.19.)*

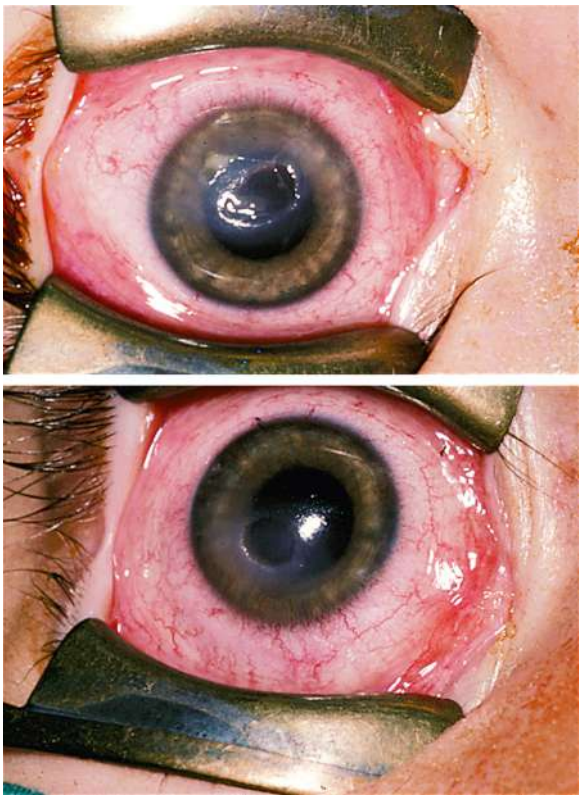

Fig. 667.6 Riley-Day syndrome. This child had a combination of anesthetic corneas and dry eyes that had been treated for several months by topical wetting agents without success. He responded well to a bilateral tarsorrhaphy and lubricant ointment. Later, punctal occlusion allowed enough wetting of his eyes to allow the tarsorrhaphies to be undone. *(From Hoyt CS, Taylor D, eds. Pediatric Ophthalmology and Strabismus, 4th ed. Philadelphia: Elsevier; 2013: Fig. 33.9, p. 315.)*

of mucopolysaccharidosis (MPS; see Chapter 109), particularly MPS IH (Hurler), MPS IS (Scheie), MPS I H/S (Hurler-Scheie compound), MPS IV (Morquio), MPS VI (Maroteaux-Lamy), and sometimes MPS VII (Sly). Corneal deposits may develop in patients with GM_1 (generalized) gangliosidosis (see Chapter 106.4). In Fabry disease, fine opacities radiating in a whorl or fanlike pattern occur, and corneal changes can be important in identifying the carrier state (see Chapter 106.4). A spraylike pattern of corneal opacities may also be seen in the Bloch-Sulzberger syndrome (incontinentia pigmenti; see Chapter 636.7). In Wilson disease (see Chapter 405.2), the distinctive corneal sign is the Kayser-Fleischer ring, a golden-brown ring in the peripheral cornea resulting from changes in Descemet's membrane. Pigmented corneal rings may develop in neonates with cholestatic liver disease. Corneal changes may occur in autoimmune hypoparathyroidism and band keratopathy in patients with hypercalcemia (see Chapters 611 and 613.1). Transient keratitis may occur with measles and sometimes with rubella (see Chapter 294).

Visit Elsevier eBooks+ at eBooks.Health.Elsevier.com for Bibliography.

Table 667.3 Partial List of Causative Agents in Microbial Keratitis

BACTERIA

Gram-Positive Cocci

- *Staphylococcus aureus*
- *Staphylococcus epidermidis*
- *Streptococcus pneumoniae, Streptococcus pyogenes,* viridans streptococci
- *Enterococcus faecalis*
- *Peptostreptococcus* spp.

Gram-Positive Bacilli

- *Bacillus coagulans, Bacillus cereus, Bacillus licheniformis*
- *Brevibacillus (Bacillus) brevis, Brevibacillus (Bacillus) laterosporus*
- *Corynebacterium diphtheriae*
- *Clostridium perfringens, Clostridium tetani*

Gram-Negative Coccobacilli

- *Neisseria gonorrhoeae*
- *Moraxella lacunata, Moraxella nonliquefaciens, Moraxella catarrhalis*
- *Acinetobacter calcoaceticus*
- *Pasteurella multocida*
- *Achromobacter xylosoxidans*

Gram-Negative Bacilli

- *Pseudomonas aeruginosa, Pseudomonas stutzeri, Pseudomonas fluorescens*
- *Burkholderia (Pseudomonas) mallei*
- *Proteus mirabilis*
- *Serratia marcescens*
- *Escherichia coli*
- *Klebsiella pneumoniae*
- *Morganella morganii*
- *Aeromonas hydrophila*
- *Bartonella henselae*

Mycobacteria

- *Mycobacterium tuberculosis, Mycobacterium chelonae, Mycobacterium gordonae, Mycobacterium mucogenicum*

Actinomycetes

- *Nocardia* spp.

Spirochetes

- *Treponema pallidum*
- *Borrelia burgdorferi*

VIRUSES

- Herpes simplex virus
- Varicella-zoster virus
- Adenovirus
- Vaccinia virus
- Epstein-Barr virus
- Rubeola
- Enteroviruses
- Coxsackievirus

FUNGI

- *Fusarium* spp.
- *Candida* spp.
- *Aspergillus* spp.
- *Acremonium* spp.
- *Alternaria* spp.
- *Penicillium* spp.
- *Bipolaris* spp.
- *Nosema* spp.
- *Vittaforma (Nosema) corneae*
- *Encephalitozoon* spp.
- *Edenia gomezpompae*
- *Exophiala phaeomuriformis*

CHLAMYDIA

- *Chlamydia trachomatis*

PARASITES

- *Acanthamoeba polyphaga, Acanthamoeba castellanii*
- *Onchocerca volvulus*
- *Leishmania brasiliensis*
- *Trypanosoma* spp.

From Azar DT, Hallak J, Barnes SD, et al. Microbial keratitis. In: Bennett JE, Dolin R, Blaser MJ, eds. *Mandell, Douglas, and Bennett's Principles and Practices of Infectious Diseases.* 9th ed. Saunders; 2020: Table 113.1, p. 1509.

Chapter 668

Abnormalities of the Lens

Scott E. Olitsky and Justin D. Marsh

CATARACTS

A cataract is any opacity of the lens (Fig. 668.1). Some are clinically unimportant; others significantly affect visual function. The incidence of infantile cataracts is approximately 2-13/10,000 live births. Approximately 60% of cataracts are an isolated defect, 22% are part of a syndrome, and the remaining cases are associated with other unrelated major birth defects. Cataracts are more common in low birthweight infants. Infants who weigh at or below 2,500 g have a three- to fourfold increased odds of developing infantile cataracts. Some cataracts are associated with other ocular or systemic diseases.

Differential Diagnosis

The differential diagnosis of cataracts in infants and children includes a wide range of developmental disorders, infectious and inflammatory processes, metabolic diseases, and toxic and traumatic insults (Table 668.1). Cataracts may also develop secondary to intraocular processes, such as retinopathy of prematurity, persistent hyperplastic primary vitreous, retinal detachment, retinitis pigmentosa, and uveitis. Finally, a fraction of cataracts in children are inherited (Fig. 668.2).

Developmental Variants

Early developmental processes may lead to various congenital lens opacities. Discrete dots or white plaquelike opacities of the lens capsule are common and sometimes involve the contiguous subcapsular region. Small opacities of the posterior capsule may be associated with persistent remnants of the primitive hyaloid vascular system (the common Mittendorf dot), whereas those of the anterior capsule may be associated with persistent strands of the pupillary membrane or vascular sheath of the lens. Congenital cataracts of this type are usually stationary and rarely interfere with vision, but in some cases, progression occurs.

Prematurity

A special type of lens change seen in some preterm newborn infants is the so-called *cataract of prematurity*. The appearance is of a cluster of tiny vacuoles in the distribution of the Y sutures of the lens. They can be visualized with an ophthalmoscope and are best seen with the pupil well dilated. The pathogenesis is unclear. In most cases, the opacities disappear spontaneously, often within a few weeks.

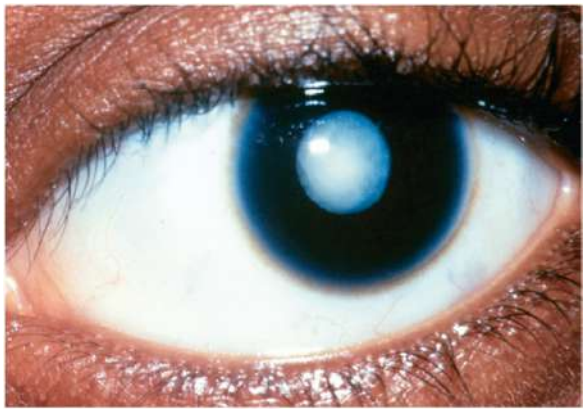

Fig. 668.1 Leukocoria secondary to cataract.

Mendelian Inheritance

Many isolated, idiopathic cataracts unassociated with other diseases are hereditary. There are ~35 genes associated with isolated pediatric cataracts; ~40% are inherited as autosomal dominants, ~20% are autosomal recessive, and ~35% have both dominant and recessive traits. Twelve crystallin gene pathologic variants are the most frequently identified genetic etiologies for both autosomal dominant and recessive inheritance patterns. Other involved genes include transcription factors, membrane proteins, and cytoskeletal proteins.

Congenital Infection Syndrome

Cataracts in infants and children can be a result of prenatal infection. Lens opacity may occur in any of the major congenital infection syndromes (e.g., toxoplasmosis, cytomegalovirus, syphilis, rubella, herpes simplex virus). Cataracts may also occur secondary to other perinatal infections, including measles, poliomyelitis, influenza, varicella-zoster, and vaccinia.

Metabolic Disorders

Cataracts are a prominent manifestation of many metabolic diseases, particularly certain disorders of carbohydrate, amino acid, calcium, and copper metabolism. A primary consideration in any infant with cataracts is the possibility of **galactosemia** (see Chapter 107.2). In classic infantile galactosemia, galactose-1-phosphate uridyltransferase deficiency, the cataract is typically of the zonular type, with haziness or opacification of one or more of the perinuclear layers of the lens. Haziness or clouding of the nucleus also often occurs. In its early stages, the cataract generally has a distinctive oil droplet appearance and is best detected with the pupil fully dilated. Progression to complete opacification of the lens may occur within weeks. With early treatment (galactose-free diet), the lens changes may be reversible.

In **galactokinase deficiency**, cataracts are the sole clinical manifestation. The cataracts are usually zonular and may appear in the first few months of life, first few years of life, or later in childhood.

In children with juvenile-onset diabetes mellitus, lens changes are uncommon. Some develop snowflake-like white opacities and vacuoles of the lens. Others develop cataracts that may progress and mature rapidly, sometimes in a matter of days, especially during adolescence. An antecedent event may be the sudden development of myopia caused by changes in the optical density of the lens. Congenital lens opacities may be seen in children of diabetic and prediabetic mothers (see Chapter 147).

Hypoglycemia in neonates can also be associated with early development of cataracts. Ketotic hypoglycemia is also associated with cataracts.

An association between cataracts and hypocalcemia is well established. Various lens opacities may be seen in patients with hypoparathyroidism (see Chapter 611).

The **oculocerebral renal syndrome of Lowe** is associated with cataracts in infants. Affected male children frequently have dense bilateral cataracts at birth, often in association with glaucoma and miotic pupils. Punctate lens opacities are frequently present in heterozygous females.

The distinctive sunflower cataract of **Wilson disease** is not commonly seen in children. Various lens opacities may be seen in children with certain of the sphingolipidoses, mucopolysaccharidoses, and mucolipidoses, particularly Niemann-Pick disease, mucosulfatidosis, Fabry disease, and aspartylglycosaminuria.

Cerebrotendinous xanthomatosis (CTX) is an autosomal recessive metabolic storage disease involving a pathogenic variant in an enzyme used during bile acid synthesis, leading to accumulation of cholesterol in the brain and elsewhere. In addition to cataract formation in childhood, patients may develop chronic diarrhea in infancy and progressive cognitive and neurologic impairment later in life. Early detection is vital as cataract formation may occur before permanent neurologic impairment, providing a window of time to treat the condition. Treatment typically consists of oral chenodeoxycholic acid.

Table 668.1 Differential Diagnosis of Cataracts

DEVELOPMENTAL VARIANTS
Prematurity (Y-suture vacuoles) with or without retinopathy of prematurity
Mittendorf dot (remnant of hyaloid artery)
Persistent pupillary membrane (remnant of embryonic lens vasculature)

GENETIC DISORDERS
Simple Mendelian Inheritance
Autosomal dominant (most common)
Autosomal recessive
X-linked

Major Chromosomal Defects
Trisomy disorders (13, 15, 18, 21)
Turner syndrome (45X)
Deletion syndromes (1p36, 1q43-44, 5p, 11p13, 18p, 18q, 22q11.2)
Duplication syndromes (3q, 20p, 10q)

Multisystem Syndromic Disorders
Alport syndrome (hearing loss, renal disease)
Alström syndrome (nerve deafness, diabetes mellitus)
Apert disease (craniosynostosis, syndactyly)
Branchiooculofacial syndrome
Cerebrooculofacial skeletal syndrome
Cockayne syndrome (premature senility, skin photosensitivity)
Congenital cataracts–facial dysmorphism–neuropathy (CCFDN) syndrome
Conradi disease (chondrodysplasia punctata)
Crouzon disease (dysostosis craniofacialis)
Ectodermal dysplasia
Hallermann-Streiff syndrome (microphthalmia, small pinched nose, skin atrophy, and hypotrichosis)
Hypohidrotic ectodermal dysplasia (anomalous dentition, hypohidrosis, hypotrichosis)
Ichthyosis (keratinizing disorder with thick, scaly skin)
Incontinentia pigmenti (dental anomalies, mental retardation, cutaneous lesions)
Laurence Moon Bardet Biedl Syndrome
Lowe syndrome (oculocerebrorenal syndrome: hypotonia, renal disease)
Marfan syndrome
Meckel-Gruber syndrome (renal dysplasia, encephalocele)
Myotonic dystrophy
Nail-patella syndrome (renal dysfunction, dysplastic nails, hypoplastic patella)
Marinesco-Sjögren syndrome (cerebellar ataxia, hypotonia)
Martsolf syndrome
Nevoid basal cell carcinoma syndrome (autosomal dominant, basal cell carcinoma erupts in childhood)
Norrie disease
Oculofaciocardiodental syndrome
Progeria
Rothmund-Thomson syndrome (poikiloderma: skin atrophy)
Rubinstein-Taybi syndrome (broad great toe, mental retardation)
Smith-Lemli-Opitz syndrome (toe syndactyly, hypospadias, mental retardation)
Sotos syndrome (cerebral gigantism)
Spondyloepiphyseal dysplasia (dwarfism, short trunk)
Warburg-Micro syndrome types 1-4
Werner syndrome (premature aging in second decade of life)

INBORN ERRORS OF METABOLISM
Abetalipoproteinemia (absent chylomicrons, retinal degeneration)
Fabry disease (α-galactosidase A deficiency)
Galactokinase deficiency
Galactosemia (galactose-1-phosphate uridyltransferase deficiency)
Homocystinemia (subluxation of lens, mental retardation)
Infantile neuronal ceroid lipofuscinosis
Mannosidosis (acid α-mannosidase deficiency)
Niemann-Pick disease (sphingomyelinase deficiency)
Refsum disease (phytanic acid α-hydrolase deficiency)
Wilson disease (accumulation of copper leads to cirrhosis and neurologic symptoms)
Zellweger syndrome

ENDOCRINOPATHIES
Albright hereditary osteodystrophy
Hypocalcemia (hypoparathyroidism)
Hypoglycemia
Diabetes mellitus

CONGENITAL INFECTIONS
Toxoplasmosis
Cytomegalovirus infection
Syphilis
Rubella
Perinatal herpes simplex infection
Measles (rubeola)
Poliomyelitis
Influenza
Varicella-zoster

OCULAR ANOMALIES
Peters' anomaly (corneal opacifications with iris-corneal dysgenesis)
Rieger syndrome (iris dysplasia, myotonic dystrophy)
Microphthalmia
Coloboma
Aniridia
Mesodermal dysgenesis
Norrie disease
Posterior lenticonus
Persistent hyperplastic primary vitreous
Primitive hyaloid vascular system
Retinitis pigmentosa

MISCELLANEOUS DISORDERS
Atopic dermatitis
Drugs (corticosteroids)
Radiation
Trauma
Juvenile idiopathic arthritis
Retinopathy of prematurity
Spherocytosis

IDIOPATHIC

Chromosomal Defects

Lens opacities of various types may occur in association with chromosomal defects, including trisomies 13, 18, and 21; Turner syndrome; and a number of deletion and duplication syndromes (Table 668.1).

Drugs, Toxic Agents, and Trauma

Of the various drugs and toxic agents that may produce cataracts, corticosteroids are of major importance in the pediatric age group. Steroid-related cataracts characteristically are posterior subcapsular lens opacities. The incidence and severity vary. The relative significance of dose, mode of administration, duration of treatment, and individual susceptibility is controversial, and the pathogenesis of steroid-induced cataracts is unclear. The effect on vision depends on the extent and density of the opacity. In many cases, the acuity is only minimally or moderately impaired. Reversibility of steroid-induced cataracts may occur in some cases. All children receiving long-term steroid treatment should have periodic eye examinations.

Trauma to the eye is a major cause of cataracts in children (Fig. 668.3). Opacification of the lens may result from blunt or penetrating injury. Cataracts can be an important manifestation of child abuse.

Cataract formation after exposure to therapeutic radiation is dose and duration dependent. Adult research shows 50% occurrence in lens dose of 15 Gy. Delayed onset is the rule.

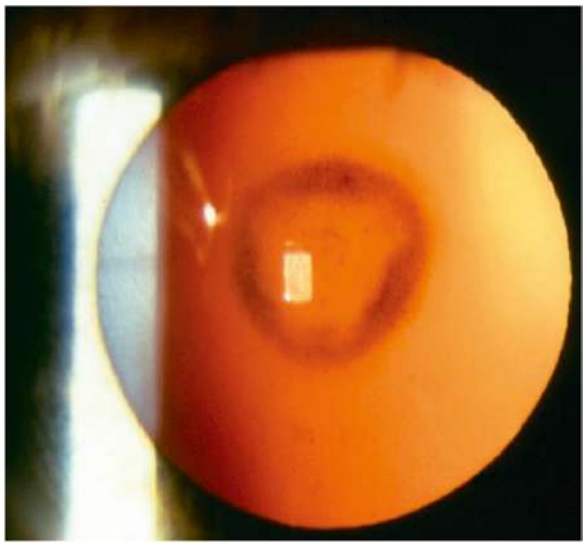

Fig. 668.2 Central lamellar cataract.

Miscellaneous Disorders

The list of multisystem syndromes and diseases associated with lens opacities and other eye anomalies is extensive (see Table 668.1).

Treatment

The treatment of cataracts that significantly interfere with vision includes the following: (1) surgical removal of lens material to provide an optically clear visual axis; (2) correction of the resultant aphakic refractive error with spectacles, contact lenses, or intraocular lens implantation; and (3) correction of any associated sensory deprivation amblyopia. Because the use of spectacles may not be possible in children after cataract removal, the use of contact lenses for visual rehabilitation is sometimes a medical necessity. Intraocular lens implantation is the mainstay for visual rehabilitation in children 2 years or older. A multicenter trial studied the visual outcomes in very young children treated with a contact lens versus an intraocular lens implant. One year after treatment, the children randomized into the intraocular lens implant group had more intraoperative complications, adverse events, and need for additional intraocular surgery. Although the median visual acuity was better in the contact lens group, the difference did not reach statistical significance. Treatment of the amblyopia may be the most demanding and difficult step in the visual rehabilitation of infants or children with cataracts. Not all cataracts require surgical intervention. Cataracts that are not visually significant should be monitored for change, and the child should be monitored for the development of amblyopia.

Prognosis

Prognosis depends on many factors, including the nature of the cataract, the underlying disease, age at onset, age at intervention, duration and severity of any attendant amblyopia, and presence of any associated ocular abnormalities (e.g., microphthalmia, retinal lesions, optic atrophy, glaucoma, nystagmus, and strabismus). Persistent amblyopia is the most common cause of poor visual recovery after cataract surgery in children. Secondary conditions and complications may develop in children who have had cataract surgery, including inflammatory sequelae, secondary membranes, glaucoma, retinal detachment, and changes in the axial length of the eye. All of these should be considered in planning treatment.

ECTOPIA LENTIS

Normally the lens is suspended in place behind the iris diaphragm by the zonular fibers of the ciliary body. Abnormalities of the suspensory system resulting from a developmental defect, disease, or trauma may result in instability or displacement of the lens. Displacement of the lens is classified as luxation, which is complete displacement of the lens (also known as dislocation) (Fig. 668.4), or as subluxation, which is a partial displacement (Fig. 668.5). Symptoms include blurring of vision, which is often the result of refractive changes such as myopia, astigmatism, or aphakic hyperopia. Some patients experience diplopia (double vision). An important sign of displacement is **iridodonesis**, a tremulousness of the iris caused by the loss of its usual support. Also, the anterior chamber may appear deeper than normal. Sometimes the equatorial region ("edge") of the displaced lens may be visible in the pupillary aperture. On ophthalmoscopy, this may appear as a black crescent. Also, the difference between the phakic and aphakic portions can be appreciated when focusing on the fundus.

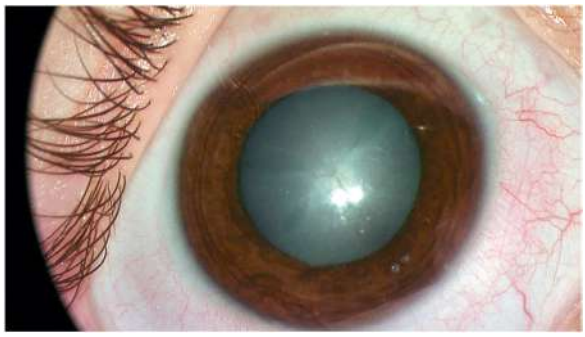

Fig. 668.3 Diffuse cataract related to blunt trauma.

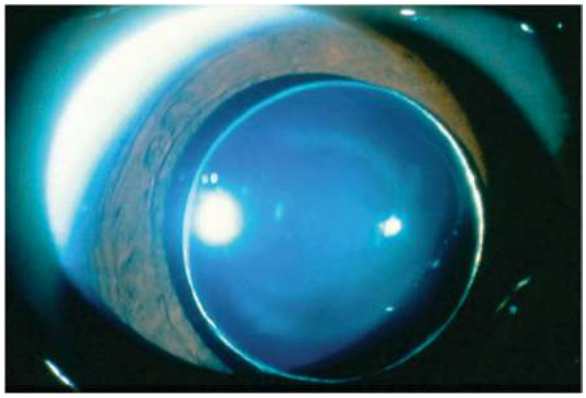

Fig. 668.4 Complete dislocation of lens into the anterior chamber seen in Weill-Marchesani syndrome.

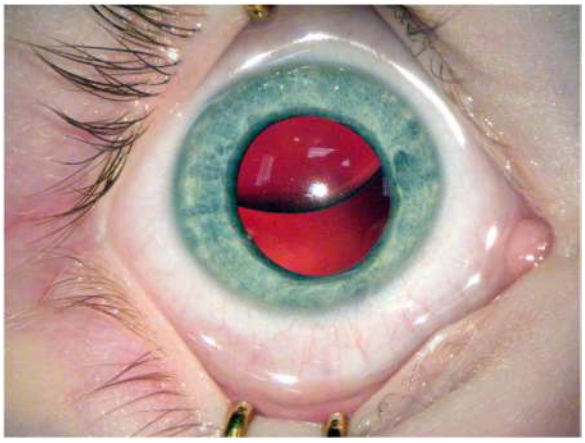

Fig. 668.5 Marfan syndrome. Upward lens subluxation. *(From Hoyt CS, Taylor D. Pediatric Ophthalmology and Strabismus. 4th ed. Philadelphia: Elsevier; 2013: Fig. 35.9A, p. 333.)*

Differential Diagnosis

A major cause of lens displacement is trauma. Displacement may also occur as a result of ocular disease, such as uveitis, intraocular tumor, congenital glaucoma, high myopia, megalocornea, or aniridia, or in association with cataract. Ectopia lentis may also be inherited or associated with systemic disease.

Displacement of the lens occurring as a heritable ocular condition unassociated with systemic abnormalities is referred to as *simple ectopia lentis*. Simple ectopia lentis is usually transmitted as an autosomal dominant condition. The lens is generally displaced upward and temporally. The ectopia may be present at birth or may appear later in life. Another form of heritable dislocation is ***ectopia lentis et pupillae*** (see Chapter 662). In this condition, both the lens and pupil are displaced, usually in opposite directions. This condition is generally bilateral, with one eye being almost a mirror image of the other. *Ectopia lentis et pupillae* is an autosomal recessive condition, although variable expression with some intermingling with simple ectopia lentis has been reported.

Systemic disorders associated with displacement of the lens include Marfan syndrome, homocystinuria, Weill-Marchesani syndrome, and sulfite oxidase deficiency. Ectopia lentis occurs in approximately 80% of patients with Marfan syndrome. In approximately 50% of patients with Marfan syndrome, the ectopia is evident by 5 years of age. In most cases, the lens is displaced superiorly and temporally; it is almost always bilateral and relatively symmetric. In homocystinuria, the lens is usually displaced inferiorly and somewhat nasally. The subluxation of the lens occurs early in life and is often evident by 5 years of age. In Weill-Marchesani syndrome, the displacement of the lens is often downward and forward, and the lens tends to be small and round.

Ectopia lentis is also associated occasionally with other conditions, including Ehlers-Danlos, Sturge-Weber, Crouzon, and Klippel-Feil syndromes; oxycephaly; and mandibulofacial dysostosis. A syndrome of dominantly inherited blepharoptosis, high myopia, and ectopia lentis has also been described.

Treatment and Prognosis

Displacement of the lens often results only in optical problems. In some cases, however, more serious complications may develop, such as glaucoma, uveitis, retinal detachment, or cataract. Management must be individualized according to the type of displacement, its cause, and the presence of any complicating ocular or systemic conditions. For many patients, optical correction by spectacles or contact lenses can be provided. Manipulation of the iris diaphragm with mydriatic or miotic drops may sometimes help improve vision. In selected cases, the best treatment is surgical removal of the lens. In many children, treatment of any associated amblyopia must be instituted early. In addition, for children with ectopia lentis, safety precautions should be taken to prevent injury to the eye.

OTHER DISORDERS OF THE LENS

Microspherophakia

The term *microspherophakia* refers to a small, round lens that may occur as an isolated anomaly (probably autosomal recessive) or in association with other ocular abnormalities, such as ectopia lentis, myopia, or retinal detachment (possibly autosomal dominant). Microspherophakia may also occur in association with various systemic disorders, including Marfan syndrome, Weill-Marchesani syndrome, Alport syndrome, mandibulofacial dysostosis, and Klinefelter syndrome.

Anterior Lenticonus

Anterior lenticonus is a rare bilateral condition in which the anterior capsule of the lens thins, allowing the lens to bulge forward centrally. It may be accompanied by lens opacities or other eye anomalies and is a prominent feature of Alport syndrome. The increased curvature of the central area may cause high myopia. Spontaneous rupture of the anterior capsule may occur, requiring prompt surgical intervention.

Posterior Lenticonus

Posterior lenticonus, which occurs more commonly than anterior lenticonus, is characterized by a circumscribed round or oval bulge of the posterior lens capsule and cortex, involving the central region of the lens. In the early stages, by the red reflex test, this may look like an oil droplet. It occurs in infants and young children and tends to increase with age. Usually the lens material within and surrounding the capsular bulge eventually becomes opacified. Posterior lenticonus usually occurs as an isolated ocular anomaly. It is generally unilateral but may be bilateral. It is believed to be sporadic, although autosomal dominant and X-linked inheritance has been suggested in some cases. Infants or children with posterior lenticonus may require optical correction, amblyopia treatment, and surgery for progressive cataract.

Visit Elsevier eBooks+ at eBooks.Health.Elsevier.com for Bibliography.

Chapter 669

Disorders of the Uveal Tract

Scott E. Olitsky and Justin D. Marsh

UVEITIS (IRITIS, CYCLITIS, CHORIORETINITIS)

The uveal tract (the inner vascular coat of the eye, consisting of the iris, ciliary body, and choroid) (Fig. 669.1) is subject to inflammatory involvement in numerous systemic diseases, both infectious and noninfectious, and in response to exogenous factors, including trauma and toxic agents (Table 669.1). Inflammation may affect any one portion of the uveal tract preferentially or all parts together. Uveitis may be classified as anterior (iris, ciliary body), intermediate (vitreous-choroid locations), posterior (choroid, retina) or panuveitis, with subclassification as infectious, inflammatory, or systemic disease associated and eye limited.

Iritis may occur alone or in conjunction with inflammation of the ciliary body as iridocyclitis or in association with pars planitis. Pain, photophobia, and lacrimation are the characteristic symptoms of acute anterior uveitis, but the inflammation may develop insidiously without disturbing symptoms. Signs of anterior uveitis include conjunctival hyperemia, particularly in the perilimbal region (ciliary flush), and cells and protein ("flare") in the aqueous humor (Figs. 669.2 and 669.3). Inflammatory deposits on the posterior surface of the cornea (keratic precipitates) and congestion of the iris may also be seen. More chronic cases may show degenerative changes of the cornea (band keratopathy), lenticular opacities (cataract), development of glaucoma, and impairment of vision. The cause of anterior uveitis is often idiopathic; primary considerations in children are rheumatoid disease, particularly pauciarticular arthritis, Kawasaki disease, postinfectious reactive arthritis syndrome, tubulointerstitial nephritis (TINU), HLA-B27 associated syndromes, and sarcoidosis. Iritis may be secondary to corneal disease, such as herpetic keratitis or a bacterial or fungal corneal ulcer, or to a corneal abrasion or foreign body. Traumatic iritis and iridocyclitis are especially common in children.

Iridocyclitis that occurs in children with juvenile idiopathic arthritis deserves special mention. Unlike most forms of anterior uveitis, it rarely creates pain, photophobia, or conjunctival hyperemia. Loss of vision may not be noticed until severe and irreversible damage has occurred. Because of the lack of symptoms and the high incidence of uveitis in these children, routine periodic screening is necessary. Ophthalmic screening guidelines are based on 3 factors that predispose children with arthritis to uveitis (Fig. 669.4):

1. Type of arthritis
2. Age of onset of arthritis
3. Antinuclear antibody (ANA) status

Choroiditis, inflammation of the posterior portion of the uveal tract, invariably also involves the retina; when both are obviously affected, the condition is termed *chorioretinitis*. The causes of posterior uveitis are numerous; the more common are toxoplasmosis, histoplasmosis, cytomegalovirus, sarcoidosis, syphilis, tuberculosis, and toxocariasis

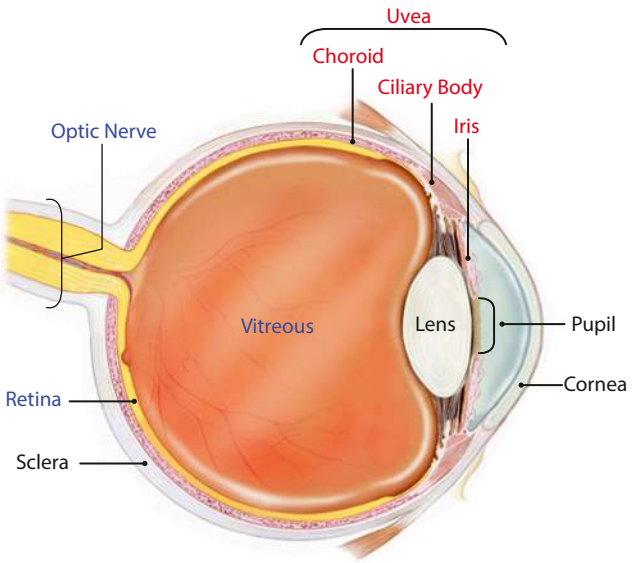

Fig. 669.1 Anatomic locations for uveitis. *(From National Eye Institute: Uveitis. Courtesy National Eye Institute, National Institutes of Health, Bethesda, Maryland.* https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/uveitis*)*

(Fig. 669.5). Depending on the etiology, the inflammatory signs may be diffuse or focal. Vitreous reaction often occurs as well. With many types, the result is atrophic chorioretinal scarring demarcated by pigmentation, often with visual impairment. Secondary complications include retinal detachment, glaucoma, and phthisis.

Panophthalmitis is inflammation involving all parts of the eye. It is frequently suppurative, most often as a result of a perforating injury or of septicemia. It produces severe pain, marked congestion of the eye, inflammation of the adjacent orbital tissues and eyelids, and loss of vision. In many cases, the eye is lost despite intensive treatment of the infection and inflammation. Enucleation of the eye or evisceration of the orbit may be necessary.

Sympathetic ophthalmia is a rare type of uveal inflammatory response that affects the uninjured eye after a perforating injury to the other eye. It may occur weeks, months, or even years after the injury. A hypersensitivity phenomenon is the most probable cause. Loss of vision in the uninjured (sympathizing) eye may result. Removal of the injured eye prevents the development of sympathetic ophthalmia but does not stop the progression of the disease once it has occurred. High-dose intravenous methylprednisolone is the initial treatment of choice. Immune therapy (immune suppression or modulators) may need to be added to steroids; these agents include cyclosporine, azathioprine, mycophenolate mofetil, cytoxan and TNF-alpha blocking agents (infliximab, adalimumab).

Treatment

The various forms of intraocular inflammation are treated according to their underlying systemic causal factors. When infection is proved or suspected, appropriate systemic antimicrobial or antiviral therapy is used. In some cases, intravitreal injection is indicated.

Elimination of the intraocular inflammation is important to reduce the risk of severe, and often permanent, vision loss. Untreated, the inflammatory process may lead to the development of band keratopathy (calcium deposition in the cornea), cataracts, glaucoma, and irreversible retinal damage. Anterior inflammation may respond well to topical corticosteroid treatment. Posterior cases often require systemic therapy. The use of topical and systemic corticosteroids can lead to the development of glaucoma and cataracts. To reduce the need for topical and systemic corticosteroids, systemic immunosuppression is often used in patients requiring long-term treatment. Immunosuppressive agents include methotrexate, cyclosporine, and tumor necrosis factor inhibitors. Multiple agents may be needed in recalcitrant cases.

Table 669.1 Uveitis in Childhood

ANTERIOR UVEITIS
Juvenile idiopathic arthritis (pauciarticular)
Sarcoidosis including Blau syndrome
Trauma
Tuberculosis
Kawasaki disease
MIS-C
Ulcerative colitis
Crohn syndrome
HLA-B27 associated
Reactive postinfectious (enteric or genital) with arthritis and rash
Spirochetal (syphilis, leptospiral)
Lyme disease
Brucellosis
Heterochromic iridocyclitis (Fuchs)
Viral (herpes simplex, herpes zoster)
Ankylosing spondylitis
Stevens-Johnson syndrome
Chronic infantile neurologic cutaneous arthritis syndrome (CINCA)
Familial Mediterranean fever
Hyperimmunoglobulin D syndrome
Tumor necrosis factor receptor–associated periodic syndrome
Muckle-Wells syndrome
Celiac disease
Psoriasis
Multiple sclerosis
Cyclic neutropenia
Chronic granulomatous disease
X-linked lymphoproliferative disease
Hypocomplementemic vasculitis
Tubulointerstitial nephritis and uveitis syndrome
Idiopathic
Drugs (rifabutin, anti-tumor necrosis factor agents, interferon)
INTERMEDIATE AND POSTERIOR UVEITIS (CHOROIDITIS—MAY INVOLVE RETINA)
Toxoplasmosis
Toxocariasis
Sarcoidosis including Blau syndrome
Cat-scratch disease
Tuberculosis
Histoplasmosis
Viral (rubella, herpes simplex, HIV, cytomegalovirus, West Nile)
Subacute sclerosing panencephalitis
Tubulointestinal nephritis and uveitis syndrome
Diffuse unilateral subacute neuroretinitis (DUSN) secondary to *Ancylostoma caninum* or *Baylisascaris procyonis*
Idiopathic
ANTERIOR AND/OR POSTERIOR (PAN) UVEITIS
Sympathetic ophthalmia (trauma to other eye)
Vogt-Koyanagi-Harada syndrome (uveootocutaneous syndrome: poliosis, vitiligo, alopecia, deafness, tinnitus, uveitis, aseptic meningitis, retinitis)
Behçet syndrome
Juvenile xanthogranulomatosis
Lyme disease
Sarcoidosis
UVEO-MENINGEAL SYNDROMES
Vogt-Koyanagi-Harada disease
Behçet
Sarcoidosis
Granulomatosis with polyangiitis
Cat-scratch disease
Whipple disease
Syphilis
Lyme disease
Acute posterior multifocal placoid pigment epitheliopathy
Lymphoma, leukemia
Herpes simplex
Cytomegalovirus

MIS-C, Multisystem inflammatory system in children associated with COVID-19

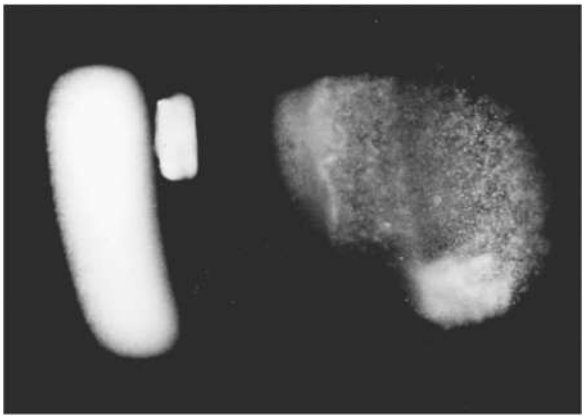

Fig. 669.2 Cell and flare in the anterior chamber. The flare represents protein leakage. *(Courtesy Peter Buch, CRA.)*

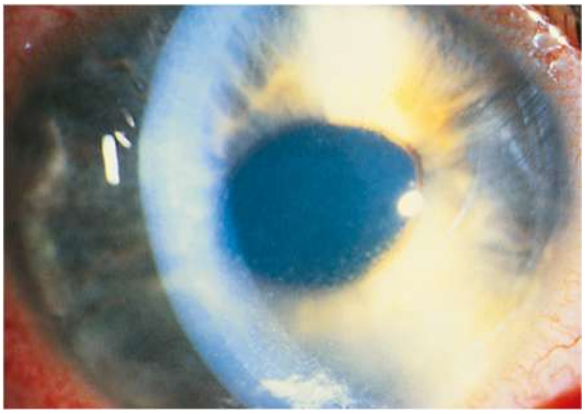

Fig. 669.3 Iritis. Conjunctival injection is most marked immediately around the cornea (ciliary flush). *(From Zitelli BJ, McIntire SC, Nowald AJ, Garrison J, eds. Zitelli and Davis' Atlas of Pediatric Physical Diagnosis. 8th ed. Philadelphia: Elsevier; 2023: Fig. 20.88, p. 721)*

Noninfectious inflammatory uveitis in adolescents has been treated with adalimumab, a human antitumor necrosis factor-α monoclonal antibody resulting in improved vision, lack of disease progression, and an ability to wean steroids. Cycloplegic agents, particularly atropine, are also used to reduce inflammation and to prevent adhesion of the iris to the lens (posterior synechiae), especially in anterior uveitis. Extensive posterior synechiae formation can lead to acute angle closure glaucoma. Other complications are noted in Table 669.2.

Surgery may be required for patients who develop glaucoma because of the underlying disease process or the need for corticosteroid treatment. Cataract surgery should be delayed until the inflammation has been under control for a period of time. Cataract surgery in children with a history of prolonged uveitis can carry significant risk. There is no universal agreement concerning the use of intraocular lenses in these patients.

Pars planitis is an uncommon idiopathic form of intermediate uveitis characterized by anterior chamber involvement, anterior vitreous cells and condensations, and peripheral retinal vasculitis. The average age of onset is 9 years. It is predominately bilateral and seen more frequently in males. Painless decreased vision is the usual presenting sign. The prognosis is good when adequate medical treatment is sought early in the course of the disease.

Masquerade syndromes can sometimes mimic intraocular inflammation. Retinoblastoma, leukemia, retained intraocular foreign body, juvenile xanthogranuloma, and peripheral retinal detachments may produce signs similar to those seen in uveitis. These syndromes should be kept in mind when evaluating a patient with suspected uveitis or if a patient does not respond as anticipated to appropriate treatment.

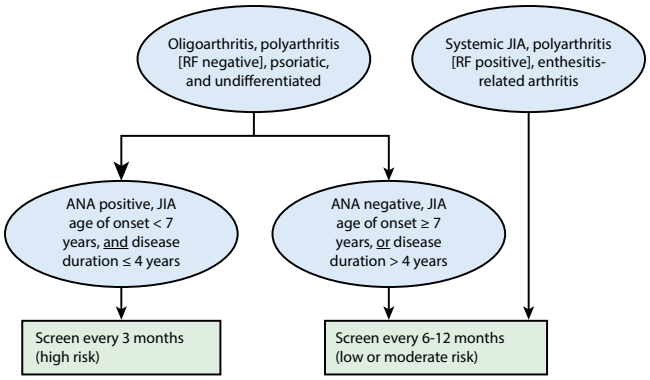

Fig. 669.4 Ophthalmology screening recommendations. ANA, Antinuclear antibody; JIA, juvenile idiopathic arthritis; RF, rheumatoid factor. *(From Angeles-Han ST, Ringold S, Beukelman T, et al. 2019 American College of Rheumatology/Arthritis Foundation guideline for the screening, monitoring, and treatment of juvenile idiopathic arthritis-associated uveitis. Arthritis Care Res (Hoboken). 2019;71:703–716.)*

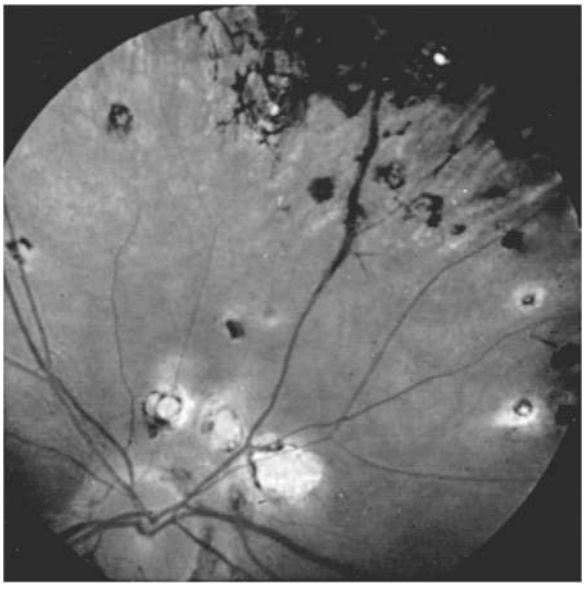

Fig. 669.5 Focal atrophic and pigmented scars of chorioretinitis.

Table 669.2 Comorbidities and Complications of Uveitis in Pediatric Group

Band keratopathy
Posterior synechia
Peripheral anterior synechia
Cataract
Ocular hypertension
Glaucoma
Ocular hypotension
Cystoid macular edema (CME)
Vitreous hemorrhage
Tractional and rhegmatogenous retinal detachment
Epiretinal membrane
Neovascularization of cornea
Neovascular or fibrovascular proliferation on retina or in vitreous
Phthisis bulbi

From Maleki A, Anesi SD, Look-Why S, Manhapra A, Foster CS. Pediatric uveitis: A comprehensive review. *Surv Ophthalmol.* 2022;67(2):510–529. Table 4.

Visit Elsevier eBooks+ at eBooks.Health.Elsevier.com for Bibliography.

Chapter 670

Disorders of the Retina and Vitreous

Scott E. Olitsky and Justin D. Marsh

RETINOPATHY OF PREMATURITY

Retinopathy of prematurity (ROP) is a complex disease of the developing retinal vasculature in infants born prematurely. It may be acute (early stages) or chronic (late stages). Clinical manifestations range from mild, usually transient changes of the peripheral retina to severe progressive vasoproliferation, scarring, and potentially blinding retinal detachment. ROP includes all stages of the disease and its sequelae.

Pathogenesis

Beginning at 16 weeks of gestation, retinal angiogenesis normally proceeds from the optic disc to the periphery, reaching the outer rim of the retina (ora serrata) nasally at about 36 weeks and extending temporally by approximately 40 weeks. Injury to this process results in various pathologic and clinical changes. The first observation in the acute phase is cessation of vasculogenesis. Rather than a gradual transition from a vascularized to avascular retina, there is an abrupt termination of the vessels marked by a line in the retina. The line may then grow into a ridge composed of mesenchymal and endothelial cells. Cell division and differentiation may later resume, and vascularization of the retina may proceed. Alternatively, there may be progression to an abnormal proliferation of vessels out of the plane of the retina, into the vitreous, and over the surface of the retina. Cicatrization and traction on the retina may follow, leading to retinal detachment.

The risk factors associated with ROP are not fully known, but prematurity and the associated retinal immaturity at birth represent the major factors. Oxygenation, respiratory distress, apnea, bradycardia, heart disease, infection, hypercarbia, acidosis, anemia, and the need for transfusion are thought by some to be contributory factors. Generally, the lower the gestational age, the lower the birthweight, and the sicker the infant, the greater the risk for ROP.

The basic pathogenesis of ROP is still unknown. Exposure to the extrauterine environment, including the necessarily high inspired oxygen concentrations, produces cellular damage, perhaps mediated by free radicals. Later in the course of the disease, peripheral hypoxia develops and vascular endothelial growth factors (VEGFs) are produced in the nonvascularized retina. These growth factors stimulate abnormal vasculogenesis, causing neovascularization to occur. Because of poor pulmonary function, a state of relative retinal hypoxia occurs. This causes upregulation of VEGF, which, in susceptible infants, can cause abnormal fibrovascular growth. This neovascularization may then lead to scarring and loss of vision.

Classification

The international classification of ROP describes the location, extent, and severity of the disease. To delineate location, the retina is divided into three concentric zones centered on the optic disc (Fig. 670.1). Zone I, the posterior or inner zone, extends twice the disc-macular distance, or 30 degrees in all directions from the optic disc. Zone II, the middle zone, extends from the outer edge of zone I to the ora serrata nasally and to the anatomic equator temporally. Zone III, the outer zone, is the residual crescent that extends from the outer border of zone II to the ora serrata temporally. The extent of involvement is described by the number of circumferential clock hours involved.

The phases and severity of the disease process are classified into five stages. Stage 1 is characterized by a demarcation line that separates vascularized from avascular retina. This line lies within the plane of the retina and appears relatively flat and white. Often noted is abnormal branching or arcading of the retinal vessels leading into the line. Stage 2 is characterized by a ridge; the demarcation line has grown, acquiring height, width, and volume and extending up and out of the plane of the retina. Stage 3 is characterized by the presence of a ridge and the development of extraretinal fibrovascular tissue (Fig. 670.2A). Stage 4 is characterized by subtotal retinal detachment caused by traction from the proliferating tissue in the vitreous or on the retina. Stage 4 is subdivided into two phases: (1) subtotal retinal detachment not involving the macula and (2) subtotal retinal detachment involving the macula. Stage 5 is total retinal detachment.

When signs of posterior retinal vascular changes accompany the active stages of ROP, the term *plus disease* is used (see Fig. 670.2B and C). Patients reaching the point of dilation and tortuosity of the retinal vessels also frequently demonstrate the associated findings of engorgement of the iris, pupillary rigidity, and vitreous haze.

The Early Treatment for Retinopathy of Prematurity Cooperative has described types 1 and 2 ROP as follows:

Type 1 ROP

- Zone I: Any stage with plus
- Zone I: Stage 3 without plus
- Zone II: Stage 2 to three with plus type 2 ROP
- Zone I: Stage 1 to two without plus
- Zone II: Stage 3 without plus

Clinical Manifestations and Prognosis

In more than 90% of at-risk infants, the course is one of spontaneous arrest and regression, with little or no residual effects or visual disability. Fewer than 10% of infants have progression toward severe disease, with significant extraretinal vasoproliferation, cicatrization, detachment of the retina, and impairment of vision.

Some children with arrested or regressed ROP are left with demarcation lines, undervascularization of the peripheral retina, or abnormal branching, tortuosity, or straightening of the retinal vessels. Some are left with retinal pigmentary changes, dragging of the retina, ectopia of the macula, retinal folds, or retinal breaks. Others proceed to total retinal detachment, which commonly assumes a funnel-like configuration. The clinical picture is often that of a retrolental membrane, producing leukocoria (a white reflex in the pupil). Some patients develop cataract, glaucoma, and signs of inflammation. The end stage is often a painful blind eye or a degenerated phthisical eye. The spectrum of ROP also includes myopia, which is often progressive and of significant degree in infancy. The incidence of anisometropia, strabismus, amblyopia, and nystagmus may also be increased.

Diagnosis

Systematic serial screening ophthalmologic examinations of infants at risk are recommended. Infants with a birthweight of less than 1,500 g or gestational age of 32 weeks or less and selected infants with a birthweight between 1,500 and 2,000 g or gestational age of more than 32 weeks with an unstable clinical course, including those requiring cardiorespiratory support and who are believed by their pediatrician or neonatologist to be at high risk, should have retinal screening examinations. The timing of the initial screening exam is based on the infant's age. Table 670.1 was developed from an evidence-based analysis of the Multicenter Trial of Cryotherapy for ROP. The examination can be stressful to fragile preterm infants, and the dilating drops can have untoward side effects. Infants must be carefully monitored during and after the examination. Some neonatologists and ophthalmologists advocate the use of topical tetracaine and/or oral sucrose to reduce the discomfort and stress to the infant. Follow-up is based on the initial findings and risk factors but is usually 2 weeks or less.

Treatment

In selected cases, laser photocoagulation of the avascular retina reduces the more severe complications of progressive ROP (Table 670.2). Advances in vitreoretinal surgical techniques have had limited success in reattaching the retina in infants with total retinal detachment (stage 5 ROP), but the visual results are often disappointing. The Early Treatment for Retinopathy of Prematurity Cooperative study did find

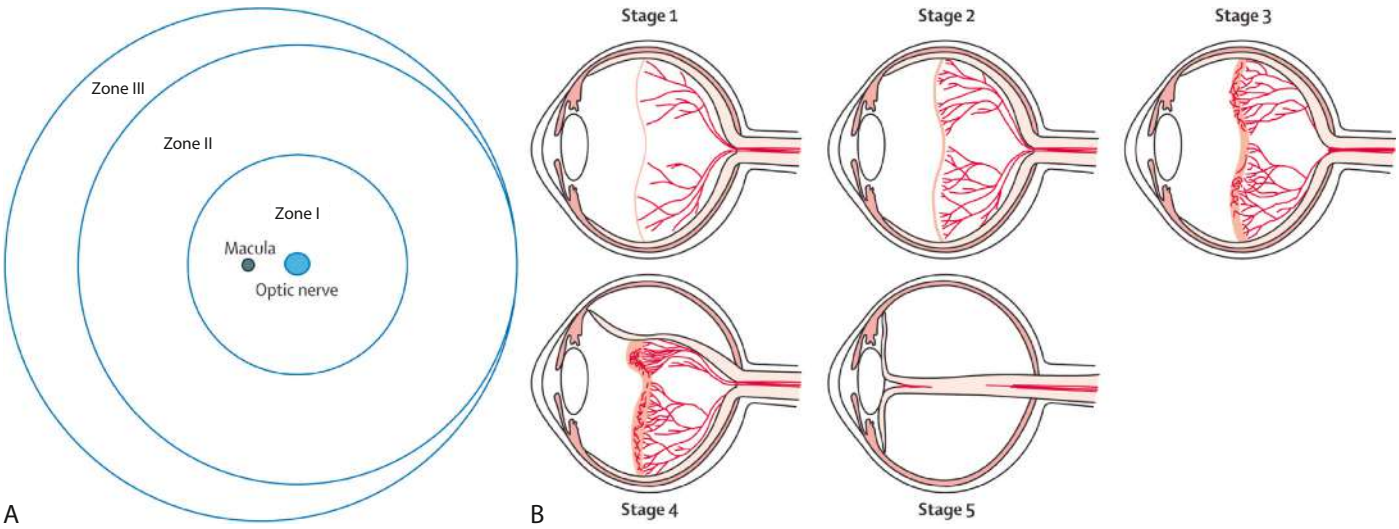

Fig. 670.1 The retina is divided into three zones and the extent or severity of retinopathy in these zones is classified in terms of five stages. **A,** Diagram of right eye. **B,** Stage 1 is characterized by a thin demarcation line between vascularized and nonvascularized retina, stage 2 by a ridge, stage 3 by extraretinal fibrovascular proliferation, stage 4 by partial retinal detachment, and stage 5 by total retinal detachment. In stage 3, extraretinal neovascularization can become severe enough to cause retinal detachment (stages 4-5), which usually leads to blindness. *(***A** *from Hellström A, Smith LEH, Dammann O. Retinopathy of prematurity. Lancet. 2013;382:1445–1454, Fig. 3, p. 1450;* **B** *courtesy Lisa Hård.)*

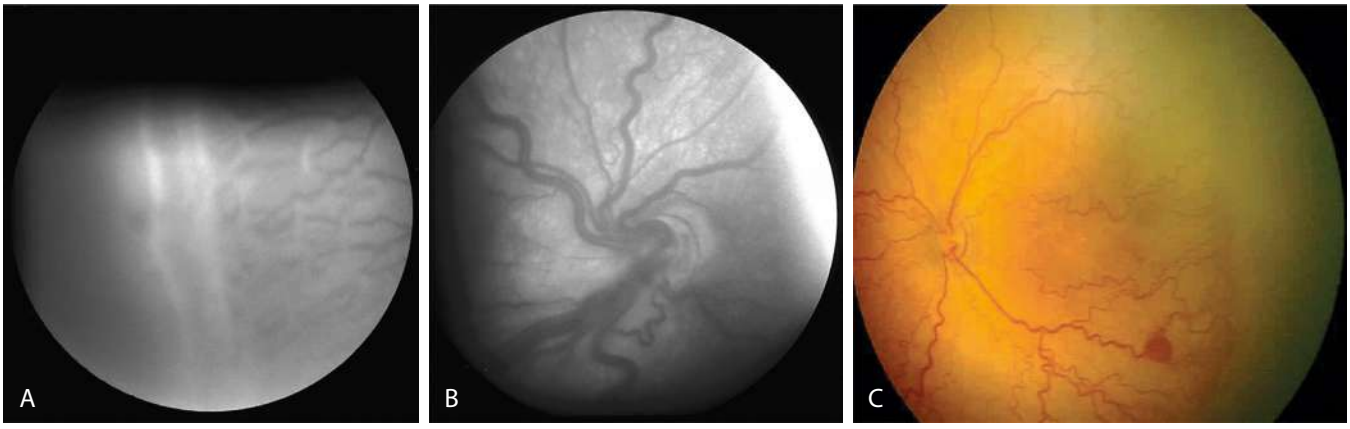

Fig. 670.2 Retinopathy of prematurity (ROP). **A,** In stage 3, there is a ridge and extraretinal vascular tissue. **B,** Retinal vessels are dilated and tortuous in active zone I ROP with plus disease. **C,** Zone I ROP with plus disease.

Table 670.1 Timing of First Eye Examination Based on Gestational Age at Birth

GESTATIONAL AGE AT BIRTH	AGE AT INITIAL EXAMINATION IN WEEKS	
	POSTMENSTRUAL	CHRONOLOGICAL
22	31	9
23	31	8
24	31	7
25	31	6
26	31	5
27	31	4
28	32	4
29	33	4
30	34	4
31	35	4
32	36	4

Table 670.2 Criteria for Peripheral Ablative Therapy for Retinopathy of Prematurity

1. Zone II: Plus disease with stage 2 or 3 ROP
2. Zone I: Plus disease with stage 1 or 2 ROP
3. Zone I: Stage 3 ROP

ROP, Retinopathy of prematurity.
Data from Early Treatment for Retinopathy of Prematurity Cooperative Group: Revised indications for the treatment of retinopathy of prematurity: Results of the Early Treatment for Retinopathy of Prematurity Randomized Trial. *Arch Ophthalmol* 2003;121:1684.

improved structural and visual outcomes with a redefined threshold for treatment. It demonstrated the importance of plus disease and the presence of posterior retinal involvement in the determination of when to treat ROP. Treatment should be considered for any eye with type 1 ROP. Serial examinations are indicated for any eye with type 2 ROP; treatment is considered if type 2 progresses to type 1 or if threshold ROP develops.

Intravitreal injections of VEGF antagonists may be recommended as first or second therapy for ROP, particularly in neonates with disease in zone 1. This treatment rapidly reduces intravitreal VEGF levels, often

improving plus disease and extraretinal fibrovascular tissue (stage 3 disease) within days of treatment. Theoretical advantages of these agents include not only the potential for improved peripheral retinal vascularization after treatment but also an apparent reduction in myopia later in childhood. Because the effects of intravitreal VEGF antagonists are temporary, neonates treated in this manner must be followed closely, often for months, after treatment to ensure additional therapy is not warranted.

Prevention

Prevention of ROP ultimately depends on the prevention of premature birth and its attendant problems (see Chapters 116 and 119.2). However, a number of other potential factors have been studied to decrease the occurrence of ROP in these premature infants. Ambient light had been considered by some to be a potential agent that could hopefully be manipulated. The LIGHT-ROP study definitively found that ambient light reduction had no impact on ROP. The association between ROP and oxygen saturation has been studied for decades. Recent research has focused on maintaining oxygen saturation levels for severely premature infants at levels sufficiently low to minimize the risk of ROP and sufficiently high to optimize survival.

PERSISTENT FETAL VASCULATURE

Persistent fetal vasculature (PFV; formerly called *persistent hyperplastic primary vitreous*) includes a spectrum of manifestations caused by the persistence of various portions of the fetal hyaloid vascular system and associated fibrovascular tissue.

Pathogenesis

During development of the eye, the hyaloid artery extends from the optic disc to the posterior aspect of the lens; it sends branches into the vitreous and ramifies to form the posterior portion of the vascular capsule of the lens. The posterior portion of the hyaloid system normally regresses by the seventh fetal month and the anterior portion by the eighth fetal month. Small remnants of the system, such as a tuft of tissue at the disc (Bergmeister papilla) or a tag of tissue on the posterior capsule of the lens (Mittendorf dot), are common findings in healthy persons. More extensive remnants and associated complications constitute PFV. Two major forms are described: anterior PFV and posterior PFV. Variability is great, and mixed or intermediate forms occur.

Clinical Manifestations

The usual clinical feature of anterior PFV is the presence of a vascularized plaque of tissue on the back surface of the lens in an eye that is microphthalmic or slightly smaller than normal. The condition is usually unilateral and may occur in infants with no other abnormalities and no history of prematurity. The fibrovascular tissue tends to undergo gradual contracture. The ciliary processes become elongated, and the anterior chamber may become shallow. The lens is usually smaller than normal and may be clear, but it often becomes cataractous and may swell or absorb fluid. Large or anomalous vessels of the iris may be present. The anterior chamber angle may have abnormalities. In time, the cornea may become cloudy.

Anterior PFV is usually noted in the first weeks or months of life. The most frequent presenting signs are leukocoria (white pupillary reflex), strabismus, and nystagmus. The course is usually progressive, and the outcome is poor. Major complications are spontaneous intraocular hemorrhage, swelling of the lens caused by rupture of the posterior capsule, and glaucoma. The eye may eventually deteriorate. The spectrum of posterior PFV includes fibroglial veils around the disc and macula, vitreous membranes and stalks containing hyaloid artery remnants projecting from the disc, and meridional retinal folds. Traction detachment of the retina may occur. Vision may be impaired, but the eye is usually retained.

Treatment

Surgery is performed to prevent complications, to preserve the eye and a reasonably good cosmetic appearance, and, in some cases, to salvage vision. Surgical treatment usually involves aspirating the lens and excising the abnormal tissue. If useful vision is to be attained, refractive correction and aggressive amblyopia therapy are required. In some cases, the affected eye is enucleated because distinguishing between this white mass and retinoblastoma can be difficult. Ultrasonography and CT are valuable diagnostic aids.

RETINOBLASTOMA

Retinoblastoma (Fig. 670.3) is the most common primary malignant intraocular tumor of childhood. It occurs in approximately 1/15,000 live births; 250-300 new cases are diagnosed in the United States annually. Hereditary and nonhereditary patterns of transmission occur; there is no predilection for gender or race. The hereditary form occurs earlier and is usually bilateral and multifocal, whereas the nonhereditary form is generally unilateral and unifocal. Fifteen percent of unilateral cases are hereditary. Bilateral cases often present earlier than unilateral cases. Unilateral tumors are often large by the time they are discovered. The average age at diagnosis is 15 months for bilateral cases compared with 27 months for unilateral cases. It is unusual for a child to present with a retinoblastoma after 3 years of age. Rarely, the tumor is discovered at birth, during adolescence, or even in early adulthood.

Clinical Manifestations

The clinical manifestations of retinoblastoma vary depending on the stage at which the tumor is detected. The initial sign in the majority of patients is a white pupillary reflex (leukocoria). Leukocoria results because of the reflection of light off the white tumor. The second most frequent initial sign of retinoblastoma is strabismus. Less frequent presenting signs include pseudohypopyon (tumor cells layered inferiorly in front of the iris) caused by tumor seeding in the anterior chamber of the eye, hyphema (blood layered in front of the iris) secondary to iris neovascularization, vitreous hemorrhage, and signs of orbital cellulitis. On examination, the tumor appears as a white mass, sometimes small and relatively flat, sometimes large and protuberant. It may appear nodular. Vitreous haze or tumor seeding may be evident.

The retinoblastoma gene is a recessive suppressor gene located on chromosome 13 at the 13q14 region. Because of the hereditary nature of retinoblastoma, family members of affected children should undergo a complete ophthalmologic examination and genetic counseling. Newborn siblings and children of affected patients should be referred to an ophthalmologist shortly after birth, when the peripheral retina can be evaluated without the need for an examination under anesthesia.

Diagnosis

Retinoblastoma is diagnosed by direct observation by an experienced ophthalmologist. Ancillary testing such as CT or ultrasonography may help to confirm the diagnosis and demonstrate calcification within the mass. MRI may better detect the presence of an associated pineoblastoma (trilateral retinoblastoma). A definitive diagnosis occasionally cannot be made, and removal of the eye must be considered to avoid the possibility of lethal metastasis of the tumor. Because a biopsy can lead to spread of the tumor, histologic confirmation before enucleation is not possible in most cases. Therefore removal of a blind eye in which the diagnosis of retinoblastoma is likely may be appropriate.

Treatment

Therapy varies, depending on the size and location of the tumor as well as whether it is unilateral or bilateral. Advanced tumors may be treated by enucleation. Other treatment modalities include the use of external beam irradiation, radiation plaque therapy, laser or cryotherapy, and chemoreduction (systemic chemotherapy) followed by local therapies (i.e., laser therapy, cryotherapy, and brachytherapy). During the last decade, there has been a dramatic shift in the treatment of retinoblastomas. Intraarterial chemotherapy involves delivery of chemotherapeutic agents via the ophthalmic artery and has dramatically reduced the need for enucleation in many cases of retinoblastoma.

Nonocular secondary tumors are common in patients with germinal pathogenic variants; they are estimated to occur with an incidence of 1% per years of life. The most common secondary tumor is osteogenic sarcoma of the skull and long bones; the risk is higher in patients

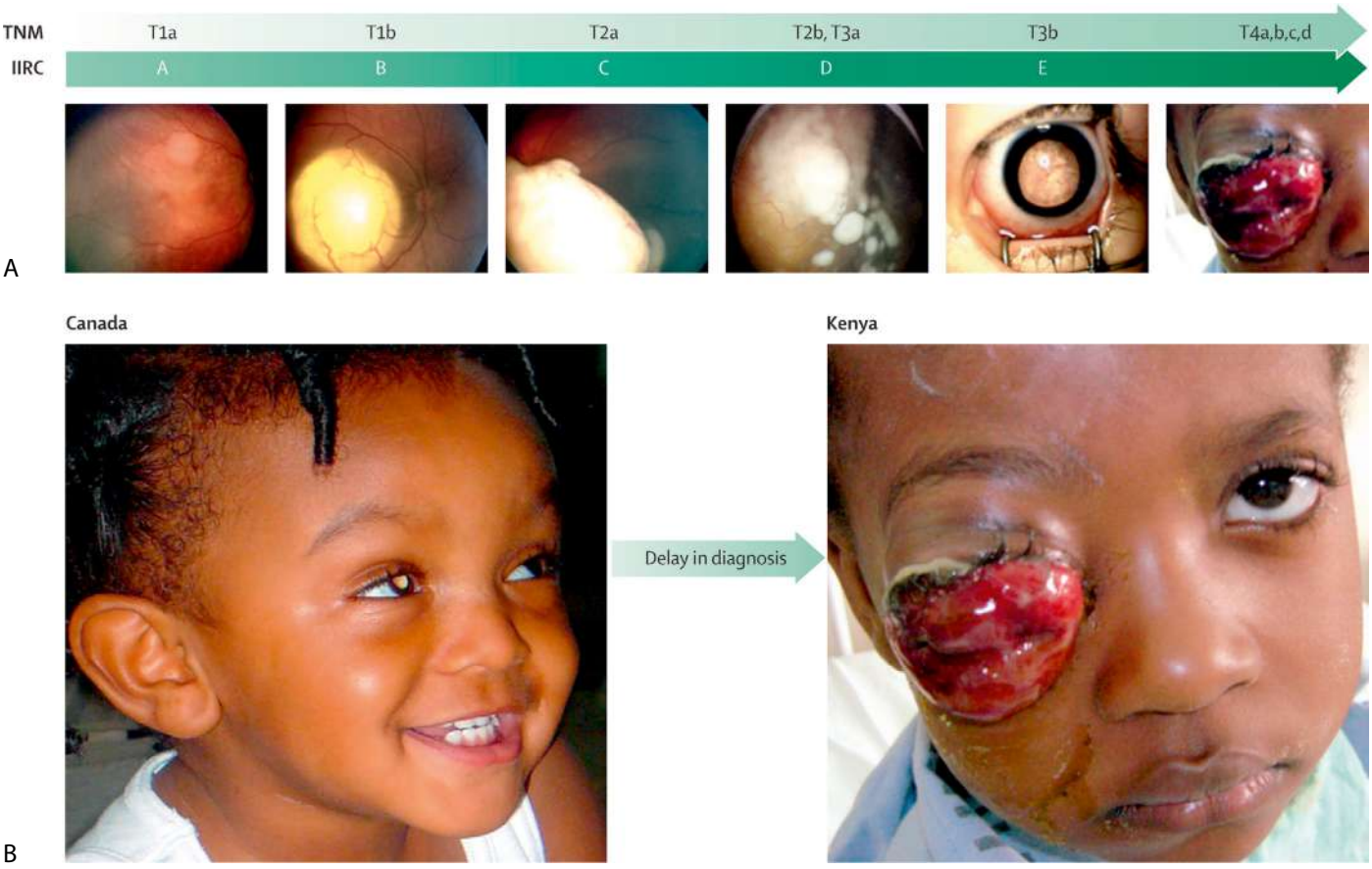

Fig. 670.3 Progression of retinoblastoma from small intraretinal tumors to a massive orbital retinoblastoma probably extending into the brain. A, Progression of retinoblastoma from small intraretinal tumors that can be cured by laser treatment and cryotherapy (TNM T1a, IIRC A) to massive orbital retinoblastoma probably extending into the brain (TNM T4a-b). B, A difference in age at diagnosis recorded between Canada and Kenya could mean the difference between possible cure and certain death. The Canadian child with leukocoria was diagnosed because of the left-hand image, which was taken by his sister with his mother's mobile phone. IIRC, International Intraocular Retinoblastoma Classification; TNM, tumor node metastasis cancer staging. *(From Dimaras H, Kimani K, Dimba EAO, et al. Retinoblastoma. Lancet. 2012;379:1436–1444, Fig. 1, p. 1438.)*

treated with radiation. Other malignancies include lung, brain, soft tissue, and skin.

The prognosis for children with retinoblastoma depends on the size and extension of the tumor. When confined to the eye, most tumors can be cured. The prognosis for long-term survival is poor when the tumor has extended into the orbit or along the optic nerve.

INHERITED RETINAL DYSTROPHIES

Inherited retinal dystrophies (IRDs) represent a wide spectrum of disorders (~280 affected genes) causing loss of photoreceptors and involving various locations (peripheral vs. macular or central) (Fig. 670.4) and affecting ~1/3,000 people. Most cases are monogenetic or isolated and nonsyndromic (~75%). Inheritance may be autosomal recessive or dominant, X-linked, mitochondrial, uniparental disomy, or digenic. There is significant genetic heterogenicity and overlap of the involved genes (Fig. 670.5). The IRDs are classified as retinitis pigmentosa, macular dystrophies, cone, or cone-rod dystrophies, syndromic (Usher syndrome with deafness), and the Leber congenital amaurosis disorders (>20 genes).

Retinitis Pigmentosa

This progressive peripheral retinal degeneration is the most common IRD and is characterized by pigmentary changes, arteriolar attenuation, usually some degree of optic atrophy, and progressive

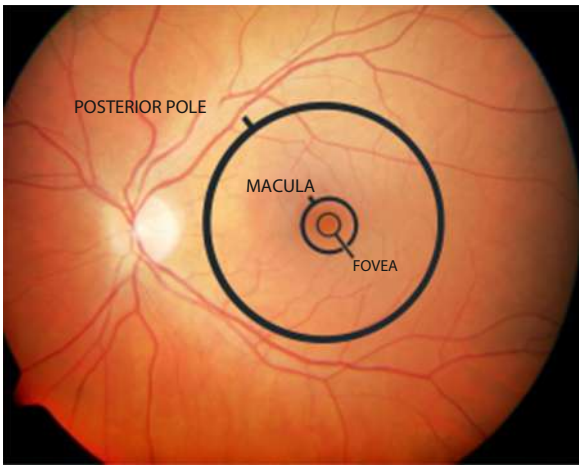

Fig. 670.4 Fundus image of a normal retina. The macula contains a high proportion of cone cells, which are most densely clustered in the fovea. The posterior pole marks the area of the retina between the optic disc (the *bright yellow oval* on the left of the image) and the macula. *(From Broadgate S, Yu J, Downes SM, Halford S. Unraveling the genetics of inherited dystrophies: Past, present, and future. Prog Retinal Eye Res. 2017;59:53–96. Fig. 1, p. 55).*

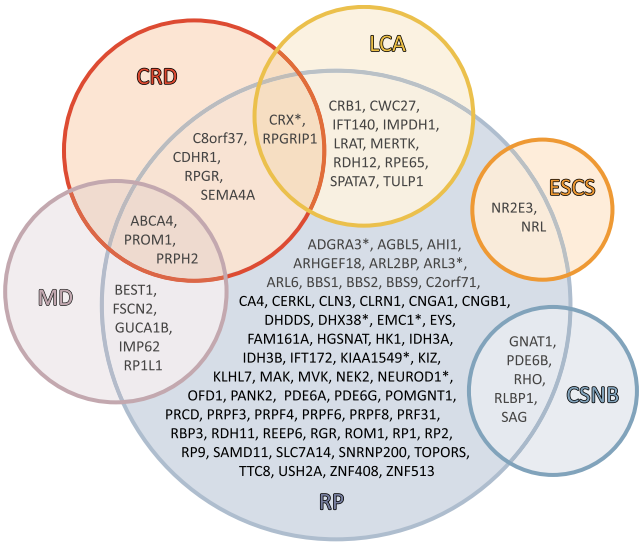

Fig. 670.5 Venn diagram summarizing the genetic overlap between retinitis pigmentosa and other inherited retinal dystrophies. Each circle represents a specific clinical diagnosis. The gene names listed in the overlapping areas indicate that mutations in these genes can lead to different phenotypes. Genes marked with an asterisk are candidate genes for nonsyndromic RP. CRD, cone-rod dystrophy; CSNB, congenital stationary night blindness; ESCS, enhanced S-cone syndrome; LCA, Leber congenital amaurosis; MD, macular dystrophy; RP, retinitis pigmentosa. *(From Verbakel SK, van Huet RAC, Boon CJF, et al. Non-syndromic retinitis pigmentosa. Prog Retin Eye Res. 2018;66:157–186. Fig 1.)*

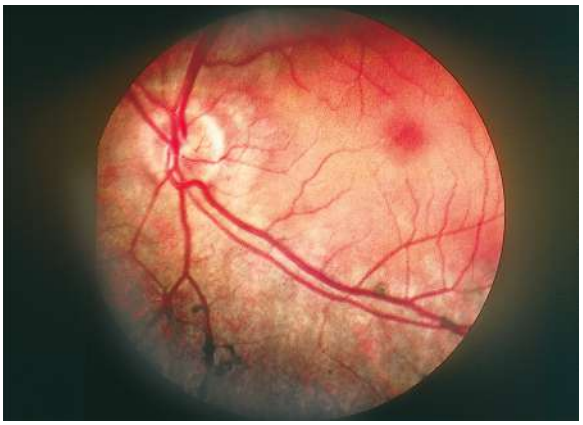

Fig. 670.6 Retinitis pigmentosa. Fundus photograph shows "bone spicule" pigmentation of the midperipheral fundus, waxy pallor of the optic disc, and attenuated retinal vessels, the most consistent finding in retinitis pigmentosa. *(Courtesy Dr. John I. Loewenstein.)*

impairment of visual function. Dispersion and aggregation of the retinal pigment produce various ophthalmoscopically visible changes ranging from granularity or mottling of the retinal pigment pattern to distinctive focal pigment aggregates with the configuration of bone spicules (Fig. 670.6). Other ocular findings include subcapsular cataract, glaucoma, and keratoconus.

Impairment of night vision (nyctalopia) or dark adaptation is often the first clinical manifestation. Progressive loss of peripheral vision (tunnel vision), often in the form of an expanding ring scotoma or concentric contraction of the field, is usual. There may also be loss of central vision. Retinal function, as measured by electroretinography (ERG), is characteristically reduced. The disorder may be autosomal recessive, autosomal dominant, or X-linked with ~70 affected genes (see Fig. 670.5). Children with autosomal recessive retinitis pigmentosa are more likely to become symptomatic at an earlier age (median age 10.7 years). Those with autosomal dominant retinitis pigmentosa are more likely to present in their 20s.

Another form of nonsyndromic IRD is **Leber congenital retinal amaurosis** (LCA), in which the retinal changes tend to be pleomorphic, with various degrees of pigment disorder, arteriolar attenuation, and optic atrophy. The incidence is approximately 1/81,000 births. Patients develop poor vision, nystagmus, poor pupillary response to light, and a behavioral pattern of eye rubbing. There are pathogenic variants in ~20 different genes producing this early (infancy) onset autosomal recessive severe retinal degenerative disease (see Fig. 670.5). Ten percent have pathogenic variants in the *LRAT* or *RPE65* genes, involved in retinoid metabolism. Although the retina may initially appear normal during infancy, the child typically shows evidence of visual impairment, nystagmus, and poor pupillary reaction soon after birth. ERG findings are abnormal early and confirm the diagnosis. Visual loss can be profound and may progress with age.

Gene replacement therapy via subretinal injections shows promise for *RPE65*-related IRDs, including those phenotypes of retinitis pigmentosa, Leber congenital amaurosis, and other IRD with this pathologic gene variant. Individuals who received subretinal injection of vector genomes of voretigene neparvovec improved in their ability to navigate a dimly lit course when compared with controls, with outcomes measured at 1 year. Similar gene replacement studies have been conducted or are being conducted for other retinal dystrophies, including choroideremia, Stargardt disease, cone-rod dystrophy, and X-linked retinoschisis.

Usher syndrome, an autosomal recessive disorder, is the most common cause of syndromic IRD *and* sensorineural deafness (incidence, 1/25,000). Type 1 Usher syndrome presents at birth with profound hearing loss and poor balance; vision loss progresses more slowly and begins during adolescence. Patients with type 3 disease have normal hearing at birth but develop hearing loss and night blindness around puberty. To date, 11 genetic loci have been located (5 for type 1, 3 for type 2; 1 for type 3).

A similar clinical picture may occur in the setting of secondary pigmentary retinal degenerations, which must be differentiated from retinitis pigmentosa, when associated with a wide variety of metabolic diseases, neurodegenerative processes, and multifaceted syndromes. Examples include the progressive retinal changes of the mucopolysaccharidoses (particularly Hurler, Hunter, Scheie, and Sanfilippo syndromes; see Chapter 109) and certain of the late-onset gangliosidoses (Batten-Mayou, Spielmeyer-Vogt, and Jansky-Bielschowsky diseases; see Chapters 106.4 and 639.2), the progressive retinal degeneration associated with progressive external ophthalmoplegia (Kearns-Sayre syndrome; see Chapter 638.2), and the retinitis pigmentosa–like changes in the Laurence-Moon and Bardet-Biedl syndromes. The retinal manifestations of abetalipoproteinemia (Bassen-Kornzweig syndrome; see Chapter 106) and Refsum disease (see Chapter 106.2) are also similar to those found in retinitis pigmentosa. The diagnosis of the latter two disorders in a patient with presumed retinitis pigmentosa is important because treatment is possible. There is also an association of retinitis pigmentosa and congenital hearing loss, as in Usher syndrome.

STARGARDT DISEASE (FUNDUS FLAVIMACULATUS)

This autosomal recessive IRD/macular dystrophy is characterized by slowly progressive bilateral macular degeneration and impairment of vision. It usually appears at 8-14 years of age, and affected children are often initially misdiagnosed as having functional visual loss. The foveal reflex becomes obtunded or appears grayish, pigment spots develop in the macular area, and macular depigmentation and chorioretinal atrophy eventually occur. Macular hemorrhages may also develop. Some patients also have white or yellow spots beyond the macula or pigmentary changes in the periphery; the term *fundus flavimaculatus* is commonly used for this condition. It is now recognized that Stargardt disease and fundus flavimaculatus represent different entities on the spectrum of the same disease. Central visual acuity is reduced, often to 20/200, but total loss of vision does not occur. ERG findings vary. The condition is not associated with central nervous system abnormalities and is to be differentiated from the macular changes of many

progressive metabolic neurodegenerative diseases. The most common (95%) genetic pathogenic variant (autosomal recessive) responsible for Stargardt macular dystrophy involves the *ABCA4* gene. Pathologic variants in *ELOVL4* are less common and are inherited as an autosomal dominant trait. Gene replacement therapy is being investigated for this condition.

BEST VITELLIFORM DEGENERATION

This macular dystrophy is characterized by a distinctive yellow or orange discoid subretinal lesion in the macula, resembling the intact yolk of a fried egg. Diagnosis is usually made at 3-15 years of age, with a mean age of presentation of 6 years. Vision is usually normal at this stage. The condition may be progressive; the yolklike lesion may eventually degenerate ("scramble") and result in pigmentation, chorioretinal atrophy, and vision impairment. The condition is usually bilateral. There is no association with systemic abnormalities. Inheritance is usually autosomal dominant. The vitelliform macular dystrophy gene *(VMD2)* has been identified, and DNA testing is available. In vitelliform macular degeneration, the ERG response is normal. Electrooculographic findings are abnormal in affected patients and carriers, and this test is useful in diagnosis and genetic counseling.

CHERRY-RED SPOT

Because of the special histologic features of the macula, certain pathologic processes affecting the retina produce an ophthalmoscopically visible sign referred to as a *cherry-red spot*, a bright to dull red spot at the center of the macula surrounded and accentuated by a grayish-white or yellowish halo (Fig. 670.7). The halo is a result of a loss of transparency of the retinal ganglion cell layer secondary to edema, lipid accumulation, or both. Because ganglion cells are not present in the fovea, the retina surrounding the fovea is opacified but the fovea transmits the normal underlying choroidal color (red), accounting for the presence of the cherry-red spot. A cherry-red spot typically occurs in certain sphingolipidoses, principally in Tay-Sachs disease (GM_2 type 1), in the Sandhoff variant (GM_2 type 2), and in generalized gangliosidosis (GM_1 type 1). Similar but less distinctive macular changes occur in some cases of metachromatic leukodystrophy (sulfatide lipidosis), in some forms of neuronopathic Niemann-Pick disease, in galactosialidosis, and in certain mucolipidoses. The cherry-red spot that characteristically occurs as a result of retinal ischemia secondary to vasospasm, ocular contusion, or occlusion of the central retinal artery must be differentiated from the cherry-red spot of neurodegenerative disease (see Chapters 106.4 and 639).

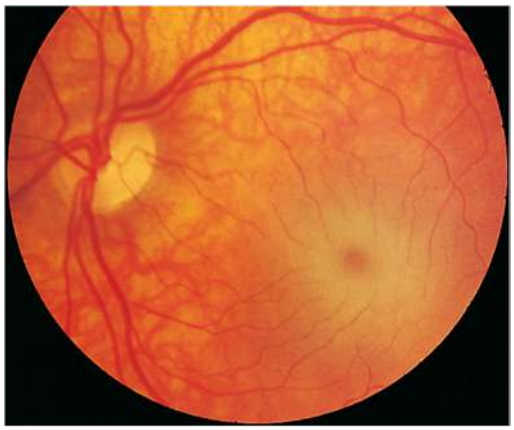

Fig. 670.7 Cherry-red spot seen in a case of Tay-Sachs disease. Because the parafoveal area has many retinal ganglion cells and the fovea has none, the fovea retains its orange-red color but is surrounded by a retina that is whitish. This produces the cherry-red spot in the macula. *(From Cheng KP, Biglan AW. Ophthalmology. In Zitelli BJ, McIntire SC, Nowald AJ, eds. Zitelli and Davis' Atlas of Pediatric Physical Diagnosis, 6th ed. Philadelphia: Saunders, 2012. Fig. 19.102.)*

PHAKOMATOSIS

See also Chapter 636.

These are the herald lesions of the hamartomatous disorders. **Tuberous sclerosis**, the distinctive ocular lesion is a refractile, yellowish, multinodular cystic lesion arising from the disc or retina; the appearance of this typical lesion is often compared with that of an unripe mulberry (Fig. 670.8). Equally characteristic and more common in tuberous sclerosis are flatter, yellow to whitish retinal lesions that vary in size from minute dots to large lesions approaching the size of the disc. These lesions are benign astrocytic proliferations. Rarely, similar retinal phakomas occur in neurofibromatosis. In **von Hippel-Lindau disease** (angiomatosis of the retina and cerebellum), the distinctive fundus lesion is a hemangioblastoma; this vascular lesion usually appears as a reddish globular mass with large, paired arteries and veins passing to and from the lesion. In **Sturge-Weber syndrome** (encephalofacial angiomatosis), the fundus abnormality is a choroidal hemangioma; the hemangioma may impart a dark color to the affected area of the fundus, but the lesion is best seen with fluorescein angiography.

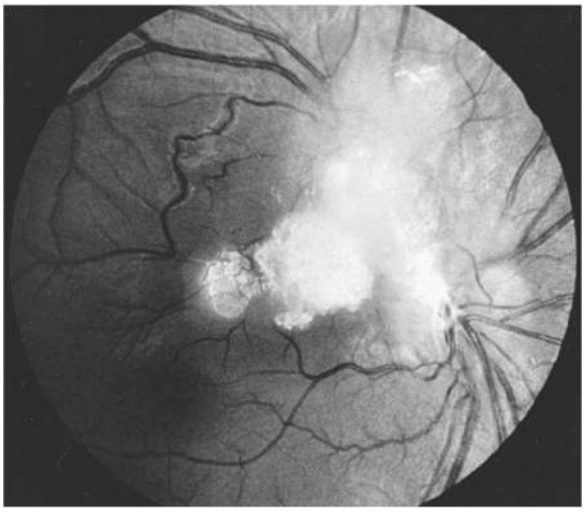

Fig. 670.8 Retinal phakoma of tuberous sclerosis.

RETINOSCHISIS

Congenital hereditary retinoschisis, also referred to as juvenile X-linked retinoschisis, is a bilateral vitreoretinal dystrophy that has a bimodal age of presentation. The first group presents with strabismus and nystagmus at a mean age of 1.5-2 years and is the most severely affected. The second group presents at 6-7 years with poor vision. Retinoschisis is characterized by splitting of the retina into inner and outer layers. The usual ophthalmoscopic finding in affected males is an elevation of the inner layer of the retina, most commonly in the inferotemporal quadrant of the fundus, often with round or oval holes visible in the inner layer. Schisis of the fovea is virtually pathognomonic and is found in almost 100% of patients. Ophthalmoscopically, this appears in early stages as small, fine striae in the internal limiting membrane. These striae radiate outward in a petaloid or spoke-wheel configuration. In some cases, frank retinal detachment or vitreous hemorrhage occurs.

Vision impairment varies from mild to severe; visual acuity may worsen with age, but good vision is often retained. Carrier females are asymptomatic, but linkage studies may be useful to help detect carriers. In some cases, treatment with a topical carbonic anhydrase inhibitor may improve visual acuity.

RETINAL DETACHMENT

A retinal detachment is a separation of the outer layers of the retina from the underlying retinal pigment epithelium (RPE). During embryogenesis, the retina and RPE are initially separated. During ocular development, they join together and are held in apposition to each other by various physiologic mechanisms. Pathologic events leading to a retinal

detachment return the retina–RPE to its former separated state. The detachment can occur as a congenital anomaly but more commonly arises secondary to other ocular abnormalities or trauma. Three types of detachment are described, and each may occur in children. Rhegmatogenous detachments result from a break in the retina that allows fluid to enter the subretinal space. In children, these are usually a result of trauma (such as child abuse) but may occur secondary to myopia or ROP or after surgery for congenital cataract. Tractional retinal detachments result when vitreoretinal membranes pull on the retina. They can occur in diabetes, sickle cell disease, and ROP. Exudative retinal detachments result when exudation exceeds absorption. This can be seen in Coats disease, retinoblastoma, and ocular inflammation.

The presenting sign of retinal detachment in an infant or child may be loss of vision, secondary strabismus or nystagmus, or leukocoria (white pupillary reflex). In addition to direct examination of the eye, special diagnostic studies such as ultrasonography and neuroimaging (CT, MRI) may be necessary to establish the cause of the detachment and the appropriate treatment. Prompt treatment is essential if vision is to be salvaged.

COATS DISEASE

This idiopathic, nonfamilial exudative retinopathy is characterized by telangiectasia of retinal vessels with leakage of plasma to form intraretinal and subretinal exudates and by retinal hemorrhages and detachment (Fig. 670.9). The condition is usually unilateral. It predominantly affects previously healthy males, usually appearing in the first decade. The most frequent presenting signs are blurring of vision, leukocoria, and strabismus. Rubeosis of the iris, glaucoma, and cataract may develop. The differential diagnosis includes retinoblastoma, ROP, Norrie disease, angiomatosis, chorioretinitis (see Table 669.1), systemic vasculitis, and Coats plus syndrome (leukodystrophy, osteopenia, anemia, retinitis) due to pathogenic variants in *CTC1* (autosomal recessive). **Treatment** with photocoagulation, cryotherapy, or VEGF inhibitors may be helpful.

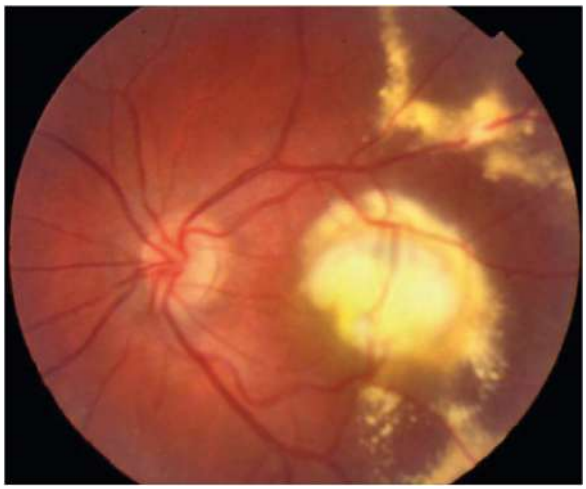

Fig. 670.9 Coats disease with massive retinal exudation.

FAMILIAL EXUDATIVE VITREORETINOPATHY

This progressive genetic retinal vascular disorder has clinical and angiographic findings that suggest an aberration of vascular development. Avascularity of the peripheral temporal retina is a significant finding in most cases, with abrupt cessation of the retinal capillary network in the region of the equator. The avascular zone often has a wedge- or V-shaped pattern in the temporal meridian. Glial proliferation or well-marked retinochoroidal atrophy may be found in the avascular zone. Excessive branching of retinal arteries and veins, dilation of the capillaries, arteriovenous shunt formation, neovascularization, and leakage from retinal vessels of the farthest vascularized retina occur. Vitreoretinal adhesions are usually present at the peripheral margin of the vascularized retina. Traction, retinal dragging and temporal displacement of the macula, falciform retinal folds, and retinal detachment are common. Intraretinal or subretinal exudation, retinal hemorrhage, and recurrent vitreous hemorrhages may develop. Patients may also develop cataracts and glaucoma. Vision impairment of varying severity occurs. The condition is usually bilateral. Familial exudative vitreoretinopathy (FEVR) is usually an autosomal dominant condition (*FZD4* or *LRP5*) with incomplete penetrance. Autosomal recessive *(LRP5)* and X-linked *(CNDP)* have also been reported. Asymptomatic family members often display a zone of avascular peripheral retina.

The findings in FEVR may resemble those of ROP in the cicatricial stages, but unlike ROP, the neovascularization of FEVR seems to develop years after birth, and most patients with FEVR have no history of prematurity, oxygen therapy, prenatal or postnatal injury or infection, or developmental abnormalities. FEVR is also to be differentiated from Coats disease, angiomatosis of the retina, peripheral uveitis, and other disorders of the posterior segment.

HYPERTENSIVE RETINOPATHY

In the early stages of hypertension, no retinal changes may be observable. Generalized constriction and irregular narrowing of the arterioles are usually the first signs in the fundus. Other alterations include retinal edema, flame-shaped hemorrhages, cotton-wool spots (retinal nerve fiber layer infarcts), and papilledema (Fig. 670.10). These changes are reversible if the hypertension can be controlled in the early stages, but in long-standing hypertension, irreversible changes may occur. Thickening of the vessel wall may produce a silver- or copper-wire appearance. Hypertensive retinal changes in a child should alert the physician to renal disease, pheochromocytoma, collagen disease, and cardiovascular disorders, particularly coarctation of the aorta.

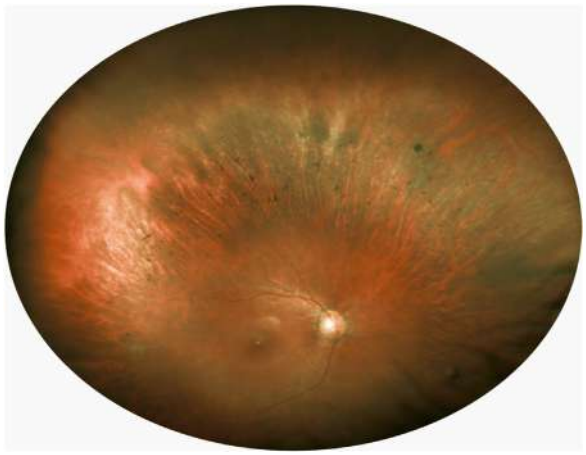

Fig. 670.10 Hypertension retinopathy with narrowed arterioles whose sclerosed walls create the appearance of "nicking" when the arterioles cross venules. *(From Yanoff M, Duker JS, eds. Ophthalmology. Elsevier, 2009.)*

DIABETIC RETINOPATHY

The retinal changes of diabetes mellitus are classified as nonproliferative or proliferative. Nonproliferative diabetic retinopathy is characterized by retinal microaneurysms, venous dilation, retinal hemorrhages, and exudates. The microaneurysms appear as tiny red dots. The hemorrhages may be of both the dot and blot type, representing deep intraretinal bleeding, and the splinter or flame-shaped type, involving the superficial nerve fiber layer. The exudates tend to be deep and to appear waxy. There may also be superficial nerve fiber infarcts called cytoid bodies or cotton-wool spots, as well as retinal edema. These signs may wax and wane. They are seen primarily in the posterior pole, around the disc and macula, or well within the range of direct ophthalmoscopy. Involvement of the macula may lead to decreased vision.

Proliferative retinopathy, the more serious form, is characterized by neovascularization and proliferation of fibrovascular tissue on the

retina, extending into the vitreous. Neovascularization may occur on the optic disc, elsewhere on the retina, or on the iris and in the anterior chamber angle (or rubeosis irides) (Fig. 670.11). Traction on these new vessels leads to hemorrhage and, eventually, scarring. The vision-threatening complications of proliferative diabetic retinopathy are retinal and vitreous hemorrhages, cicatrization, traction, and retinal detachment. Neovascularization of the iris may lead to secondary glaucoma if not treated promptly.

Diabetic retinopathy involves the alteration and nonperfusion of retinal capillaries, retinal ischemia, and neovascularization, but its pathogenesis is not yet completely understood, either in terms of location of the primary pathogenetic mechanism (retinal vessels vs surrounding neuronal or glial tissue) or the specific biochemical factors involved. The better the degree of long-term metabolic control, the lower the risk of diabetic retinopathy.

The prevalence and course of retinopathy relate to a patient's age and to disease duration. Detectable microvascular changes are rare in prepubertal children, with the prevalence of retinopathy increasing significantly after puberty, especially after the age of 15 years. The incidence of retinopathy is low during the first 5 years of disease and increases progressively thereafter, with the incidence of proliferative retinopathy becoming substantial after 10 years and with increased risk of visual impairment after 15 years or more.

Ophthalmic examination guidelines have been proposed by the American Academy of Pediatrics. An initial exam is recommended at age 9 years if the diabetes is poorly controlled. If the diabetes is well controlled, an initial exam 3 years after puberty with annual follow-up is recommended.

In addition to retinopathy, patients with juvenile-onset diabetes may develop optic neuropathy, characterized by swelling of the disc and blurring of vision. Patients with diabetes may also develop cataracts, even at an early age, sometimes with rapid progression.

Treatment

Macular edema is the leading cause of visual loss in diabetic persons. Photocoagulation may be used to decrease the risk of continued vision loss in patients with macular edema.

Proliferative retinopathy causes the most severe vision loss and can lead to total loss of vision and even loss of the eye. Patients who have proliferative disease and who display certain high-risk characteristics should undergo panretinal photocoagulation to preserve their central vision. Neovascularization of the iris is also treated with panretinal photocoagulation to stop the development of neovascular glaucoma.

Vitrectomy and other intraocular surgery may be necessary in patients with nonresolving vitreous hemorrhage or traction retinal detachment. The value of technologic advances, such as insulin infusion pumps and pancreatic transplants, in preventing ocular complications is under investigation (see Chapter 629).

SUBACUTE BACTERIAL ENDOCARDITIS

At some time during the disease, retinopathy is present in approximately 40% of cases of subacute bacterial endocarditis (see Chapter 486). The lesions include hemorrhages, hemorrhages with white centers (Roth spots), papilledema, and, rarely, embolic occlusion of the central retinal artery (Fig. 670.12).

BLOOD DISORDERS

In primary and secondary anemias, retinopathy in the form of hemorrhages and cotton-wool patches may occur. Vision can be affected if hemorrhage occurs in the macular area. The hemorrhages may be light and feathery or dense and preretinal. In polycythemia vera, the retinal veins are dark, dilated, and tortuous. Retinal hemorrhages, retinal edema, and papilledema may be observed. In leukemia, the veins are characteristically dilated, with sausage-shaped constrictions; hemorrhages, particularly white-centered hemorrhages and exudates, are common during the acute stage. In the sickling disorders, fundus changes include vascular tortuosity, arterial and venous occlusions, "salmon patches," refractile deposits, pigmented lesions, arteriolar-venous anastomoses, and neovascularization (with "sea-fan" formations), sometimes leading to vitreous hemorrhage and retinal detachment. Individuals with sickle cell hemoglobin C and sickle cell hemoglobin β-thalassemia hemoglobinopathies are at a higher risk of the development of retinopathy than are those with homozygous hemoglobin S disease. It is thought that the more anemic state of those patients with homozygous hemoglobin S disease offers protection from vascular occlusions in the retina.

TRAUMA-RELATED RETINOPATHY

Retinal changes may occur in patients who suffer trauma to other parts of the body. The occurrence of retinal hemorrhages in infants who have been physically abused is well documented (Fig. 670.13; see Chapter 17). Retinal, subretinal, subhyaloid, and vitreous hemorrhages have been described in infants and young children with inflicted neurotrauma. Often there are no signs of direct trauma to the eye, periocular region, or head. Such cases may result from violent shaking of an infant, and permanent retinal damage may result.

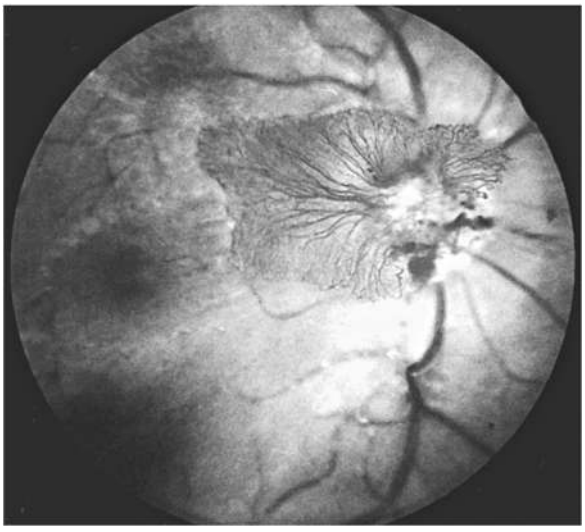

Fig. 670.11 Proliferative diabetic retinopathy with neovascularization of the disc.

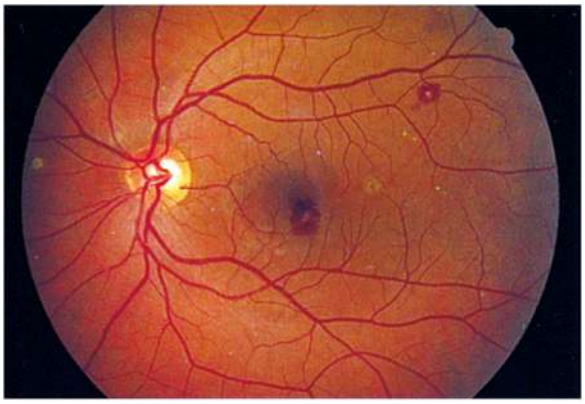

Fig. 670.12 Roth's spots. Multiple white-centered hemorrhages in a man with recurrent subacute bacterial endocarditis. White-centered hemorrhages are also seen with leukemia and diabetes. The small white scars are probably the residua of previous episodes. *(From Goldman L, Schafer AI, eds. Goldman-Cecil Medicine. 25th ed. Philadelphia: Elsevier, 2016. Fig. 423.28, p. 2569.)*

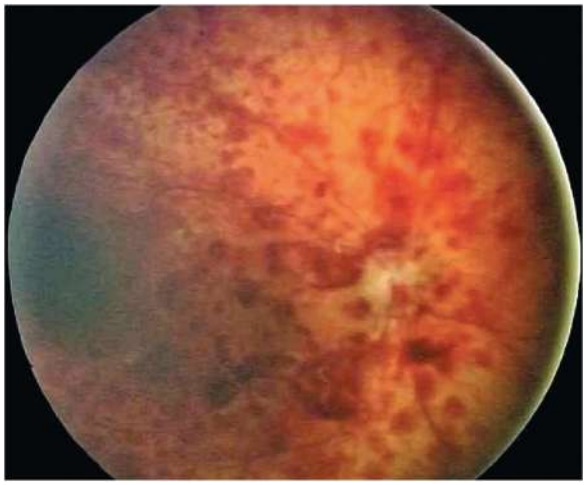

Fig. 670.13 Shaken baby syndrome (inflicted neurotrauma). Retinal hemorrhages in multiple layers too numerous to count into the far periphery.

In patients with severe head or chest compressive trauma, a traumatic retinal angiopathy known as **Purtscher retinopathy** may occur. This is characterized by retinal hemorrhage, cotton-wool spots, possible disc swelling, and decreased vision. The pathogenesis is unclear, but there is evidence of arteriolar obstruction in this condition. A Purtscher-like fundus picture may also occur in several nontraumatic settings, such as acute pancreatitis, lupus erythematosus, and childbirth. **Laser pointers** may produce vision loss with varying findings depending on the retinal area exposed to the nonionizing radiation.

MYELINATED NERVE FIBERS

Myelination of the optic nerve fibers normally terminates at the level of the disc, but in some individuals, ectopic myelination extends to nerve fibers of the retina. The condition is most commonly seen adjacent to the disc, although more peripheral areas of the retina may be involved. The characteristic ophthalmoscopic picture is a focal white patch with a feathered edge or brushstroke appearance. Because the macula is generally unaffected, the visual prognosis is good. A relative or absolute visual field defect corresponding to areas of ectopic myelination is usually the only associated ocular abnormality. Extensive unilateral involvement, however, is associated with ipsilateral myopia, amblyopia, and strabismus. If unilateral high myopia and amblyopia are present, appropriate optical correction and occlusion therapy should be instituted. For unknown reasons, the disorder is more commonly encountered in patients with craniofacial dysostosis, oxycephaly, neurofibromatosis, and Down syndrome.

CHORIORETINAL COLOBOMA

The term *coloboma* describes a defect such as a gap, notch, fissure, or hole (see Chapter 662). The typical fundus coloboma is a result of malclosure of the embryonic fissure, which leaves a gap in the retina, RPE, and choroid, thus baring the underlying sclera. The defect may be extensive, involving the optic nerve, ciliary body, and iris and even the lens, or it may be localized to one or more portions of the fissure. The usual appearance is of a well-circumscribed, wedge-shaped white area extending inferonasally below the disc, sometimes involving or engulfing the disc. In some cases, there is ectasia or cyst formation in the area of the defect. Less extensive colobomatous defects may appear as only single or multiple focal punched-out chorioretinal defects or anomalous pigmentation of the fundus in the line of the embryonic fissure. Colobomas may occur in one or both eyes. A visual field defect usually corresponds to the chorioretinal defect. Visual acuity may be impaired, particularly if the defect involves the disc or macula.

Fundus colobomas may occur in isolation as sporadic defects or as an inherited condition. Isolated colobomatous anomalies are commonly inherited in an autosomal dominant manner with highly variable penetrance and expressivity. Family members of affected patients should receive appropriate genetic counseling. Colobomas may also be associated with such abnormalities as microphthalmia, glioneuroma of the eye, cyclopia, or encephalocele. They occur in children with various chromosomal disorders, including trisomies 13 and 18, triploidy, cat-eye syndrome, and 4p−. Ocular colobomas also occur in many multisystem disorders, including the CHARGE (*C,* coloboma; *H,* heart disease; *A,* atresia choanae; *R,* retarded growth, and development and/or central nervous system anomalies; *G,* genetic anomalies and/or hypogonadism; *E,* ear anomalies and/or deafness) association; Joubert, Aicardi, Meckel, Warburg, and Rubinstein-Taybi syndromes; linear sebaceous nevus; Goldenhar and Lenz microphthalmia syndromes; and Goltz focal dermal hypoplasia.

Visit Elsevier eBooks+ at eBooks.Health.Elsevier.com for Bibliography.

Chapter 671

Abnormalities of the Optic Nerve

Scott E. Olitsky and Justin D. Marsh

OPTIC NERVE APLASIA

This rare congenital anomaly of unknown etiology is typically unilateral. The optic nerve, retinal ganglion cells, and retinal blood vessels are absent. A vestigial dural sheath usually connects with the sclera in a normal position, but no neural tissue is present within this sheath. Optic nerve aplasia typically occurs sporadically in an otherwise healthy person.

OPTIC NERVE HYPOPLASIA

Hypoplasia of the optic nerve is a nonprogressive, idiopathic condition characterized by a subnormal number of optic nerve axons with normal mesodermal elements and glial supporting tissue. In typical cases, the nerve head is small and pale, with a pale or pigmented peripapillary halo or double ring sign (Fig. 671.1).

This anomaly is associated with defects of vision and of visual fields of varying severity, ranging from blindness to normal or near-normal vision. It may be associated with systemic anomalies that most commonly involve the central nervous system (CNS). CNS defects such as hydranencephaly or anencephaly or more focal lesions compatible with continued development may accompany optic nerve hypoplasia, but unilateral or bilateral optic nerve hypoplasia may be found without any concomitant defects.

Optic nerve hypoplasia is a principal feature of **septo-optic dysplasia (SOD),** a developmental disorder characterized by the association of anomalies of the midline structures of the brain

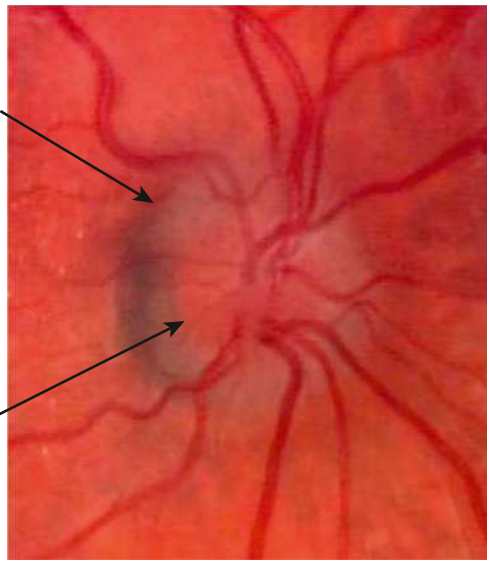

Fig. 671.1 Optic nerve hypoplasia: the "double ring sign." The first ring shows the border of the nerve sheath, and the second ring is formed by the actual border of the optic nerve tissue edge. *(From Martin RJ, Fanaroff AA, Walsh MC, eds. Fanaroff & Martin's Neonatal-Perinatal Medicine. 10th ed. Philadelphia: Elsevier; 2015: Fig. 103.24, p. 1753.)*

with hypoplasia of the optic nerves, optic chiasm, and optic tracts; typically noted are agenesis of the septum pellucidum, partial or complete agenesis of the corpus callosum, and malformation of the fornix, with a large chiasmatic cistern. Patients may have hypothalamic abnormalities and endocrine defects ranging from panhypopituitarism to isolated deficiency of growth hormone, hypothyroidism, or diabetes insipidus. Neonatal hypoglycemia and seizures are important presenting signs in affected infants. In some patients with SOD, pathologic variants in *HESX1*, *SOX2*, *SOX3*, *OTX2*, and *PROKR2* have been identified.

MRI is preferred for evaluating CNS abnormalities in patients with optic nerve hypoplasia. During MRI, special attention should be directed to the pituitary infundibulum, where ectopia of the posterior pituitary may be found. Posterior pituitary ectopia appears on MRI as an absence of the pituitary infundibulum with an abnormal bright spot at the upper infundibulum area. This abnormality is present in approximately 15% of patients and suggests a posterior pituitary hormone deficiency, requiring further endocrinologic workup. Endocrine function should be watched closely in patients with optic nerve hypoplasia. The cause of optic nerve hypoplasia remains unclear.

Children with **periventricular leukomalacia** display an unusual form of optic nerve hypoplasia. The optic nerve demonstrates a large cup within a normal-size optic disc. This form of optic nerve hypoplasia occurs secondary to transsynaptic degeneration of optic axons caused by the primary bilateral lesion in the optic radiation (periventricular leukomalacia).

OPTIC NERVE COLOBOMA

Optic nerve colobomas can be unilateral or bilateral. The visual acuity can range from normal to complete blindness. The coloboma develops secondary to incomplete closure of the embryonic fissure. The defect may produce a partial or total excavation of the optic disc (Fig. 671.2). Chorioretinal and iris colobomas may also occur (see Chapter 662). Optic nerve colobomas may be seen in a multitude of ocular and systemic abnormalities, including the CHARGE (*C*, coloboma; *H*, heart disease; *A*, atresia choanae; *R*, retarded growth and development and/or CNS anomalies; *G*, genetic anomalies and/or hypogonadism; *E*, ear anomalies and/or deafness) association.

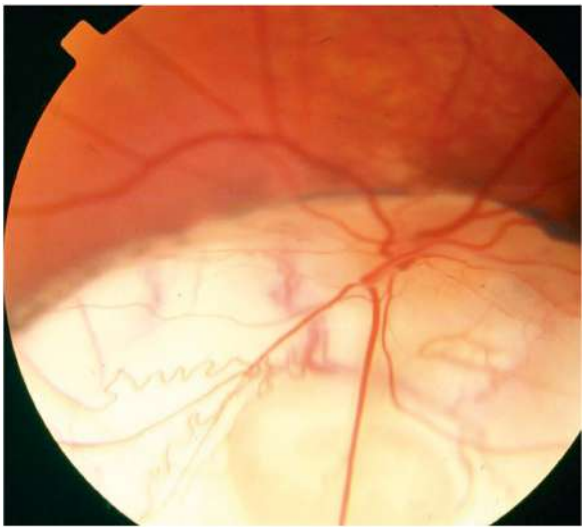

Fig. 671.2 Optic nerve coloboma.

MORNING GLORY DISC ANOMALY

This term describes a congenital malformation of the optic nerve characterized by an enlarged, excavated, funnel-shaped disc with an elevated rim resembling a morning glory flower. White glial tissue is present in the central part of the disc (Fig. 671.3). The retinal vessels are abnormal and appear at the peripheral disc, coursing over the elevated pink rim in a radial fashion. Pigmentary mottling of the peripapillary region is usually seen. Most cases are unilateral. Females are affected twice as often as males. Visual acuity is usually severely reduced. Morning glory disc anomaly has been associated with basal encephalocele in patients with midfacial anomalies. Abnormalities of the carotid circulation can also be seen in patients with morning glory anomaly. Moyamoya disease is a well-described associated finding.

TILTED DISC

In this congenital anomaly, the vertical axis of the optic disc is directed obliquely, so that the upper temporal portion of the nerve head is more prominent and anterior to the lower nasal portion of the disc. The retinal vessels emerge from the upper temporal portion of the disc rather than from the nasal side. Often noted is a peripapillary crescent or conus. Associated visual field defects and myopic astigmatism may be found. Clinical recognition of the tilted disc syndrome is important to avoid confusion of its disc and visual field signs with those of papilledema and intracranial tumor.

DRUSEN OF THE OPTIC NERVE

These globular, acellular bodies are thought to arise from axoplasmic derivatives of disintegrating nerve fibers. Drusen may be buried within the optic nerve, producing elevation of the optic nerve head (pseudopapilledema), or they may be partially or completely exposed, appearing as refractile bodies at the surface of the disc (Fig. 671.4). Visual field defects and spontaneous hemorrhages of the peripapillary nerve fiber layer may occur in association with drusen. Drusen may occur as an autosomal dominant condition with incomplete penetrance. B-scan ultrasonography can help to positively identify drusen suspected on clinical ophthalmic exam in some cases, although drusen in young children may be less likely to be visible with ultrasonography than in adults.

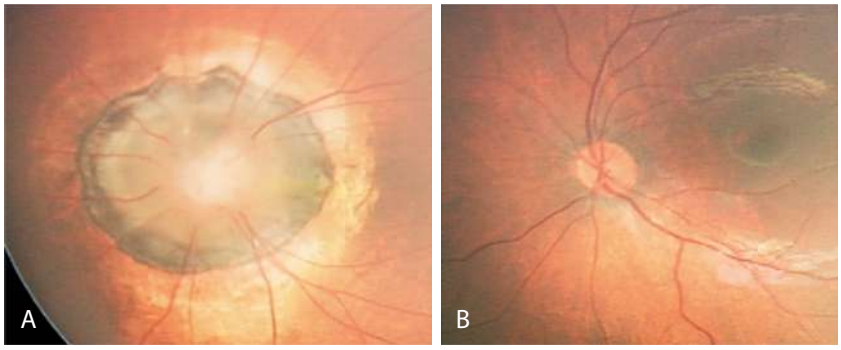

Fig. 671.3 A, Morning glory disc anomaly. The defect looks like a fully opened morning glory flower. B, Normal appearance of scaled fundus photography. *(From Martin RJ, Fanaroff AA, Walsh MC, eds. Fanaroff & Martin's Neonatal-Perinatal Medicine. 10th ed. Philadelphia: Elsevier; 2015: Fig. 103.25, p. 1754.)*

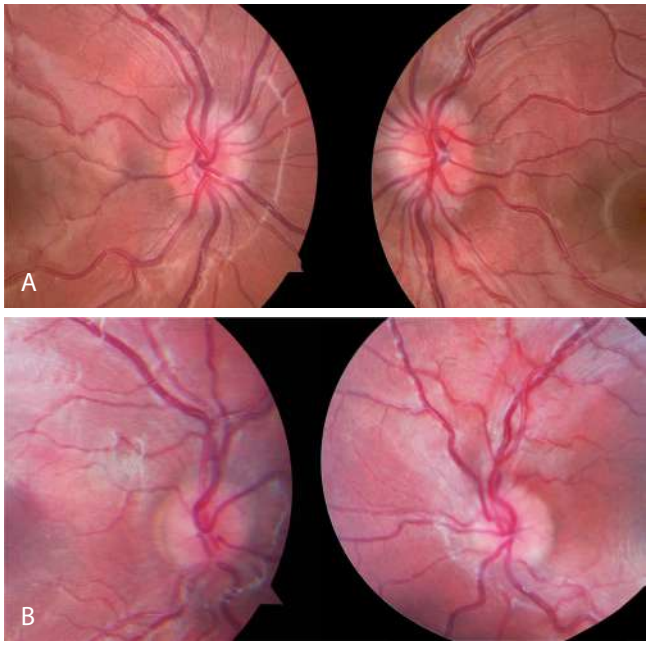

Fig. 671.4 Comparison of optic disc in children with optic disc drusen and papilledema. A, Optic disc photos of a 10-year-old child with bilateral buried optic disc drusen. The disc margins are blurred, but there are no hemorrhages, exudates, or vessel obscuration. B, Optic disc photos of a 5-year-old child with mild papilledema due to increased intracranial pressure. Disc margins are blurred with mild obscuration of vessels, but no hemorrhages or exudates. *(From Chang MY, Pineles SL. Optic disc drusen in children. Surv Ophthalmol. 2016;61:745–758: Fig. 1).*

PAPILLEDEMA

The term *papilledema* is reserved to describe swelling of the nerve head secondary to increased intracranial pressure (ICP). Clinical manifestations of papilledema include edematous blurring of the disc margins, fullness or elevation of the nerve head, partial or complete obliteration of the disc cup, capillary congestion and hyperemia of the nerve head, generalized engorgement of the veins, loss of spontaneous venous pulsation, hemorrhages in the nerve fiber layer around the disc, and peripapillary exudates (see Fig. 671.4 and 630.2). In some cases, edema extending into the macula may produce a fan- or star-shaped figure. In addition, concentric peripapillary retinal wrinkling (Paton lines) may be noted. Transient obscuration of vision may occur, lasting seconds, and is associated with postural changes. Vision, however, is usually normal in acute papilledema. Normally, when the ICP is relieved, the papilledema resolves and the disc returns to a normal or nearly normal appearance within 6-8 weeks. Sustained chronic papilledema or longstanding unrelieved increased ICP may, however, lead to permanent nerve fiber damage, atrophic changes of the disc, macular scarring, and impairment of vision.

The *pathophysiology* of papilledema is probably as follows: elevation of intracranial subarachnoid cerebrospinal fluid (CSF) pressure, elevation of CSF pressure in the sheath of the optic nerve, elevation of tissue pressure in the optic nerve, stasis of axoplasmic flow and swelling of the nerve fibers in the optic nerve head, and secondary vascular changes and the characteristic ophthalmoscopic signs of venous stasis. Associated neuro-ophthalmic signs of increased ICP in infants and children include sixth cranial nerve palsy and attendant esotropia, lid retraction, paresis of upward gaze, tonic downward deviation of the eyes, and convergent nystagmus.

The common **etiologies** of papilledema in childhood are intracranial tumors and obstructive hydrocephalus, intracranial hemorrhage, the cerebral edema of trauma, meningoencephalitis, toxic encephalopathy, idiopathic intracranial hypertension, and certain metabolic diseases. Regardless of the cause, the optic disc signs of increased ICP in early childhood may occasionally be modified by the distensibility of the young skull. In the absence of conditions associated with early closure of sutures and early obliteration of the fontanel (craniosynostosis, Crouzon disease, and Apert syndrome), infants with increased ICP may not develop papilledema.

The **differential diagnosis** of papilledema includes structural changes of the disc (pseudopapilledema, pseudoneuritis, drusen, and myelinated nerve fibers; see Fig. 671.4), with which it may be confused, and the disc swelling of papillitis associated with optic neuritis in addition to the disc changes of hypertension and diabetes mellitus. Unless retinal hemorrhage or edema involves the macular area, the preservation of good central vision and the absence of an afferent pupillary defect (Marcus Gunn pupil) help to differentiate acute papilledema from the edema of the optic nerve head found in acute optic neuritis.

Papilledema is a neurologic emergency. It can be accompanied by other signs of increased ICP, including headaches, nausea, and vomiting. Neuroimaging should be performed; if no intracranial masses are detected, a lumbar puncture and determination of CSF pressure should follow.

OPTIC NEURITIS

This is any inflammation or demyelinization of the optic nerve with attendant impairment of function (see Chapter 640.2). The process is usually acute, with rapidly progressive loss of vision. It may be unilateral or bilateral. Pain on movement or palpation of the globe may precede or accompany the onset of visual symptoms. There is decreased visual activity, decreased color vision and contrast sensitivity, a relative afferent pupillary defect, and a normal macula and peripheral retina.

When the retrobulbar portion of the nerve is affected without ophthalmoscopically visible signs of inflammation at the disc, the term *retrobulbar optic neuritis* is applied. When there is ophthalmoscopically visible evidence of inflammation of the nerve head, the term *papillitis* or *intraocular optic neuritis* is used. When there is involvement of both the retina and the papilla, the term *optic neuroretinitis* is used.

In childhood, optic neuritis may occur as an isolated condition or as a manifestation of a neurologic or systemic disease. Optic neuritis may be secondary to inflammatory diseases (systemic lupus erythematosus, sarcoidosis, Behçet disease); infections (tuberculosis, syphilis, Lyme disease, meningitis, viral encephalitis, HIV, or postinfectious disease); and toxic or nutritional disorders (methanol, ethambutol, vitamin B_{12} deficiency). It may signify one of the many demyelinating diseases of childhood (see Chapter 640.2). Although a significant percentage of adults who experience an episode of optic neuritis eventually develop other symptoms associated with multiple sclerosis (MS), young children with optic neuritis are seemingly at less risk (risk of MS is 19% within 20 years). High-risk features suggestive of MS include visual acuity better than no light perception, periocular pain, acutely normal-appearing optic nerve, no retinal abnormalities, and abnormal MRI suggesting a demyelinating disease. Bilateral optic neuritis in children may be associated with **acute disseminated encephalomyelitis (ADEM)** or **neuromyelitis optica (NMO or Devic disease).** NMO is characterized by rapid and severe bilateral visual loss accompanied by transverse myelitis and paraplegia. Involvement of the brain stem and occasionally the cortex may be seen on MRI. NMO-specific immunoglobulin G (directed to the aquaporin 4 water channel) is the diagnostic test of choice for Devic syndrome. Antibody-negative NMO patients may have anti-MOG (myelin oligodendrocyte glycoprotein) antibodies, suggesting another form of demyelinating optic neuritis. Optic neuritis may also be secondary to an exogenous toxin or drug, as with lead poisoning or as a complication of long-term high-dose treatment with chloramphenicol or vincristine. Extensive pediatric neurologic and ophthalmic investigation, including MRI and lumbar puncture, is usually required. Idiopathic NMO is associated with anti–aquaporin 4 antibodies, otherwise known as NMO antibodies.

In most cases of acute optic neuritis, some improvement in vision begins within 1-4 weeks after onset, and vision may improve to normal or near normal within weeks or months. The course varies with cause. Although central vision may recover fully, it is common to find permanent defects in other areas of visual function (contrast sensitivity, color, brightness sense, and motion perception). Recurrences may occur especially, but not universally, in patients who go on to develop MS.

A **treatment** trial has demonstrated that high-dose intravenous methylprednisolone may help to speed the visual recovery in young adults, and it may prevent the development of MS in those at risk. It is unknown to what degree the results of the aforementioned trial may be extrapolated to optic neuritis in childhood.

LEBER HEREDITARY OPTIC NEUROPATHY

Leber hereditary optic neuropathy (LHON) is characterized by an acute to subacute painless loss of central vision primarily affecting young males (male to female ratio 2.5:1). The incidence is 1:30,000-50,000 people. A characteristic peripapillary telangiectatic microangiopathy occurs not only in the presymptomatic phase of involved eyes but also in a number of asymptomatic females (Fig. 671.5). Disc hyperemia and edema mark the acute phase of central visual loss. One eye is usually affected before the other; the second eye involvement begins 2-3 months later. Visual field loss (blurring, clouding) and impaired color vision are also present. In time, progressive optic atrophy and vision loss usually ensue. The tortuous angiopathy becomes less obvious. Although visual function after the initial loss generally remains stable, partial or less often complete recovery may occur in as many as 20–30% of affected individuals. This recovery may take place years or decades after the initial episode of acute vision loss. The peripapillary angiopathy, the lack of short-term remission and inflammation and MRI, as well as the degree of symmetry or peripheral motor or sensory deficits, serve to distinguish most cases of Leber disease from the optic neuritis of MS.

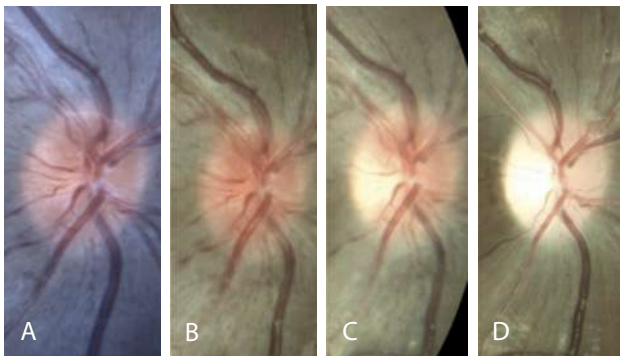

Fig. 671.5 A 9-year-old child with Leber hereditary optic neuropathy (LHON) m.11778 presents with best-corrected visual acuity of 20/20 in the right eye and no symptoms **(A).** At age 12, retinal nerve fiber layer swelling is observed before reduction in vision **(B).** His visual acuity rapidly decreases 1 month later to 20/50 and subtle temporal optic nerve pallor is visible **(C).** Three months later, his visual acuity is <20/400 and diffuse optic nerve pallor is present **(D).** Notice that peripapillary telangiectasia was present at age 9, 3 years before his visual symptoms started. The patient's left eye progressed similarly to the right eye. *(From Pilz YL, Bass SJ, Sherman J. A review of mitochondrial optic neuropathies: from inherited to acquired forms. J Optometry. 2016;10:205–214: Fig. 1, p. 208).*

LHON is maternally inherited and is caused by pathogenic gene variants in mitochondrial DNA (Fig. 671.6). Multiple point variants in the mitochondrial DNA have been identified. Pathogenic variants in *MTND1*, *MTND4* (~70%), and *MTND6* represent ~90% of cases. **LHON plus** is a related mitochondrial disorder affecting skeletal and cardiac muscle disorders, including electrocardiographic abnormalities. Only ~50% of males and 15% of females with a pathogenic gene variant develop symptomatic LHON.

The differential diagnosis includes optic neuritis (Chapter 640.2), other genetic optic neuropathies (Table 671.1; see also Fig. 671.6) and toxic or nutritional neuropathies (Table 671.2).

Gene therapy with intravitreal injection of a vector-*ND4* gene has had success improving vision in patients with LHON.

OPTIC ATROPHY

This term denotes degeneration of optic nerve axons, with attendant loss of function. The ophthalmoscopic signs of optic atrophy are pallor of the disc and loss of substance of the nerve head, sometimes with enlargement of the disc cup. The associated vision defect varies with the nature and site of the primary disease or lesion.

Optic atrophy is the common expression of a wide variety of congenital or acquired pathologic processes (Table 671.3). The cause may be traumatic, inflammatory, degenerative, neoplastic, or vascular; intracranial tumors and hydrocephalus are principal causes of optic atrophy in children. In some cases, progressive optic atrophy is hereditary. **Dominantly inherited infantile optic atrophy** is a relatively mild heredodegenerative type that tends to progress through childhood and adolescence. **Autosomal recessively inherited congenital optic atrophy** is a rare condition that is evident at birth or develops at

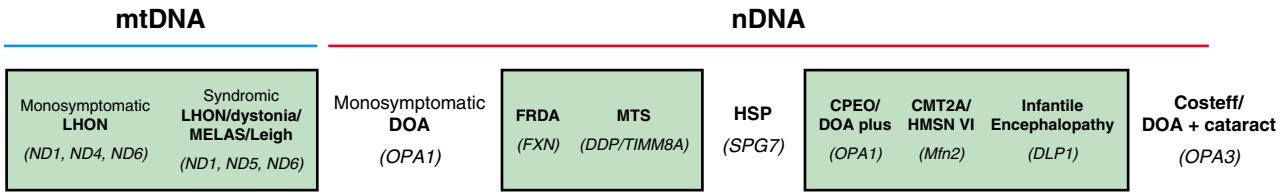

Fig. 671.6 Mitochondrial and nuclear DNA etiologies of inherited optic neuropathies. LHON, Leber hereditary optic neuropathy; DOA, dominant optic atrophy; FRDA, Friedreich ataxia; MTS, Mohr-Tranebjaerg syndrome; HSP, hereditary spastic paraplegia; CPEO, chronic progressive external ophthalmoplegia; CMT2A, Charcot Marie tooth; HMSN VI, hereditary motor and sensory neuropathy; mtDNA, mitochondrial DNA; nDNA, nuclear DNA; MELAS, mitochondrial encephalopathy, lactic acidosis, stroke. *(Modified from Carelli V, La Morgia C, Valentino ML, et al. Retinal ganglion cell neurodegeneration in mitochondrial inherited disorders. Biochim et Biophysic Acta. 2009;1787:518–528: Fig. 2).*

Table 671.1 Genetic and Clinical Features of Primary Hereditary Optic Atrophies and Their Respective Genes

	OPA1	*LHON*	*OPA3*	*TMEM126A*	*WFS1*
Inheritance	Autosomal dominant	Maternal	Autosomal dominant	Autosomal recessive	Autosomal dominant
Age of onset	Childhood	Young adult, male > female	Late childhood	Childhood	Childhood to adult
Ophthalmologic features	Slowly progressive, tritanomaly	Sudden visual loss. Frequently beginning unilateral	Often additional cataract	Early manifestation and progression	Highly variable
Loss of visual acuity	Moderate to severe	Pronounced visual impairment	Moderate	Severe visual loss	Variable
Possible extraocular signs	~20% of patients have neurologic symptoms (e.g., ataxia, neuropathy)	Mild neurologic symptoms possible; multiple sclerosis–like symptoms	Late in life; mild neurologic signs possible late in life	Subclinical hearing impairment	Hearing impairment, disturbed glucose tolerance, behavioral abnormalities

LHON, Leber hereditary optic neuropathy (*mt-ND1, mt-ND4, mt-ND46, mt-ND6*); OPA1, optic atrophy type 1; OPA3, optic atrophy type 3; TMEM126A, optic atrophy type 7; WFS1, Wolfram syndrome (diabetes mellitus, diabetes insipidus, optic neuropathy, deafness).
Modified from Neuhann T, Rautenstrauss B. Genetic and phenotypic variability of optic neuropathies. *Expert Rev Neurother.* 2013;13(4):357–367.

Table 671.2 Causes of Acquired Optic Neuropathies

TOXINS	MEDICATIONS	NUTRITIONAL DEFICIENCIES
Methanol	Ethambutol	Thiamine (Vitamin B_1)
Ethanol	Isoniazid	Riboflavin (Vitamin B_2)
Tobacco	Chloramphenicol	Pyridoxine (Vitamin B_6)
Arsenics	Linezolid	Folic Acid (Vitamin B_9)
Cobalt	Erythromycin	Cobalamin (Vitamin B_{12})
Thallium	Streptomycin	
Carbon disulfide	Ciprofloxacin	
Tetrachloride	Dapsone	
Cyanide	Antiretrovirals	
Ethylene glycol	Amiodarone	
Toluene	Infliximab	
Styrene	Clioquinol	
Perchloroethylene	Pheniprazine	
	Suramin	
	Quinine	

From Pilz YL, Bass SJ, Sherman J. A review of mitochondrial optic neuropathies: From inherited to acquired forms. *J Optometry.* 2016;10:205–214: Table 2.

a very early age; the visual defect is usually profound. **Behr optic atrophy** is a hereditary type associated with hypertonia of the extremities, increased deep tendon reflexes, mild cerebellar ataxia, some degree of mental deficiency, and possibly external ophthalmoplegia. This disorder principally afflicts boys 3-11 years of age. Some forms of heredodegenerative optic atrophy are associated with sensorineural hearing loss, as may occur in some children with juvenile-onset (insulin-dependent) diabetes mellitus. In the absence of an obvious cause, optic atrophy in an infant or child warrants extensive etiologic investigation.

OPTIC NERVE GLIOMA

Optic nerve glioma, more properly referred to as **juvenile pilocytic astrocytoma,** is the most frequent tumor of the optic nerve in childhood (Fig. 671.7). This neuroglial tumor may develop in the intraorbital, intracanalicular, or intracranial portion of the nerve; the chiasm is often involved.

The tumor is a cytologically benign hamartoma that is generally stationary or only slowly progressive. The principal *clinical manifestations* when the tumor occurs in the intraorbital portion of the nerve are unilateral loss of vision, proptosis, and deviation of the eye; optic atrophy or congestion of the optic nerve head may occur. Chiasmal involvement may be attended by defects of vision and visual fields (often bitemporal hemianopia), increased ICP, papilledema or optic atrophy, hypothalamic dysfunction, pituitary dysfunction, and sometimes nystagmus or strabismus. Juvenile pilocytic astrocytomas occur with increased frequency in patients with neurofibromatosis (see Chapter 636.1).

Treatment of optic pathway gliomas is controversial. The best management is usually periodic observation with serial radiography

Table 671.3 Causes of Childhood Optic Atrophy

Compressive intracranial lesions
Compressive bony disorders
Craniosynostosis
Fibrous dysplasia
Hydrocephalus
Postpapilledema optic atrophy
Infectious
Hereditary
Leber hereditary optic neuropathy
Dominant optic atrophy (Kjer)
Recessive optic atrophy
Behr optic atrophy
DIDMOAD (diabetes insipidus, diabetes mellitus, optic atrophy, deafness) (Wolfram) optic atrophy
Toxic or nutritional optic neuropathy
Hypoxia
Trauma
Postoptic neuritis
Radiation optic neuropathy
Paraneoplastic syndromes
Neurodegenerative disorders with optic atrophy
Krabbe disease
Canavan disease
Leigh disease
Mitochondrial encephalomyopathy, lactic acidosis, and strokelike (MELAS) episodes
Neonatal adrenoleukodystrophy
Metachromic leukodystrophy
Riley-Day syndrome
Lactic acidosis
Spinocerebellar degeneration
Mucopolysaccharidosis
Ocular disorders
Glaucoma
Retinal disease
Vascular disease
Uveitis
Optic nerve hypoplasia

From Martin RJ, Fanaroff AA, Walsh MC, eds. *Fanaroff & Martin's Neonatal-Perinatal Medicine.* 10th ed. Philadelphia: Elsevier; 2015. Box 103.5.

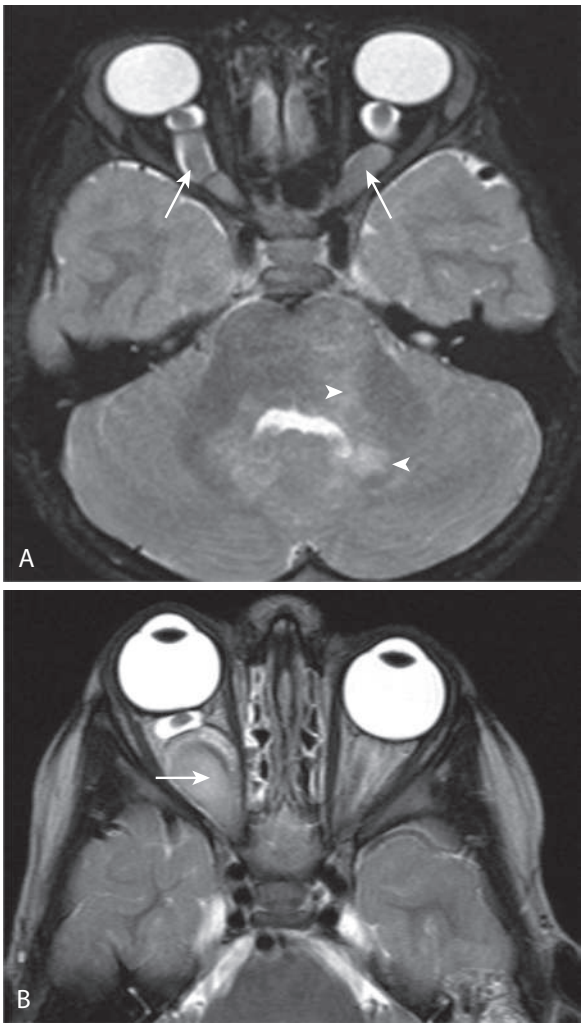

Fig. 671.7 Optic nerve glioma (ONG). **A,** ONG in a patient with neurofibromatosis NF1. Axial fat-saturated T2-weighted MR image of the orbits demonstrates bilaterally symmetrically enlarged and tortuous intracanalicular portions of the optic nerves associated *(arrows).* Areas of signal abnormality within the cerebellar white matter indicate spongiform changes of NF1 *(arrowheads).* **B,** Isolated right ONG. Axial T2-weighted MR image of the orbits demonstrates an ONG *(arrow)* with similar expansion and tortuosity of the optic nerve to the case in **A** but with unilateral involvement of the right optic nerve and without additional imaging findings of NF1. *(From Coley BD [ed]. Caffey's Pediatric Diagnostic Imaging, 13th ed. Philadelphia: Elsevier, 2019: Fig. 7.8, p. 48.)*

(preferably MRI). Only symptomatic and radiographically progressing optic nerve gliomas require strong consideration for treatment. If a patient has unsightly proptosis with complete or nearly complete loss of vision of the affected eye, surgical removal may be appropriate when the tumor is confined to the intraorbital, intracanalicular, or prechiasmal portion of the nerve. When the chiasm is involved, resection is not usually indicated, and radiation and chemotherapy may be necessary.

TRAUMATIC OPTIC NEUROPATHIES

Injury to the optic nerve may result from both direct and indirect trauma. Direct trauma to the optic nerve is a result of a penetrating injury to the orbit with transection or contusion of the nerve. Blunt trauma to the orbit may also lead to severe visual loss if the traumatic force is transmitted to the optic canal and causes disruption of the blood supply to the intracanalicular portion of the nerve. Treatment with high-dose corticosteroids has not proved to be effective; it has been shown that similar regimens involve an increased relative risk of death when they are given to patients who have experienced significant head injuries.

Visit Elsevier eBooks+ at eBooks.Health.Elsevier.com for Bibliography.

Chapter 672

Childhood Glaucoma

Scott E. Olitsky and Justin D. Marsh

Glaucoma is a general term used to indicate damage to the optic nerve with visual field loss that is caused by or related to elevated pressure within the eye. It is classified according to the age of the affected individual at presentation and the association of other ocular or systemic conditions. Glaucoma that begins within the first 5 years of life is called

Table 672.1 Primary and Secondary Childhood Glaucomas

I. PRIMARY GLAUCOMAS
A. Congenital open-angle glaucoma
  1. Congenital
  2. Infantile
  3. Late recognized
B. Autosomal dominant juvenile glaucoma
C. Primary angle-closure glaucoma
D. Associated with systemic abnormalities
  1. Sturge-Weber syndrome
  2. Neurofibromatosis type I (NF-1)
  3. Stickler syndrome
  4. Oculocerebrorenal (Lowe) syndrome
  5. Rieger syndrome
  6. Hepatocerebrorenal syndrome
  7. Marfan syndrome
  8. Rubinstein-Taybi syndrome
  9. Infantile glaucoma associated with cognitive disability and paralysis
  10. Oculodentodigital dysplasia
  11. Open-angle glaucoma associated with microcornea and absence of frontal sinuses
  12. Mucopolysaccharidosis
  13. Trisomy 13
  14. Cutis marmorata telangiectasia congenita
  15. Warburg syndrome
  16. Kniest syndrome (skeletal dysplasia)
  17. Michel syndrome
  18. Nonprogressive hemiatrophy
E. Associated with ocular abnormalities
  1. Congenital glaucoma with iris and pupillary abnormalities
  2. Aniridia
    a. Congenital glaucoma
    b. Acquired glaucoma
  3. Congenital ocular melanosis
  4. Sclerocornea
  5. Iridotrabecular dysgenesis
  6. Peters syndrome
  7. Iridotrabecular dysgenesis and ectropion uveae
  8. Posterior polymorphous dystrophy
  9. Idiopathic or familial elevated episcleral venous pressure
  10. Anterior corneal staphyloma
  11. Congenital microcornea with myopia
  12. Congenital hereditary endothelial dystrophy
  13. Congenital hereditary iris stromal hypoplasia

II. SECONDARY GLAUCOMAS
A. Traumatic glaucoma
  1. Acute glaucoma
    a. Angle concussion
    b. Hyphema
    c. Ghost cell glaucoma
  2. Late-onset glaucoma with angle recession
  3. Arteriovenous fistula
B. Secondary to intraocular neoplasm
  1. Retinoblastoma
  2. Juvenile xanthogranuloma
  3. Leukemia
  4. Melanoma
  5. Melanocytoma
  6. Iris rhabdomyosarcoma
  7. Aggressive nevi of the iris
C. Secondary to uveitis
  1. Open-angle glaucoma
  2. Angle-blockage glaucoma
    a. Synechial angle closure
    b. Iris bombé with pupillary block
D. Lens-induced glaucoma
  1. Subluxation-dislocation and pupillary block
    a. Marfan syndrome
    b. Homocystinuria
  2. Spherophakia and pupillary block
  3. Phacolytic glaucoma
E. Secondary to surgery for congenital cataract
  1. Lens material blockage of the trabecular meshwork (acute or subacute)
  2. Pupillary block
  3. Chronic open-angle glaucoma associated with angle defects
F. Steroid-induced glaucoma
G. Secondary to rubeosis
  1. Retinoblastoma
  2. Coats disease
  3. Medulloepithelioma
  4. Familial exudative vitreoretinopathy
H. Secondary angle-closure glaucoma
  1. Retinopathy of prematurity
  2. Microphthalmos
  3. Nanophthalmos
  4. Retinoblastoma
  5. Persistent hyperplastic primary vitreous
  6. Congenital pupillary iris-lens membrane
I. Glaucoma associated with increased venous pressure
  1. Carotid or dural-venous fistula
  2. Orbital disease
J. Secondary to maternal rubella
K. Secondary to intraocular infection
  1. Acute recurrent toxoplasmosis
  2. Acute herpetic iritis

From Nelson LB. *Harley's Pediatric Ophthalmology*. 4th ed. Philadelphia: Saunders; 1998: p. 294.

infantile (congenital); that which begins between the ages of 5 and 30 years is called juvenile.

Primary glaucoma indicates that the cause is an isolated anomaly of the drainage apparatus of the eye (trabecular meshwork). More than 50% of infantile cases are primary glaucoma. In secondary glaucoma, other ocular or systemic abnormalities are associated, even if a similar developmental defect of the trabecular meshwork is also present. Primary infantile glaucoma occurs with an incidence of 0.03% (Table 672.1).

CLINICAL MANIFESTATIONS

The symptoms of infantile glaucoma include the classic triad of epiphora (tearing), photophobia (sensitivity to light), and blepharospasm (eyelid squeezing; Fig. 672.1). Each can be attributed to corneal irritation. Only approximately 30% of affected infants demonstrate the classic symptom complex. Signs of glaucoma include corneal edema, corneal and ocular enlargement, and conjunctival injection (Fig. 672.2).

The sclera and cornea are more elastic in early childhood than later in life. An increase in intraocular pressure (IOP) therefore leads to an expansion of the globe, including the cornea, and the development of buphthalmos ("ox eye"). If the cornea continues to enlarge, breaks occur in the endothelial basement membrane (Descemet's membrane) and may lead to permanent corneal scarring. These breaks in Descemet's membrane (Haab striae) are visible as horizontal edematous lines that cross or curve around the central cornea. They rarely occur beyond 3 years of age or in corneas <12 mm in diameter. The cornea also becomes edematous and cloudy, with increased IOP. The corneal edema leads to tearing and photophobia. If any of these other signs or symptoms are present, glaucoma should be considered in a child suspected of having a nasolacrimal duct obstruction.

Children with unilateral glaucoma generally present early because the difference in the corneal size between the eyes can be noticed. When the disease is bilateral, parents may not recognize the increased corneal size.

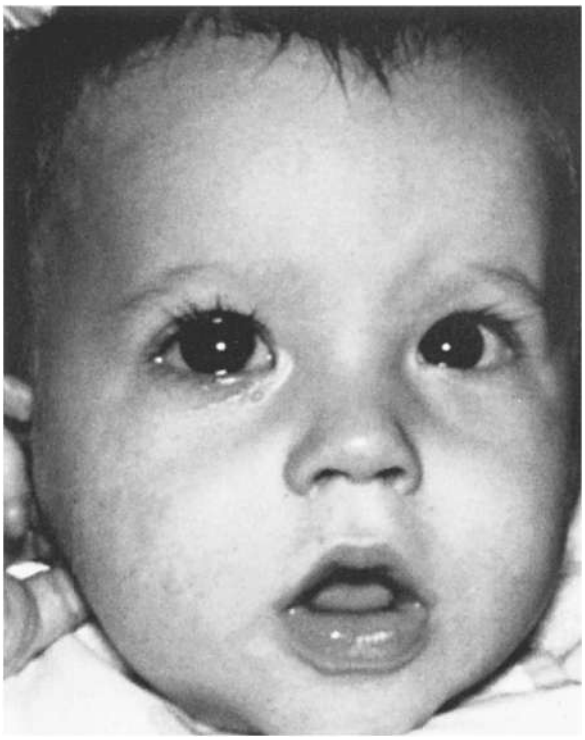

Fig. 672.1 Tearing of the right eye caused by glaucoma. Note the increased corneal diameter of the right eye. *(From Nelson LB. Harley's Pediatric Ophthalmology. 4th ed. Philadelphia: WB; 1998; p. 285.)*

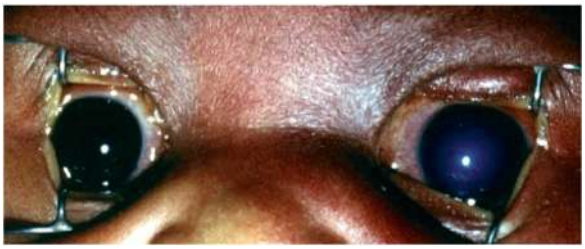

Fig. 672.2 Infantile glaucoma. The left cornea is enlarged and edematous.

Many parents view the large eyes as attractive and do not seek help until other symptoms develop.

Cupping of the optic nerve head is detected by ocular examination. The optic nerve of an infant is easily distended by excessive pressure. Deep central cupping readily occurs and may regress with normalization of pressure.

Some infants and children with early-onset glaucoma have more extensive maldevelopment of the anterior segment of the eye. The neurocristopathies, particularly those involving the anterior segment (Axenfeld-Rieger syndrome: *FOXC1, PITX2, CYP1B1, PRDM5* genes), produce early-onset glaucoma. They are usually bilateral and may include abnormalities of the iris, cornea, and lens. Other ocular anomalies that may be associated with glaucoma in infants and children are aniridia, cataract, spherophakia, and ectopia lentis. Glaucoma may also develop secondary to persistent hyperplastic primary vitreous or retinopathy of prematurity.

Trauma, intraocular hemorrhage, ocular inflammatory disease, and intraocular tumor are also important causes of glaucoma in the pediatric population. Systemic disorders associated with glaucoma in infants and children are Sturge-Weber syndrome (see Chapter 636.3), neurofibromatosis (see Chapter 636.1), Lowe syndrome, Marfan syndrome (see Chapter 743), congenital rubella (see Chapters 149 and 294), and a number of chromosomal syndromes (see Chapter 99).

Table 672.2 Differential Diagnosis of Primary Congenital Glaucoma

I. OTHER GLAUCOMAS
- A. Glaucoma associated with congenital anomalies
- B. Secondary glaucoma

II. OTHER CAUSES OF CORNEAL ENLARGEMENT OR CLOUDING
- A. Megalocornea
- B. Sclerocornea
- C. High myopia
- D. Metabolic diseases
  1. Cystinosis
  2. Mucopolysaccharidoses
     - a. MPS I H = Hurler's syndrome
     - b. MPS I S = Scheie's syndrome
     - c. MPS II = Hunter's syndrome
     - d. MPS IV = Morquio's syndrome
     - e. MPS VI = Maroteaux-Lamy syndrome
     - f. MPS VII = b-Glucuronidase deficiency
  3. Hand-Schüller-Christian disease (histiocytosis)
  4. Acrodermatitis enteropathica
  5. Peroxisomal disorders
  6. Zellweger syndrome
- E. Posterior polymorphous dystrophy
- F. Congenital hereditary endothelial dystrophy
- G. Obstetric trauma
- H. Inflammation (keratitis, iridocyclitis)

III. OTHER CAUSES OF EPIPHORA OR PHOTOPHOBIA
- A. Nasolacrimal duct obstruction
- B. Conjunctivitis
- C. Corneal abrasion
- D. Meesmann's corneal dystrophy
- E. Reis-Buckler's dystrophy

IV. OTHER CAUSES OF OPTIC NERVE ABNORMALITIES
- A. Pit
- B. Coloboma
- C. Hypoplasia
- D. Tilted disc
- E. Large physiologic cup

From Stamper RL, Lieberman MF, Drake MV, eds. *Becker-Shaffer's Diagnosis and Therapy of the Glaucomas.* 8th ed. Philadelphia: Mosby, 2009: Box 19.3, p. 307.

Glaucoma occurs frequently in children with a history of congenital cataracts. Glaucoma may develop in up to 25% of children who have undergone cataract surgery early in life. The cause of aphakic glaucoma is not known but is thought to be the result of a coexistent anterior chamber deformity. Children treated for cataracts must be monitored closely for this complication, which may threaten vision.

DIAGNOSIS AND TREATMENT

The diagnosis of infantile glaucoma is made on recognition of the signs and symptoms. Once the diagnosis is established, treatment is started promptly. Unlike adult glaucoma, in which medication is often the first line of therapy, for infantile glaucoma the treatment is primarily surgical. The differential diagnosis is noted in Table 672.2.

Procedures used to treat glaucoma in children include surgery to establish a more normal anterior chamber angle (goniotomy and trabeculotomy), to create a site for aqueous fluid to exit the eye (trabeculectomy and Seton surgery), or to reduce aqueous fluid production (cyclocryotherapy and cyclophotocoagulation). Many children frequently require several operations to lower and maintain their IOP adequately, and long-term medical therapy may be necessary as well. Patients with multiple ocular abnormalities and those with aphakic glaucoma generally require more surgeries to achieve and maintain adequate IOP control. Although vision may be reduced secondary to glaucomatous optic nerve damage or corneal scarring, amblyopia is the most common cause of loss of vision in these children.

Visit Elsevier eBooks+ at eBooks.Health.Elsevier.com for Bibliography.

Chapter 673

Orbital Abnormalities

Scott E. Olitsky and Justin D. Marsh

HYPERTELORISM AND HYPOTELORISM

Hypertelorism is wide separation of the eyes or an increased interorbital distance, which may occur as a morphogenetic variant, a primary deformity, or a secondary phenomenon in association with developmental abnormalities, such as frontal meningocele or encephalocele or the persistence of a facial cleft. Often-associated conditions are strabismus, exotropia, and sometimes optic atrophy.

Hypotelorism refers to narrowness of the interorbital distance, which may occur as a morphogenetic variant alone or in association with other anomalies, such as epicanthus or holoprosencephaly, or secondary to a cranial dystrophy, such as scaphocephaly.

EXOPHTHALMOS AND ENOPHTHALMOS

Protrusion of the eye is referred to as *exophthalmos* or *proptosis* and is a common indicator of orbital disease. It may be caused by shallowness of the orbits, as in many craniofacial malformations, or by increased tissue mass within the orbit, as with neoplastic, vascular, and inflammatory disorders. Ocular complications include exposure keratopathy, ocular motor disturbances, and optic atrophy with loss of vision.

Posterior displacement or sinking of the eye back into the orbit is referred to as *enophthalmos*. This may occur with orbital fracture or with atrophy of orbital tissue.

ORBITAL INFLAMMATION

Nonspecific Orbital Inflammation/Idiopathic Orbital Inflammation/Orbital Pseudotumor

Nonspecific orbital inflammation (NSOI) is an acute or subacute, usually benign, idiopathic inflammatory process of unknown etiology manifesting in specific orbital structures but usually with no systemic features. After thyroid-associated disease and lymphoproliferative disorders, it is the third most common noninfectious masslike inflammatory lesion of the orbit. It is unilateral in ~80% of patients, who often present with periorbital edema, ptosis, limited extraocular motion, pain, proptosis, conjunctival injection, chemosis or, less often, decreased visual acuity. There are five categories involving specific orbit tissues: dacryoadenitis (Fig. 673.1A), myositis (see Fig. 673.1B), anterior orbit (see Fig. 673.1C), posterior orbit apex (optic nerve; Fig. 673.2), and diffuse. Lacrimal gland inflammation and orbital myositis are the most common manifestations. The apical (**orbital apex syndrome**) often affects visual acuity and cranial nerves III, IV, and VI, as well as the first division of CN V. There is an association with a sclerosing IgG4-related disease variant, which may also manifest with inflammation and fibrosis in extraorbital tissue (pancreas, retroperitoneal); systemic IgG4-related disease is more common in patients with bilateral lacrimal gland involvement.

The differential diagnosis of NSOI includes sarcoidosis, granulomatosis with polyangiitis, lymphoma, and thyroid orbitopathy (Fig. 673.3). In addition, **Tolosa Hunt syndrome** may mimic NSOI; manifestations include unilateral headache, brow and eye pain, and cranial nerve palsies with associated cavernous sinus granulomatosis (Fig. 673.4). Biopsy is not initially needed for patients with NSOI who have a typical presentation (usually myositis) or a higher biopsy risk (orbital apex-optic nerve). Therapy is usually initiated with systemic corticosteroids.

Thyroid-related ophthalmopathy (see Chapter 601) is believed to be secondary to an immune mechanism, leading to inflammation and deposition of mucopolysaccharides and collagen in the extraocular muscles and orbital fat. Involvement of the extraocular muscles may lead to a restrictive strabismus. Lid retraction and exophthalmos may cause corneal exposure and infection or perforation. Involvement of the posterior orbit can compress the optic nerve. Treatment of thyroid-related ophthalmopathy may include the use of systemic corticosteroids, radiation of the orbit, eyelid surgery, strabismus surgery, or orbital decompression to eliminate symptoms and protect vision. The degree of orbital involvement is often independent of the status of the systemic disease.

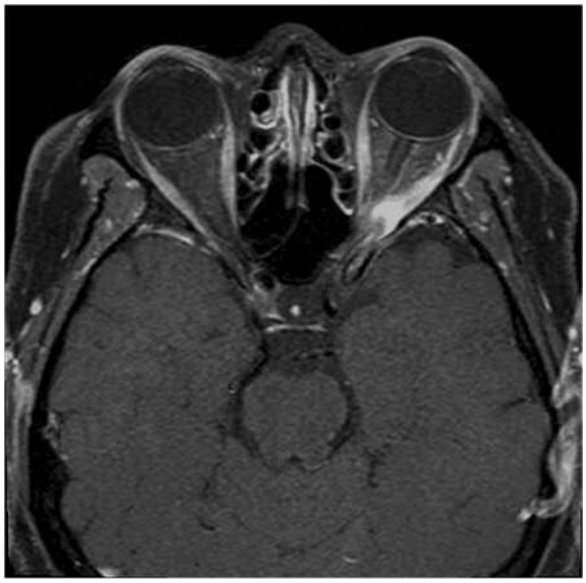

Fig. 673.2 Nonspecific orbital inflammation involving the orbital apex. Contrast-enhanced T1-weighted axial MRI with fat suppression showing inflammatory tissue at the left orbital apex resulting in compression and obliteration of the optic nerve. *(From Maamari RN, Couch SM. Nonspecific orbital inflammation. Adv Ophthalmol Optom. 2018;3:315–335: Fig. 7.)*

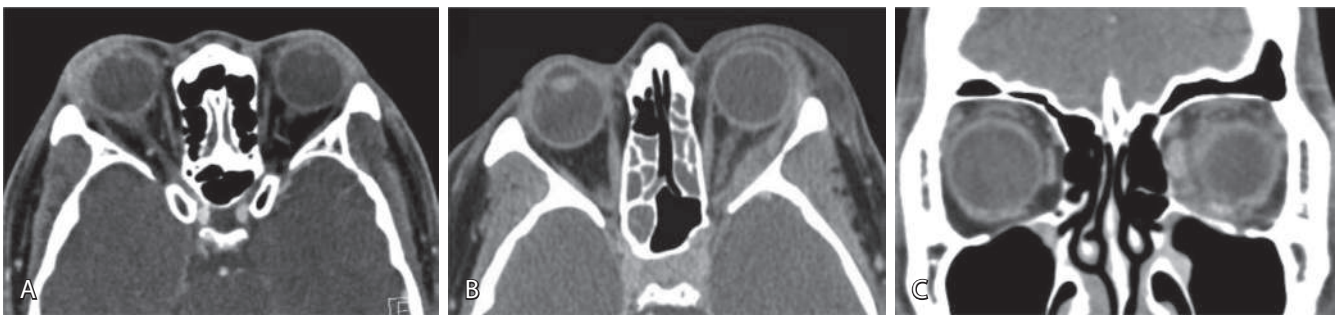

Fig. 673.1 Anatomic localization of nonspecific orbital inflammation. **A,** Lacrimal gland (right eye). **B,** Extraocular muscle (left lateral rectus). **C,** Orbital fat (left inferomedial extraconal space). *(From Lee MJ, Planck SR, Choi D, et al. Non-specific orbital inflammation: current understanding and unmet needs. Prog Retinal Eye Res. 2021;81:100885: Fig. 5).*

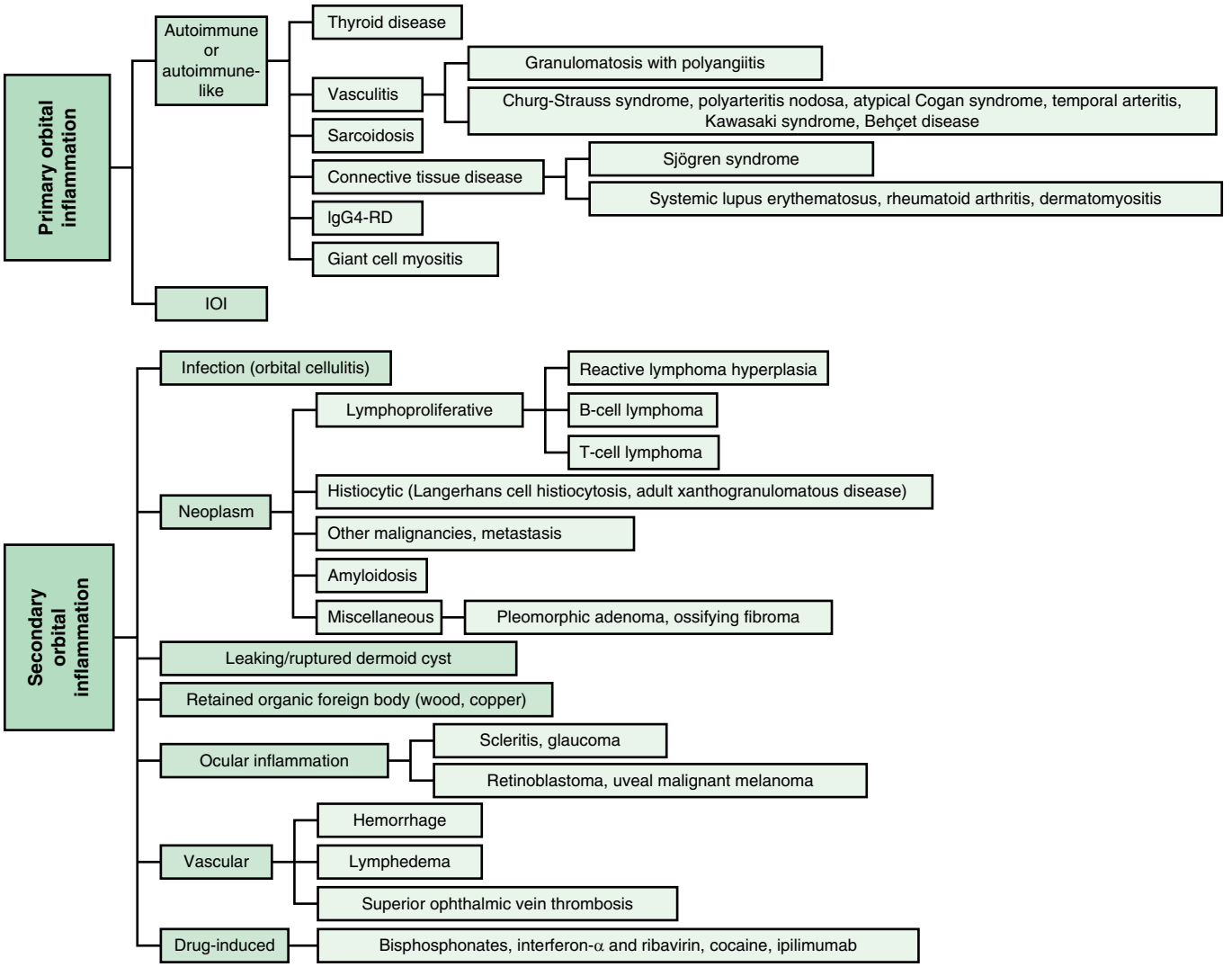

Fig. 673.3 Classification for possible causes of orbital inflammation. NSOI, nonspecific orbital inflammation. *(From Mombaerts I, Rose GE, Garrity JA. Orbital inflammation: biopsy first. Surv Ophthalmol. 2016;61:664–669: Table 1.)*

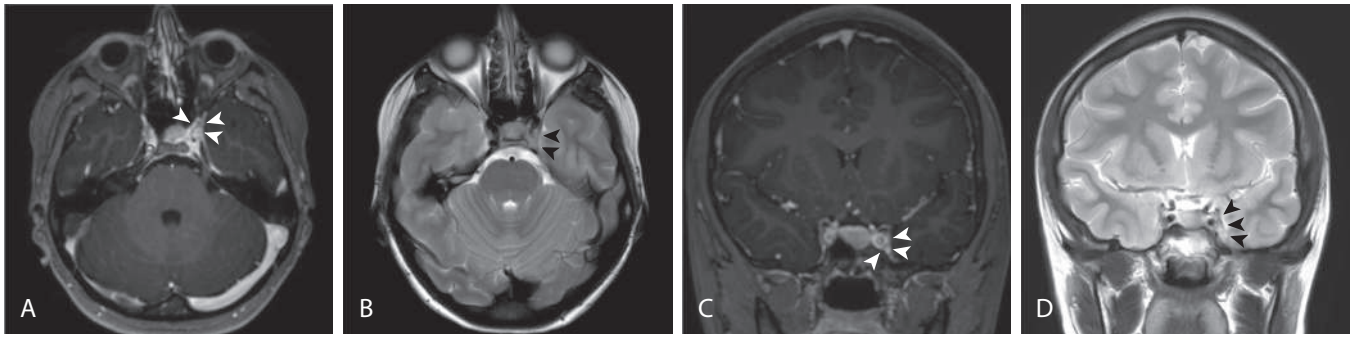

Fig. 673.4 MR scan of the brain showing an enhancing space-occupying lesion within the left cavernous sinus *(arrowheads)*. Postgadolinium T1-weighted (**A**) and T2-weighted (**B**) axial views. Postgadolinium T1-weighted (**C**) and T2-weighted (**D**) coronal views. *(From Pérez CA, Evangelista M. Evaluation and management of Tolosa-Hunt syndrome in children: a clinical update. Pediatr Neurol. 2016;62:18–26: Fig. 2.)*

Other systemic disorders that may cause inflammatory disease within the orbit include lymphoma (see Chapter 545), sarcoidosis (see Chapter 209), amyloidosis (see Chapter 206), polyarteritis nodosa (see Chapter 210.3), systemic lupus erythematosus (see Chapter 199), dermatomyositis (see Chapter 200), granulomatosis with polyangiitis (see Chapter 210), and juvenile xanthogranuloma (see Chapter 556).

TUMORS OF THE ORBIT

Various tumors occur in and about the orbit in childhood. Among benign tumors, the most common are vascular lesions (principally hemangiomas; Fig. 673.5) and dermoids. Among malignant neoplasms, rhabdomyosarcoma, lymphosarcoma, and metastatic neuroblastoma are the most frequent. Optic nerve gliomas (see Chapter 671)

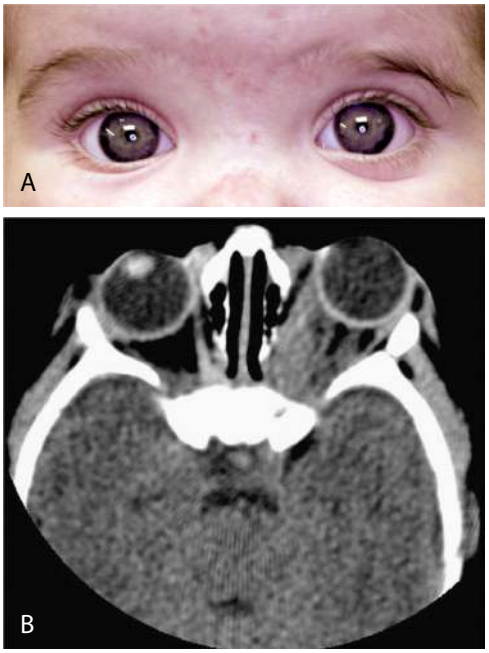

Fig. 673.5 Orbital hemangioma. **A**, Note the proptosis. **B**, CT scan. *(Courtesy Amy Nopper, MD, and Brandon Newell, MD.)*

are most commonly seen in patients with neurofibromatosis and may present with poor vision or proptosis. Retinoblastoma (see Chapter 551) may extend into the orbit if it is discovered late or goes untreated. Teratomas are rare tumors that typically grow rapidly after birth and exhibit explosive proptosis.

The effects of orbital tumors vary with their locations and growth patterns. The principal signs are proptosis, resistance to retroplacement of the eye, and impairment of eye movement. A palpable mass may be found. Other significant signs are ptosis, optic nerve head congestion, optic atrophy, and loss of vision. Bruit and visible pulsation of the globe are important clues to vascular lesions.

Evaluation of orbital tumors includes ultrasonography, MRI, and CT. Pseudotumor of the orbit also must be considered in children with signs of a mass lesion. In selected cases, an incisional or excisional biopsy of the lesion may be warranted.

Visit Elsevier eBooks+ at eBooks.Health.Elsevier.com for Bibliography.

Chapter 674

Orbital Infections

Scott E. Olitsky, Justin D. Marsh, and Mary Anne Jackson

Orbital infections are common in children. It is important to be able to distinguish the different forms of infection that occur in the orbital region to allow rapid diagnosis and treatment to prevent loss of vision or spread of the infection to the nearby intracranial structures (Table 674.1).

DACRYOADENITIS

Dacryoadenitis is inflammation of the lacrimal gland; it most commonly occurs in the pediatric population and in some young adults and is related to a variety of infectious pathogens or inflammatory processes (see Chapter 673). Pain, redness, swelling, increase in tearing, and discharge over the lacrimal gland are noted and usually visible at the lateral one third of the upper eyelid; concurrent preauricular lymphadenopathy may be noted (Fig. 674.1). It may occur with mumps (in which case it is usually acute and bilateral, subsiding in a few days or weeks), with influenza, infectious mononucleosis, and herpes zoster. *Staphylococcus aureus* may produce a suppurative dacryoadenitis, and other bacterial causes include streptococci and *Neisseria gonorrhoeae*. Chronic dacryoadenitis is associated with certain systemic diseases, particularly sarcoidosis, tuberculosis, and syphilis. Some systemic diseases may produce enlargement of the lacrimal and salivary glands (Mikulicz syndrome).

DACRYOCYSTITIS

Dacryocystitis is an infection of the lacrimal sac and generally requires obstruction of the nasolacrimal system to allow its development. Acute, subacute, and chronic forms are described. Most patients with dacryocystitis present with redness and swelling over the region of the lacrimal sac (Fig. 674.2). It is treated with warm compresses and systemic antibiotics. This helps control the infection, but the obstruction usually requires definitive treatment to reduce the risk of recurrence.

Dacryocystitis may occur in newborns as a complication of a congenital dacryocystocele (see Chapter 665). If present, systemic antibiotics and digital pressure for decompression are recommended. The obstruction of the nasolacrimal system may resolve once the infection clears. If spontaneous resolution does not occur, probing should be considered within a short time frame. An intranasal cyst may be present in conjunction with the dacryocystocele. If this occurs, marsupialization of the cyst may be needed at the time of the probing.

PRESEPTAL CELLULITIS

Inflammation of the lids and periorbital tissues without signs of true orbital involvement (such as proptosis or limitation of eye movement) is generally referred to as *periorbital* or *preseptal cellulitis* and is a form of facial cellulitis. This is a common entity in young children, usually under age 5 years, and may rarely be caused by direct seeding related to bacteremia (usually seen in those <3 years), or more often sinusitis,

Table 674.1 Manifestations of Orbital Cellulitis Associated with Ethmoid Sinusitis

MANIFESTATIONS	CLINICAL AND CT IMAGING DESCRIPTION
1: Inflammatory edema	Eyelid edema and erythema; eye may be swollen shut Fever Painless extraocular muscle movement; full range of motion Visual acuity normal Edema of orbit without abscess formation
2: Orbital cellulitis	Inflammation of orbital contents without discrete abscess formation Fever, malaise
3: Subperiosteal abscess	Purulent exudate beneath medial orbital periosteum of lamina papyracea Pain on extraocular muscle movement Fever, malaise, may have pain with extraocular muscle movement Displacement of globe (down and out)
4: Orbital abscess/ orbital apex syndrome	Purulent collection within orbit Proptosis, chemosis Ophthalmoplegia; pain on extraocular muscle movement Decreased vision Fever, malaise
5: Septic cavernous sinus thrombophlebitis	Bilateral (contralateral) eye findings; ptosis, proptosis, swelling, ophthalmoplegia Severe headaches Meningismus, fever, severe malaise Decreased vision

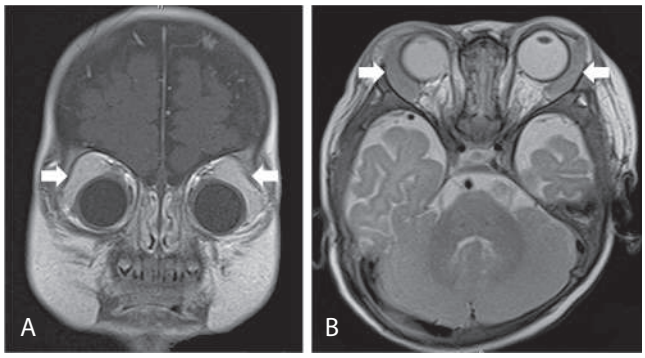

Fig. 674.1 MRI of the bilateral lacrimal glands. **A,** Coronal T1-weighted image. **B,** Axial T2-weighted image. The bilateral lacrimal glands are markedly enlarged *(arrows)*. *(From Hoshino A, Fujii T, Hibino S, Abe Y. Acute infantile dacryoadenitis. J Pediatr. 2014;164:425: Fig. 2))*

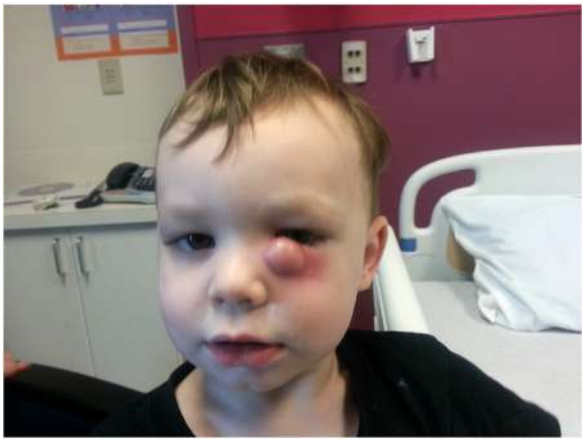

Fig. 674.2 Dacrycystitis in a child previously treated for nasolacrimal duct obstruction.

trauma, or other infected wounds in the periorbital region, or an abscess of the lid or periorbital region (pyoderma, hordeolum, conjunctivitis, dacryocystitis, insect bite). Brown recluse spider bites are often associated with considerable local swelling, and in the first 24 hours, the bite itself may not be obvious to the parent or the examiner.

Patients present with eyelid swelling; the edema may be so intense as to make it difficult to evaluate the globe. Before the *Haemophilus influenzae* type B (Hib) vaccine, the most common cause of pediatric preseptal (facial) cellulitis was bacteremia caused by Hib. Group A streptococcus (GAS), pneumococcus, and *S. aureus* (especially if related to an infected wound or bite) are the most common identifiable etiologic agents. Occasionally, young children with herpes simplex virus infection of the periorbital tissues will present first with swelling and redness, followed by the appearance of discrete tiny ulcers.

Clinical examination will show **lack of** proptosis, with normal painless ocular movements, normal vision, and normal pupil responses. CT imaging can demonstrate edema of the lids and subcutaneous tissues anterior to the orbital septum (Fig. 674.3); imaging is not necessary in those without signs of an orbital process. Antibiotic therapy and careful clinical monitoring and evaluation to identify signs of local progression are essential. In well-appearing children with infected traumatic wounds or insect bites associated with periorbital cellulitis, oral antibiotics that target *S. aureus* and GAS may be considered. For young children in whom a hematogenous process is suspected, or in any toxic, ill-appearing child, blood cultures should be obtained, and hospitalization and intravenous antibiotics are required. Most recommend intravenous ampicillin with sulbactam or intravenous clindamycin plus cefotaxime (or ceftriaxone) for hospitalized patients.

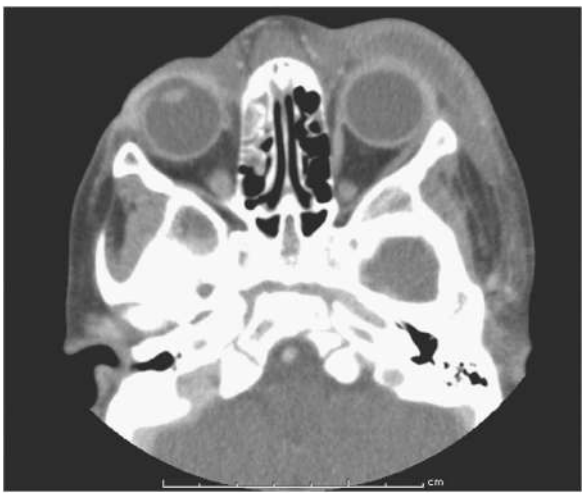

Fig. 674.3 CT scan of a patient with preseptal cellulitis.

Periorbital necrotizing fasciitis is a severe, rapidly spreading form of periorbital bacterial infection, involving both superficial and deep fascial planes. The disease may have no preceding events or may follow trauma to the periorbital skin. Initial symptoms resemble periorbital/facial cellulitis but rapidly progress to tissue necrosis, blistering, and significant systemic toxicity. Streptococci and *S. aureus* are the most common pathogens. Treatment includes broad spectrum antibiotics, surgical debridement, and, when available, hyperbaric oxygen therapy.

ORBITAL CELLULITIS

Inflammation of the tissues of the orbit, characterized by the triad of proptosis, painful limitation of movement of the eye (ophthalmoplegia), and potentially decreased visual acuity, is termed *orbital cellulitis* (see Table 674.1). Edema of the conjunctiva (chemosis) and inflammation and swelling of the eyelids may be seen. The mean age is ~7 years, ranges from 1 week to 18 years, and has a 2:1 predilection in males. An increased risk is seen in the winter because complicated obligatory sinusitis often follows respiratory viral infection (e.g., influenza). Patients often feel ill, are febrile, and appear toxic, and leukocytosis sometimes but not always may be appreciated. Practitioners should have an increased clinical suspicion for intracranial extension in those with headache, vomiting, and any focal neurologic findings.

Orbital cellulitis may follow direct infection of the orbit from a wound, hematogenous seeding of organisms during bacteremia, or *more often* direct extension or venous spread of infection from contiguous sites such as the lids, conjunctiva, globe, lacrimal gland, nasolacrimal sac, or *more commonly* from the paranasal (ethmoid) sinuses. The **differential diagnosis** includes idiopathic orbital inflammation, myositis, sarcoidosis, granulomatous vasculitis, leukemia, lymphoma, histiocytic disorders, rhabdomyosarcoma, ruptured dermoid cyst, orbital trauma, and orbital foreign body (see Chapter 673). In some cases, primary or metastatic tumor in the orbit can produce the clinical picture of orbital cellulitis.

Although the most common cause of orbital cellulitis in children is direct extension or venous spread from infected paranasal sinuses, an antecedent history of sinusitis requiring antibiotic therapy is generally not reported. The spread of infection to the orbit from the sinuses is more prevalent in children because of their thinner bony septa and sinus wall, greater porosity of bones, open suture lines, and larger vascular foramina (Fig. 674.4). The spread of infection is also facilitated by the venous and lymphatic communication between the sinuses and surrounding structures, which allow flow in either direction, facilitating retrograde thrombophlebitis. Frequently noted pathogenic organisms include *S. aureus,* streptococcus species (especially *Streptococcus anginosus* also known as the *Streptococcus milleri* group, and *S. pyogenes*), *Streptococcus pneumoniae*, and anaerobes (e.g., *Bacteroides* spp., *Prevotella* spp.).

The potential for complications is high. Visual loss can occur secondary to an increase in orbital pressure that causes retinal artery or ophthalmic vein occlusion or optic neuritis. This is more likely to occur in the presence of an orbital abscess. Extension of infection from the orbit into the cranial cavity may lead to cavernous sinus thrombosis or meningitis, epidural or subdural empyema, or brain abscesses (Fig. 674.5). Additional complications include optic atrophy, exposure keratitis, and retinal or choroidal ischemia. An interdisciplinary team involving an infectious disease specialist, ophthalmologist, otolaryngologist, and, where indicated, a pediatric neurosurgeon should be involved in the care of the patient with orbital infection.

Orbital cellulitis must be recognized promptly and treated aggressively. Hospitalization and systemic antibiotic therapy are indicated. All patients with suspected orbital cellulitis should undergo contrast CT imaging of the orbit, paranasal sinuses, and adjacent cortex. Lumbar puncture should not be considered unless there is a meningitis presentation (and only after CT imaging), assuming there are no signs of elevated intracranial pressure or focal neurologic findings on examination. Parenteral antibiotics should be initiated immediately. Antimicrobial agents should begin with intravenous ampicillin with sulbactam or intravenous clindamycin plus ceftriaxone, cefepime (or cefotaxime); in cases where there is suspicion for intracranial extension, vancomycin plus cefotaxime (or ceftriaxone) plus metronidazole should be given.

If the patient does not show evidence of improvement or if there are signs of progression, sinus and abscess drainage should be considered. The presence of an orbital or unresponsive subperiosteal abscess (see Fig. 674.4) may require urgent drainage of the orbit. The clinical presentation and course of each individual patient should dictate the need and timing of abscess drainage.

Most children (especially those <9 years of age) with a medial **subperiosteal abscess** can initially be managed with intravenous antibiotics, which usually are sufficient for resolution of the subperiosteal abscess. Adjunctive use of corticosteroids is controversial but may hasten resolution. Patients should be examined frequently for signs of visual deterioration or pupillary abnormalities. Most will become afebrile within 48 hours and have examination improvement by 72 hours. If there are pupillary abnormalities, decreased vision, or failure to improve, the subperiosteal abscess should be drained.

Many recommend drainage for a subperiosteal abscess and an orbital abscess in older children. Additionally, abscesses involving the orbital roof with associated frontal sinus disease may require more frequent surgical intervention. Operative procedures should be coordinated with the otolaryngologist to allow for sinus drainage at the same time that the subperiosteal abscess is drained, and cultures should be obtained from the sinus and the abscess. Similarly, if neurosurgical intervention is required, operative coordination should occur with ophthalmology and otolaryngology.

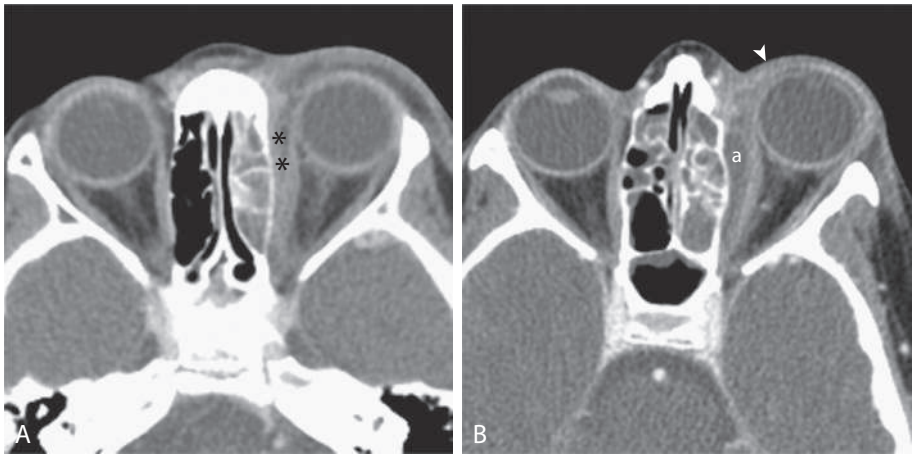

Fig. 674.4 Orbital complications of sinusitis. **A,** Orbital phlegmon and orbital cellulitis. Axial contrast-enhanced computed tomography (CECT) shows left preseptal periorbital soft tissue swelling (STS) and left ethmoid air cell opacification. There is increased density of the left medial extraconal orbital fat *(asterisks)*, consistent with phlegmon. The adjacent medial rectus muscle is thickened. There is subtle increased density of the intraconal orbital fat, consistent with orbital cellulitis. **B,** Orbital subperiosteal abscess. Axial CECT shows preseptal periorbital STS *(arrowhead)*, extensive left ethmoid air cell opacification, and an elliptical low-density, peripherally enhancing, medial subperiosteal abscess *(a)*. *(Modified from Walters MM, Robertson RL, eds. Pediatric Radiology: The Requisites, 4th ed. Philadelphia: Elsevier, 2017. Fig. 10.37, p. 377.)*

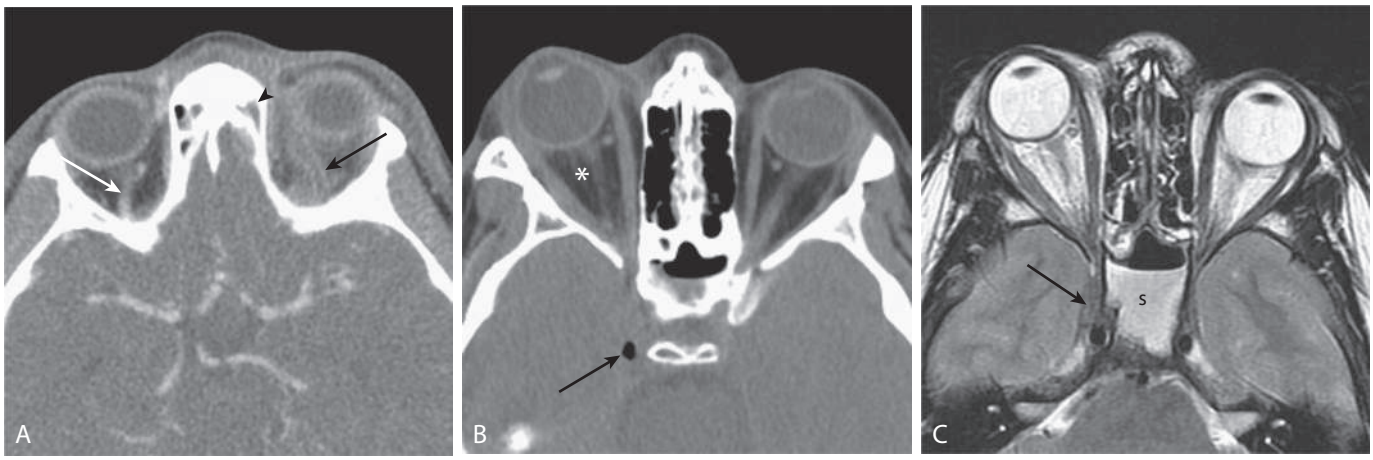

Fig. 674.5 Superior ophthalmic vein (SOV) and cavernous sinus thrombosis (CST). **A,** SOV thrombosis. Axial contrast-enhanced computed tomography (CECT) shows opacification of the partially visualized paranasal sinuses *(arrowhead)*. There is a tram-track sign due to lack of enhancement of the thrombosed left SOV *(black arrow)*. Compare with the normally enhancing right SOV *(white arrow)*. **B,** CST (new patient). Axial computed tomography image demonstrates a sphenoid sinus air–fluid level caused by sphenoid sinusitis. Gas is present within the right cavernous sinus *(arrow)* due to CST. There is resultant right ocular proptosis with minimal reticulation of the right intraconal orbital fat *(asterisk)*. **C,** Axial T2-weighted magnetic resonance (same patient) shows low signal intensity within the right cavernous sinus with lateral convexity of its lateral margin *(arrow)*, consistent with CST. Note the sphenoid sinus air–fluid level *(s)*. *(From Walters MM, Robertson RL [eds]. Pediatric Radiology: The Requisites. 4th ed. Philadelphia: Elsevier, 2017: Fig. 10.38, p. 377.)*

Table 674.2 Endophthalmitis Categories and the Most Common Pathogens in Each

CATEGORY	COMMON PATHOGENS
Acute postoperative	Coagulase-negative staphylococci
Chronic postcataract	*Propionibacterium acnes*
Postinjection	Viridans streptococci, coagulase-negative staphylococci
Bleb-related	Streptococci, *Haemophilus influenzae*
Posttraumatic	*Bacillus cereus*
Keratitis related	Molds (e.g., *Fusarium*)
Endogenous	*Staphylococcus aureus*, streptococci, gram-negative bacilli
Fungal	Candida, Aspergillus, Fusarium

From Durand ML. Endophthalmitis. In: Bennett JE, Dolin R, Blaser MJ, eds. *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases.* Philadelphia: Elsevier, 2020: Table 114.1, p. 1524.

ENDOPHTHALMITIS

Endophthalmitis is infection of the aqueous and/or vitreous humors and is rare in children; major predisposing factors are noted in Table 674.2. Endogenous hematogenous bacterial (*S. aureus*, streptococci, gram-negative bacilli) and fungal (candida, *Aspergillus* spp., *Fusarium*) may be seen in immunosuppressed and neutropenic patients, whereas histoplasmosis, blastomycosis, coccidiomycosis, and cryptococcus endophthalmitis may rarely be seen as part of disseminated systemic mycotic infection. In addition, ocular toxocariasis may mimic bacterial or fungal endophthalmitis.

The diagnosis requires vitreous sampling because aqueous samples are often negative. The pathogen may be identified by staining, culture, and molecular methods.

Treatment of bacterial endophthalmitis requires intravitreal antibiotics; systemic antibiotics alone are ineffective. Fungal disease often requires combined intraocular and systemic antifungal agents.

Visit Elsevier eBooks+ at eBooks.Health.Elsevier.com for Bibliography.

Chapter 675

Injuries to the Eye

Scott E. Olitsky and Justin D. Marsh

Approximately 30% of all blindness in children results from trauma. Children and adolescents account for a disproportionate number of episodes of ocular trauma. Males ages 11-15 years are the most vulnerable; their injuries outnumber those in females by a ratio of about 4:1. The majority of injuries are related to sports, sticks, stones, fireworks, paint balls, air-powered BB guns, and other projectiles. High-velocity projectiles and fireworks cause particularly devastating ocular and orbital injuries. Much of the trauma is avoidable (see Chapter 14). Any part of the orbit or globe may be affected (Figs. 675.1 and 675.2).

ECCHYMOSIS AND SWELLING OF THE EYELIDS

Ecchymosis and edema of the eyelids are common after blunt trauma (Fig. 675.3). These disorders are self-limiting, absorb spontaneously, and can be treated with iced compresses and analgesics. Periorbital

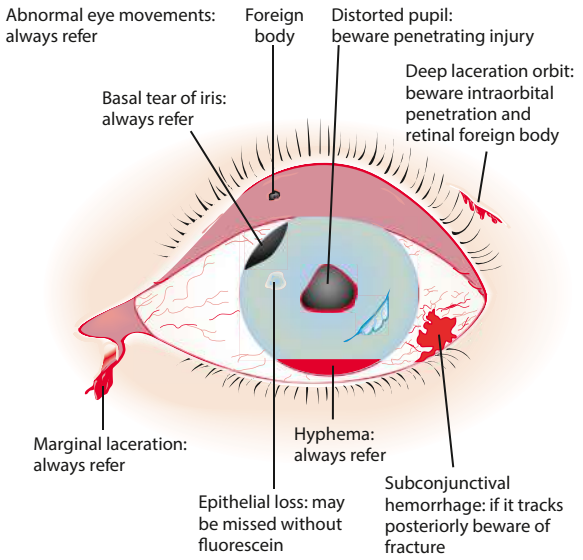

Fig. 675.1 The injured eye. *(From Khaw PT, Shah P, Elkington AR. Injury to the eye. BMJ. 2004;328:36–38.)*

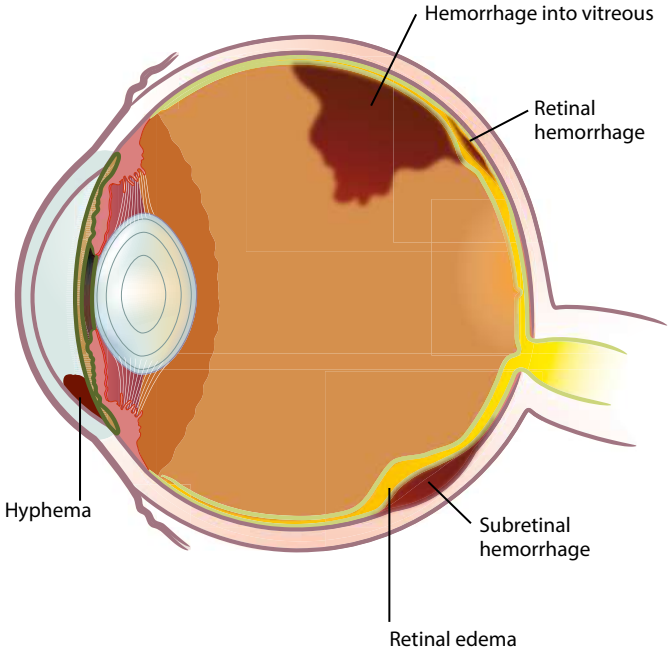

Fig. 675.2 Various types of ocular hemorrhage after blunt trauma to the globe. *(From Reilly BM. Practical Strategies in Outpatient Medicine. 2nd ed. Philadelphia: WB Saunders; 1991:68.)*

Fig. 675.3 Eyelid ecchymosis and subconjunctival hemorrhage.

ecchymosis should prompt careful examination of the eye and surrounding structures for more serious injuries such as orbital bone fracture, intraocular hemorrhage, or rupture of the globe.

LACERATIONS OF THE EYELIDS

Eyelid lacerations may vary from simple to complex. When evaluating an eyelid laceration, key findings include the depth of the laceration, its location, and whether there is involvement of the canaliculus (lacrimal ducts). Most superficial eyelid lacerations may be closed by the primary caregiver, but if a laceration is deep, involves the lid margin, or involves the canaliculus, it should be evaluated by an ophthalmologist. The levator muscle is responsible for elevation of the upper eyelid and runs deep to the skin and orbicularis oculi muscle. If the levator muscle is compromised and not recognized at initial repair, ptosis will occur. Therefore, if orbital fat is visible in the laceration, the laceration has compromised the skin, orbicularis oculi, levator muscles, and orbital septum and must be meticulously repaired to avoid ptosis. Eyelid margin involvement (Fig. 675.4) also requires careful repair to avoid lid malposition and notch formation. These can lead to ocular surface problems in the future, resulting in corneal scarring and loss of vision. Lacerations involving the canaliculus require intubation of the nasolacrimal system, in addition to repair of the laceration of the eyelid to avoid future tearing problems. Proper primary repair of eyelid lacerations often achieves a superior outcome to secondary repair at a later date. As with any eyelid injury, careful examination of the eye and surrounding tissue is required.

SUPERFICIAL ABRASIONS OF THE CORNEA

When the corneal epithelium is scratched, abraded, or denuded, it exposes the underlying epithelial basement layer and superficial corneal nerves. This is accompanied by pain, tearing, photophobia, and decreased vision. Corneal abrasions are detected by instilling fluorescein dye and inspecting the cornea using a blue-filtered light (Fig. 675.5). A slit lamp is ideal for this examination, but a direct ophthalmoscope with a blue filter or a handheld Wood lamp is adequate for young children.

Treatment of a corneal abrasion is directed at promoting healing and relieving pain. Abrasions are treated with frequent applications of a topical antibiotic ointment until the epithelium is completely healed. The use of a semipressure patch does not improve healing time or decrease pain. An improperly applied patch may itself abrade the cornea. A topical cycloplegic agent (cyclopentolate hydrochloride 1%) can relieve the pain from ciliary spasm in patients with large abrasions. Topical anesthetics should not be given at home because they retard epithelial healing and inhibit the natural blinking reflex.

FOREIGN BODY INVOLVING THE OCULAR SURFACE

This usually produces acute discomfort, tearing, and inflammation. Most foreign bodies can be detected by examination in good light with the aid of magnification (Fig. 675.6) or a direct ophthalmoscope set on a high plus lens (+10 or +12). In many cases, slit-lamp examination is necessary, especially if the particle is deep or metallic. Some conjunctival foreign bodies tend to lodge under the upper eyelid, causing the sensation of corneal foreign body, as they make contact with the globe on eyelid movement; they may also produce vertically oriented linear corneal abrasions (Fig. 675.7). Finding these abrasions should lead to a suspicion of such a foreign body, and eversion of the lid may be necessary (see Chapter 659). If a foreign body is suspected but not found, further examination is indicated. If the history suggests injury with a high-velocity particle, radiologic examination of the eye may be needed to explore the possibility of an intraocular foreign body.

Removal of a foreign body can be facilitated by instillation of a drop of topical anesthetic. Many foreign bodies can be removed by irrigation or by gently wiping them away with a moistened cotton-tipped applicator. Embedded foreign bodies or foreign bodies in the central cornea should be treated by an ophthalmologist. Removal of corneal foreign bodies may leave epithelial defects, which are treated as corneal abrasions. Metallic foreign bodies may cause rust to form in the corneal tissues; examination

Fig. 675.4 Eyelid margin laceration.

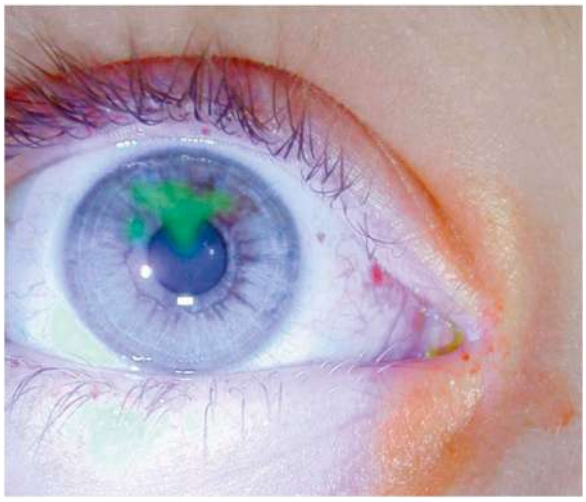

Fig. 675.5 Corneal abrasion with fluorescein staining.

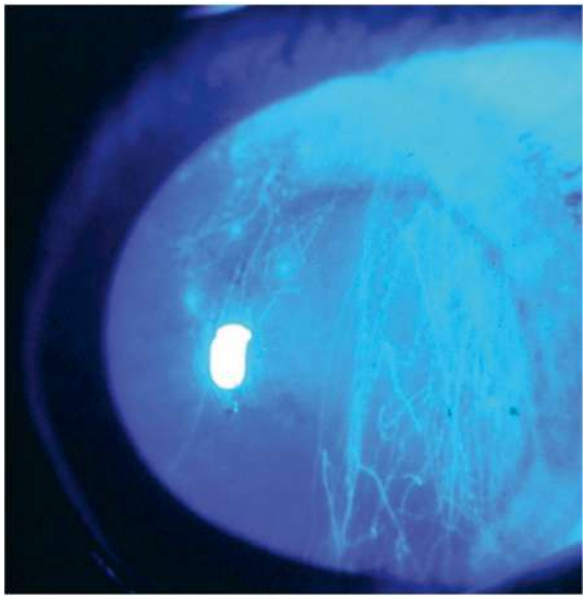

Fig. 675.6 Vertically oriented linear corneal abrasions secondary to a foreign body underneath the upper eyelid.

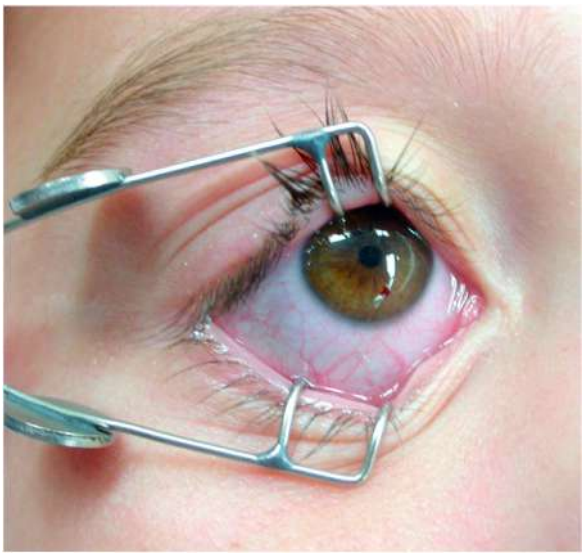

Fig. 675.7 Superficial corneal foreign body.

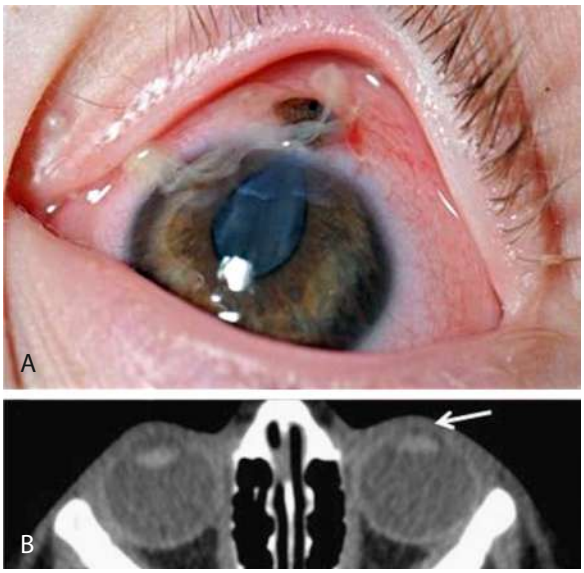

Fig. 675.8 A, Photograph of an open globe injury with a peaked pupil because of iris prolapse through the sclera, a shallow anterior chamber, and a traumatic cataract. B, CT imaging demonstrating a shallow left anterior chamber when compared to the right *(arrow)* but without evidence of an intraocular foreign body. *(From Hwang RY, Schoenberger SD. Imaging a peaked pupil in a traumatic open globe injury. J Pediatr. 2013;163:1517: Figs. A and B.)*

by an ophthalmologist 1 or 2 days after removal of a foreign body is recommended because a rust ring might require further treatment.

HYPHEMA

This is the presence of blood in the anterior chamber of the eye. It may occur with either a blunt or perforating injury and represents a situation that may threaten vision. Hyphema appears as a bright or dark red fluid level between the cornea and iris, or as a diffuse murkiness of the aqueous humor. Children with hyphema present with acute loss of vision, with or without pain. The treatment of hyphema involves efforts to minimize the vision-threatening sequelae, such as rebleeding, glaucoma, and corneal blood staining. Bedrest is necessary, ideally with elevation of the head of the bed to 30 degrees. A shield (without underlying patch) is placed on the affected eye to prevent repeat trauma, and a cycloplegic agent is used to immobilize the iris. In addition, topical or systemic steroids are used to minimize intraocular inflammation. Antiemetics should be considered if the patient is experiencing nausea. All nonsteroidal anti-inflammatories and aspirin must be avoided. Rarely, hospitalization and sedation may be necessary to ensure compliance in some children. If the intraocular pressure is elevated, topical and systemic pressure-lowering medications are used. If the pressure is not controllable by such measures, then surgical evacuation of the clot may be required to minimize the risk of permanent vision loss. Patients with sickle cell disease or trait are at higher risk of acute loss of vision secondary to elevated intraocular pressure or optic nerve infarction and may require more aggressive intervention. Individuals with a history of traumatic hyphema have an increased incidence of glaucoma later in life and should be monitored on a regular basis throughout their lives.

OPEN GLOBE

A penetrating, perforating, or blunt injury resulting in compromise of the cornea or sclera of the eye is one of the most sight-threatening injuries that can be sustained (Fig. 675.8). An open globe is a true ophthalmologic emergency that requires prompt, careful evaluation and immediate repair to minimize vision loss. Permanent vision loss can result from corneal scarring, loss of intraocular contents, or infection. Evaluation involves careful history, including time and mechanism of the injury, as well as visual acuity and inspection of the eye. A full-thickness corneal wound will often present with prolapsed iris tissue through the wound. If this is not immediately evident, a peaked or irregular pupil may be a sign of full-thickness laceration. Scleral compromise may be more difficult to identify because of overlying structures. The thinnest part of the sclera is at the corneoscleral junction (the limbus) and just posterior to the insertion of the rectus muscles. When an open globe is caused by blunt force injury, these are the two areas most likely involved. A ruptured globe occurs when the compressive traumatic force is high enough to lead to a rupture of the globe itself. Although the term *ruptured globe* is frequently used to describe any open eye, the term should be reserved for this specific form of trauma. The force required to rupture the globe often is severe enough to lead to other permanent injuries to the eye with a resultant poor prognosis even when the rupture itself can be repaired. This specific term denotes a poorer prognosis than many other forms of open globe injuries.

The overlying conjunctiva may not be compromised but a subconjunctival hemorrhage may be present, obscuring the view. In these cases, look for a shallow anterior chamber, low intraocular pressure, or pigment within the involved area. If the patient has been diagnosed with an open globe, the examination should be stopped, an eye shield placed immediately, and the ophthalmologist contacted to minimize further ocular compromise.

OPTIC NERVE TRAUMA

The optic nerve may be injured in both penetrating and blunt trauma. The injury may occur at any point between the globe and the chiasm. Traumatic injury to the optic nerve, regardless of cause or location, results in reduced vision and a pupillary defect. Direct trauma to the intraorbital optic nerve may cause transection, partial transection, or optic sheath hemorrhage. Fractures involving the skull base may cause injury to the intracranial portions of the optic nerve. Treatment decisions are difficult because there are no universally accepted guidelines, and the prognosis for good visual outcome is often poor. Medical management involves observation and the use of high-dose corticosteroids, although the use of corticosteroids has not been proven to improve visual outcomes and has been shown to increase the risk of death in patients with significant head injury. Surgical intervention involves optic nerve sheath decompression for nerve sheath hemorrhages. If compression of the optic nerve is secondary to orbital hemorrhage, prompt lateral canthotomy and cantholysis should be performed to relieve intraorbital pressure. Decompression of the optic canal may be performed if there is compression of the optic nerve by a bone fragment. Optic canal decompression is controversial in the absence of direct bone compression.

CHEMICAL INJURIES

Chemical burns of the cornea and adnexal tissue are among the most urgent of ocular emergencies, and they are most common in toddler and preschool-age children and men. Laundry detergent pods have become an increasingly common source of ocular injury to young children over the last decade. Alkali burns are usually more destructive than acid burns because they react with fats to form soaps, which damage cell membranes, allowing further penetration of the alkali into the eye. Acids generally cause less severe, more localized tissue damage. The corneal epithelium offers moderate protection against weak acids, and little damage occurs unless the pH is 2.5 or less. Most stronger acids precipitate tissue proteins, creating a physical barrier against their further penetration.

Mild acid or alkali burns are characterized by conjunctival injection and swelling and mild corneal epithelial erosions. The corneal stroma may be mildly edematous, and the anterior chamber may have mild to moderate cell and flare reactions. With strong acids, the cornea and conjunctiva rapidly become white and opaque. The corneal epithelium may slough, leaving a relatively clear stroma; this appearance may initially mask the severity of the burn. Severe alkali burns are characterized by corneal opacification.

Emergency treatment of a chemical burn begins with immediate, copious irrigation with water or saline. Local debridement and removal of foreign particles should be performed as irrigation continues. If the nature of the chemical injury is unknown, the use of pH test paper is helpful in determining whether the agent was basic or acidic. Irrigation should continue for at least 30 minutes or until 2 L of irrigant has been instilled in mild cases and for 2-4 hours or until 10 L of irrigant has been instilled in severe cases. At the end of irrigation, the pH should be within a normal range (7.3-7.7). The pH should be checked again approximately 30 minutes after irrigation to ensure that it has not changed. The goal of treatment is to minimize sequelae that may threaten vision, such as conjunctival scarring, corneal scarring/opacification, glaucoma, cataract, and phthisis.

ORBITAL FRACTURES

The orbit is the bony structure surrounding the eye. Any of these bones may fracture in a traumatic incident. Superior and lateral wall fractures are the least common of the fracture sites, but superior orbital fracture is the most significant because of the potential of intracranial injury. The medial wall of the orbit is very susceptible to fracture because of the thin nature of the lamina papyracea. Perhaps the most common site of fracture from blunt trauma is the orbital floor. This is often referred to as blowout fracture. At times, the fracture may act as a trapdoor, entrapping orbital contents within the fracture site. In some cases, there may be very little external evidence of trauma, the so called "white-eyed blow-out fracture."

The patient often presents with a recent history of periorbital trauma and pain. Diplopia, eyelid swelling, eye movement restriction, or hypesthesia may or may not be present. Eye symptoms may be associated with nausea and bradycardia if the inferior rectus is entrapped in the fracture site. A complete ophthalmic examination, including visual acuity, examination of the pupil for ocular alignment, ocular motility, anterior segment, and fundus status, as well as the history of the injury, is required because there are often accompanying ocular injuries. The diagnosis of fracture is suspected if eye misalignment, eye movement restriction, or enophthalmos (sunken eye) are present. The diagnosis can be verified by orbital CT scan, although small areas of entrapped muscle may easily be missed if careful attention is not directed toward the fracture site.

Medical management includes iced compresses to the orbit and elevation of the head of the bed for the first 24-48 hours. Broad-spectrum antibiotics are sometimes recommended for 14 days because of the exposure of the orbital contents to the sinus cavity. In medial wall fractures, instructions not to blow one's nose should be given to the patient to avoid orbital emphysema and subsequent optic nerve compression. Consider neurosurgical consultation in orbital roof fractures. Indications for surgical repair of orbital fractures are diplopia in primary gaze or downgaze that persists for 2 weeks, enophthalmos, or fracture of the orbital floor involving more than half of the floor. Extraocular muscle entrapment often requires prompt surgical repair because affected patients have significant pain, nausea, and vomiting that are difficult to control. Rarely, extraocular muscle entrapment can cause activation of the oculocardiac reflex, requiring urgent fracture repair.

PENETRATING WOUNDS OF THE ORBIT

These demand careful evaluation for possible damage to the eye, optic nerve, orbital contents, or brain. Examination should include investigation for a retained foreign body. Orbital hemorrhage and infection are common with penetrating wounds of the orbit; such injuries must be treated as emergencies.

CHILD ABUSE

See Chapter 17.

This is a major cause of injuries to the eye and orbital region. The possibility of nonaccidental trauma must be considered in any child with ecchymosis or laceration of the lids, hemorrhage in or about the eye, cataract or dislocated lens, retinal detachment, or fracture of the orbit. Inflicted childhood neurotrauma (shaken baby syndrome) occurs secondary to violent, nonaccidental, repetitive, unrestrained acceleration-deceleration head and neck movements, with or without blunt head trauma in children typically younger than 3 years of age. Inflicted childhood neurotrauma accounts for approximately 10% of all cases of child abuse and carries a mortality rate of up to 25%. Detection of abuse is not only important to treat the pathology that is discovered but also to prevent further abuse or even death. The ocular manifestations are numerous and may have a prominent role in recognition of this syndrome. Retinal hemorrhage is the most common ophthalmic finding and occurs at all levels of the retina. The pattern of hemorrhage helps distinguish this disorder from other causes of retinal hemorrhage or from accidental injuries (Fig. 675.9). Retinal hemorrhages can occur without associated intracranial pathology.

FIREWORKS-RELATED INJURIES

Injuries related to the use of fireworks can be the most devastating of all ocular traumas that occur in children. At least 20% of emergency department visits for fireworks-related injuries are for ocular trauma. In the United States, a majority of these injuries take place around Independence Day, and most occur despite adult supervision.

SPORTS-RELATED OCULAR INJURIES AND THEIR PREVENTION

Although sports injuries occur in all age-groups, far more children and adolescents participate in high-risk sports than adults. The greater number of participating children, their athletic immaturity, and the increased likelihood of their using inadequate or improper eye protection account for their disproportionate share of sports-related eye injuries (see Chapter 734).

The sports with the highest risk of eye injury are those in which no eye protection can be worn, including boxing, wrestling, and martial arts. Other high-risk sports include those that use a rapidly moving ball or puck, bat, stick, racquet, or arrow (baseball, hockey, lacrosse, racquet sports, and archery) or involve aggressive body contact (football and basketball). Related to both risk and frequency of participation, the highest percentage of eye injuries are in basketball and baseball.

Protective eyewear, designed for a specific activity, is available for most sports. For basketball, racquet sports, and other recreational activities that do not require a helmet or face mask, molded polycarbonate sports goggles that are secured to the head by an elastic strap are suggested. For hockey, football, lacrosse, and baseball (batter), specific helmets with polycarbonate face shields and guards are available. Children should also wear sports goggles under their helmets. For baseball, goggles and helmets should be worn for batting, catching, and base running; goggles alone are usually sufficient for other positions.

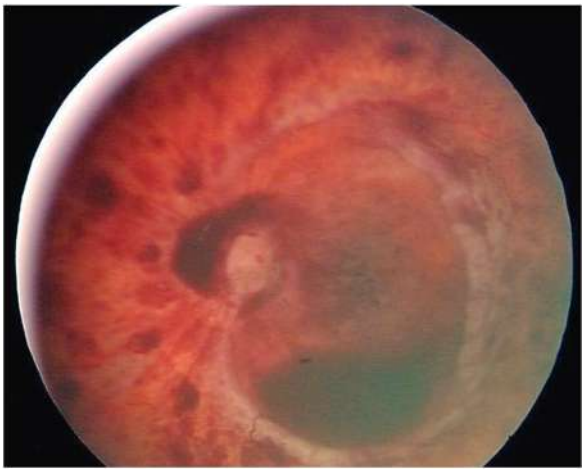

Fig. 675.9 Retinal hemorrhages in an abused child.

HANDHELD LASER RETINAL INJURY

Handheld laser pointers, often purchased to light cigarettes or for other purposes, may produce significant retinal damage if the power output is ≥150 mW. If a person looks directly at the light, direct foveal injury may occur before they have time to blink. Central (foveal) blurring and decreased visual activity are the chief complaints. Retinal injuries include retinal disruption, subretinal edema, and macular holes (Fig. 675.10), which usually require surgical repair.

Visit Elsevier eBooks+ at eBooks.Health.Elsevier.com for Bibliography.

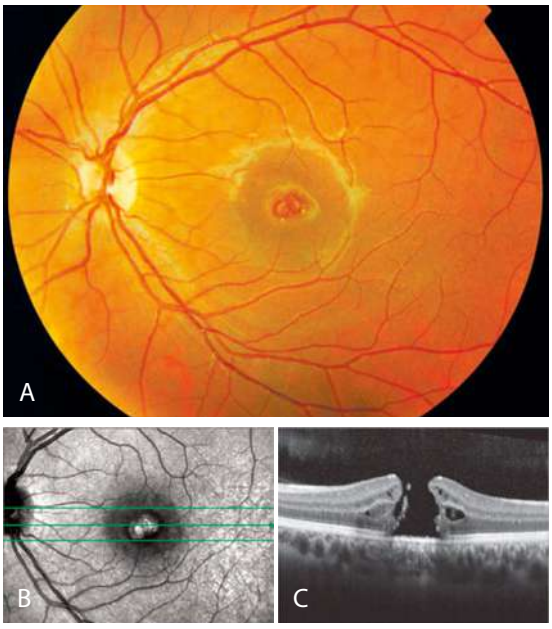

Fig. 675.10 Laser damage to the left eye. **A,** Color photo of the fundus of the left eye showing a macular hole. Note the changes at the retinal pigment epithelium. **B,** Infrared photo of the left fundus. **C,** Optical coherence tomography of the left eye showing the macular hole. *(From Petrou P, Patwary S, Banerjee PJ, et al. Bilateral macular hole from a handheld laser pointer. Lancet. 2014;383:1780.)*