Chapter 8
Ocular Infection in Children

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Introduction

Throughout the life of a child, from conception to adulthood, the human organism is consistently being exposed to organisms that may lead to an infection of the eye and ocular adnexa. To some extent these infections are related to environmental factors and exposures that are age and developmentally dependent. Thus the site of infection may vary and be tissue dependent, whether it involves the orbit, conjunctiva, cornea, or retina, all giving clues to the etiology and time of primary inoculation. Age of presentation along with the site of infection helps to determine the most likely cause and location. Primarily, infectious ocular diseases in children can be divided in four broad categories. These include intrauterine and perinatal infections, ophthalmia neonatorum, conjunctivitis, and orbital and adnexal infections.

Intrauterine and Perinatal Infections

Very early on, intrauterine infections are the fetus's first exposure to potential pathogens. Classically, these maternally transmitted congenital infections are remembered by the acronym TORCHES (toxoplasmosis; rubella; cytomegalovirus (CMV); herpes viruses, including Epstein-Barr; syphilis). Lymphocytic choriomeningitis virus is also included in the differential. While all can affect the developing eye and cause ongoing damage, they tend to do so in three major different ways: (1) direct tissue damage from the infecting organism, (2) interference in embryogenesis by a

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teratogenic effect, and (3) reactivation postconception leading to further organ damage later on in life and into adulthood. Thus the specific organism has a predilection for specific sites and potential reactivation giving clues as to its type that is dependent on the site and presentation (Tables 8.1 and 8.2).

Rubella

First trimester exposure to rubella (German measles) primarily affects the developing eye leading to microphthalmia, keratitis, cataracts, glaucoma, and a retinal pigmentary disturbance. Other organ systems are notably involved that can lead to sensorineural hearing loss, hepatosplenomegaly, mental retardation, osteopathy,

Table 8.1 Intrauterine and perinatal infection

TORCHES – intrauterine and perinatal infections
Toxoplasmosis
Rubella
Cytomegalovirus (CMV)
Herpes virus including Epstein-Barr
Syphilis
Lymphocytic choriomeningitis virus

Table 8.2 Intrauterine and perinatal infections

Causative organism	Ocular abnormalities
Toxoplasmosis	Microphthalmos
	Cataracts
	Panuveitis
	Optic atrophy
	Chorioretinitis
Rubella	Microphthalmos
	Keratitis
	Cataracts
	Glaucoma
	Pigmentary retinopathy
Cytomegalovirus	Microphthalmos
	Keratitis
	Cataracts
	Chorioretinitis
Herpes virus including Epstein-Barr	Conjunctivitis
	Keratitis
	Anterior uveitis
	Cataracts
Syphilis	Interstitial keratitis
	Iridocyclitis
	Iris atrophy
	Pigmentary retinopathy
Lymphocytic choriomeningitis virus	Chorioretinitis/pigmentary retinopathy

lymphadenopathy, thrombocytopenia purpura, and diabetes [1]. Intracerebral calcification of the white matter and basal ganglion can be seen on computed tomography (CT). Overall, its incidence has decreased substantially in the developed world since the introduction of the attenuated rubella virus vaccine in 1969. Corneal involvement presents with clouding from a keratitis. However in combination with microphthalmia and anterior segment dysgenesis, this can lead to glaucoma with secondary corneal haze or abnormal development of the endothelium (Fig. 8.1) [2]. Cataracts are more commonly present and are typically bilateral and diffusely involved [3]. This is thought to be due to viral load within the lens itself, and virus has been cultured at the time of lens extraction [4]. Most often a pigmentary retinopathy is present and characterized as fine, granular, or powdery discrete deposits that are typically limited to the posterior pole (Fig. 8.2). Vision is preserved other than in those cases that develop subretinal neovascularization [5].

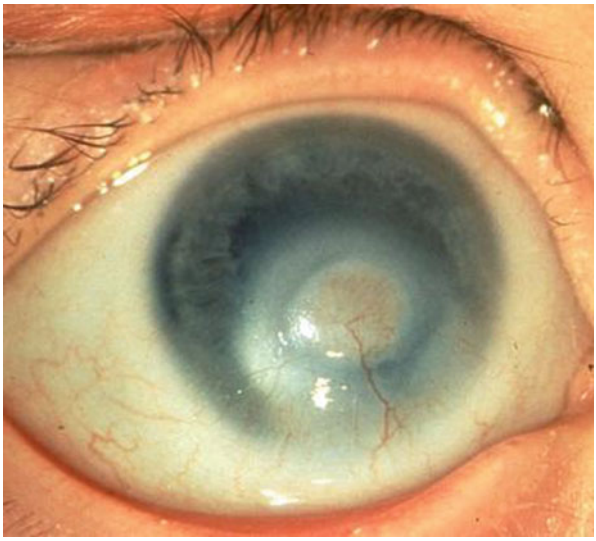

Fig. 8.1 Corneal keratitis with neovascularization from rubella

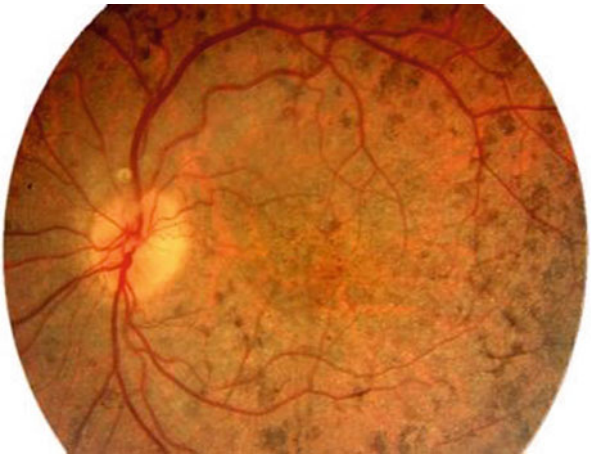

Fig. 8.2 Pigmentary retinopathy from rubella

Herpes Virus Family

The herpes virus family includes two types of simplex virus (HSV-1 and HSV-2), herpes zoster, Epstein-Barr virus, and cytomegalovirus.

Cytomegalovirus

Cytomegalovirus (CMV) is a member of the herpes virus family and is the most common intrauterine infection in the United States occurring in 1 % of all newborns, of which the majority remains asymptomatic [6]. Transmissions transplacentally and early in gestation affect the developing eye and are less common than systemic organ involvement. Ocular findings include keratitis, microphthalmos, cataracts, and chorioretinitis. The typical chorioretinitis presents with focal areas of retinal pigment epithelium atrophy, whitish areas of ischemia, and retinal hemorrhages [7]. Because CMV can also be transmitted from contact while passing through the birth canal or from breast milk, it is often difficult to determine the age at which the infection occurred. CMV can lead to periventricular calcification and hydrocephalus along with generalized cerebral atrophy and associated optic atrophy.

Herpes Simplex

Congenital herpes simplex virus (HSV) is usually acquired via passage through the birth canal in mothers who have active infection either with HSV-1 (labialis) or HSV-2 (vulvovaginitis) [8]. Primary infection is more likely to result in transmission versus secondary reactivation. HSV-2 is the most common culprit and can also occur following premature rupture of the membranes with ascending uterine involvement. Localized disease causes the typical vesicular skin lesions, oral ulceration, and keratoconjunctivitis (Fig. 8.3). However disseminated disease involves the viscera and central nervous system which portends a high mortality rate. Systemic HSV can lead to chorioretinitis, pneumonia, hepatitis, encephalitis, and disseminated intravascular coagulation.

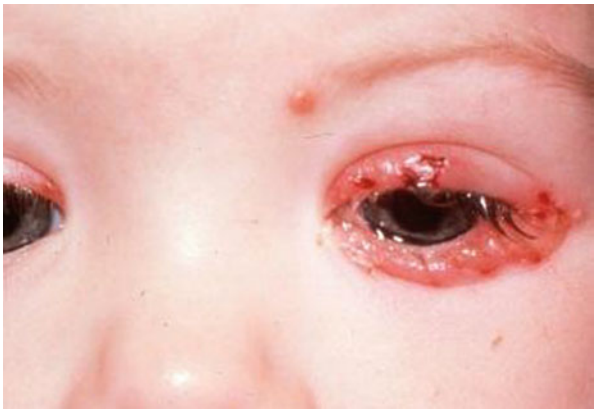

Fig. 8.3 Vesicular lid lesions from herpes simplex

Localized ocular involvement typically consists of eyelid vesicles, conjunctivitis, and a keratitis. Corneal infection may present as dendritic with epithelial involvement or as stromal infiltrates. This can be associated with anterior uveitis and lead to the development of cataracts. In neonates with disseminated disease, especially central nervous system involvement, chorioretinitis can occur with accompanying vitritis and optic atrophy. The chorioretinitis typically involves the retinal periphery and results in hyperpigmented scars that are well circumscribed. Acute retinal necrosis can occur later on in life with reactivation of the virus [9].

Epstein-Barr

Epstein-Barr virus (EBV) (infectious mononucleosis) can lead to toxic and teratogenic effects on ocular development via transplacental transmission. The case reports are limited which is thought to be due to a mild illness in the mother. This makes the diagnosis more difficult and the likelihood of clinical manifestations reduced. Anomalies are multiple and include microphthalmos, cataracts, micrognathia, cleft palate, hypotonia, hepatosplenomegaly, and cardiovascular malformations [10–12].

Varicella Zoster

Varicella and herpes zoster virus (HZV) is the same virus with the initial response considered chicken pox and reactivation herpes zoster. Varicella is not a potent teratogen. It leads to abnormalities in only 12 % of infants exposed and before 20 weeks of gestation. Maternal infection is also exceedingly low since the introduction of immunization programs against chicken pox. Clinical features of congenital varicella infection are primarily skin lesions in a dermatomal distribution and limb hypoplasia. Microcephaly, cortical atrophy, hydrocephalus, mental retardation, and abnormalities of the gastrointestinal, genitourinary, and cardiovascular systems have all been reported. The primary ocular disorders include microphthalmia, cataracts, and chorioretinitis [13]. Theoretically if the varicella virus is reactivated during pregnancy causing herpes zoster in the T10 to L4 root ganglion, intrauterine shedding could occur. However this mode of transmission to the fetus has not been reported and only in a case from a mother with disseminated herpes zoster at 12 weeks of gestation [14]. Neonatal chicken pox can develop if the mother is infected late in pregnancy. This can be transmitted either transplacental or ascending from the uterus. The mortality rate is low except in those born either premature or with low birth weight.

Toxoplasmosis

Toxoplasmosis is caused by *Toxoplasma gondii* which is an obligate intracellular parasite. Human infection occurs from exposure to cat feces, eating undercooked meat, or poorly washed vegetables. Cats are the definitive host and the parasite lives

in the intestinal mucosa. When the unsporulated oocyst is excreted into the environment, it can then be ingested by humans. The oocysts then transform into tachyzoites. They then migrate into cardiac, muscular, neural, and retinal tissue and develop into tissue cyst bradyzoites. Disease reactivation can occur with rupture of the cysts or can remain dormant indefinitely. The stimulus for cyst rupture and reactivation is unknown.

The majority of human disease was thought to result primarily from congenital infection by transplacental transmission; however, postnatal infection also occurs. From the ocular standpoint, chorioretinitis is the most recognized feature. Other findings include microphthalmos, cataracts, panuveitis, and optic atrophy [15]. The chorioretinal scarring is usually heavily pigmented with associated areas of chorioretinal atrophy. It is usually bilateral and often involves the macula (Fig. 8.4) [16]. The primary active infection or reactivation is characterized by retinal inflammation that is thickened and cream colored with overlying vitritis. This vitreous inflammation has been classically described as a "headlight in the fog."

The common systemic findings of first trimester transplacental transmission include intracranial calcification with resultant seizures, hydrocephalus, microcephaly, hepatosplenomegaly, jaundice, anemia, and fever. Second or third trimester infection is associated with mild generalized disease during the first few months of life. Some of these children can then develop central nervous system involvement and chorioretinitis later in life [17]. From the ocular standpoint, the diagnosis is often clinical, based on the typical chorioretinal findings. However, a positive enzyme-linked immunosorbent assay (ELISA) supports the diagnosis. Finding toxoplasma-specific IgM is also specific since maternal IgM does not cross the placenta.

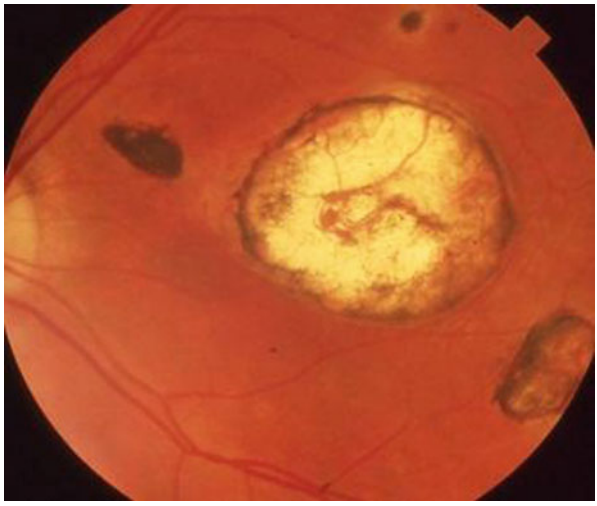

Fig. 8.4 Chorioretinal atrophy from toxoplasmosis

Syphilis

Syphilis is caused by the spirochete *Treponema pallidum*. Exposure leading to signs and symptoms of congenital syphilis typically occurs following maternal primary infection after the first trimester. The incidence of transmission decreases to 90 % in secondary syphilis and approximately 30 % in tertiary disease. Manifestations can be early or late. Early findings include skeletal abnormalities because of metaphyseal involvement or periostitis, maculopapular rash, hepatosplenomegaly with jaundice, pneumonia, anemia, and lymphadenopathy. The typical late manifestations are sensorineural hearing loss, dental abnormalities, and the ocular manifestations. Interstitial keratitis, deafness, and malformed incisors are known as Hutchinson's triad.

The interstitial keratitis is typically bilateral with associated iridocyclitis and iris atrophy. It is a hypersensitivity reaction that occurs in 10–40 % of untreated congenital syphilis cases and most commonly presents at 5–20 years of age [18]. It can be sectorial or diffuse and consists of corneal inflammation with interstitial vessels. These become "ghost vessels" that along with scarring lead to visual loss. Chorioretinitis may develop in the peripheral retina and cause pigment mottling. The primary findings are that of a salt and pepper granularity. However, pigmentation can become heavier leading to a pseudoretinitis pigmentosa-type appearance.

Diagnosis of congenital syphilis is dependent upon identification of the organism by direct-field microscopy from a scraping of a lesion or serologic testing. A positive VDRL (Venereal Disease Research Laboratory) greater than the mothers', with systemic findings, or a positive FTA-ABS (fluorescent treponemal antibody absorption) test, supports the diagnosis.

Lymphocytic Choriomeningitis Virus

Lymphocytic choriomeningitis virus (LCMV) is an arenavirus that is transmitted by exposure to infected rodents. Hydrocephalus, microcephaly, and periventricular calcifications are the most common neurologic manifestations. Ocular findings can be similar in appearance to toxoplasmosis with chorioretinal scars that may involve the entire macula, although peripheral chorioretinitis is most commonly present [19]. The retinal lesions can occur without the systemic findings. Positive antibodies to LCMV support the diagnosis since it is uncommon in the general population.

Ophthalmia Neonatorum

Conjunctivitis that occurs during the first month of life is referred to as ophthalmia neonatorum. In addition to bacterial agents which will be discussed, it can also be caused by viruses and chemicals. Prior to the worldwide institution of prophylaxis

Table 8.3 Ophthalmia neonatorum

Ophthalmia neonatorum – causative agents
Neisseria gonorrhoeae – 2–5 days of age
Chlamydia trachomatis – 7 days of age
Staphylococcus aureus
Streptococcus pneumoniae
Haemophilus
Pseudomonas aeruginosa – rarely

programs, the incidence exceeded 10 % of live births in some areas. If untreated, ocular morbidity is high leading to corneal damage and blindness. Inoculation typically occurs during passage through an infected birth canal, although inoculation can also result from ascending infection of the uterus especially as it may occur following premature rupture of membranes. The two most common organisms are *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. Other etiologic agents include *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and rarely *Pseudomonas aeruginosa* (Table 8.3).

Neisseria gonorrhoeae

Neisseria gonorrhoeae is the most serious of causative agents and typically occurs 2–5 days after birth. It begins as a mild conjunctival hyperemia with serosanguinous discharge that can rapidly progress to a thick purulent yellowish exudate with chemosis and eyelid edema. Corneal ulceration and perforation can quickly occur since the bacterium has a propensity to penetrate the cornea and replicate rapidly. Although the clinical course and findings are typical for *Neisseria gonorrhoeae*, conjunctival culture and Gram stain are paramount in making the diagnosis. Classic gram-negative intracellular diplococci are seen on Gram stain, although *Neisseria gonorrhoeae* cannot be differentiated from *Neisseria meningitidis*. Systemic infection can also occur including meningitis and sepsis [20, 21].

Chlamydia trachomatis

In the industrialized world, *Chlamydia trachomatis*, an obligate intracellular organism, is the most common cause of ophthalmia neonatorum. Also known as trachoma-inclusion conjunctivitis (TRIC), it usually occurs at around 1 week of age and often begins in one eye and then becomes bilateral. Clinically there is a mild mucopurulent discharge with moderate lid swelling and chemosis. Pseudomembranes can develop and if untreated this leads to scarring of the tarsal conjunctiva and corneal micropannus. The concern with *Chlamydia* is systemic involvement of the pharynx and lungs which can be fatal [22]. The diagnosis is made by conjunctival culture and scrapings. The culture material must include epithelial cells. Testing with

polymerase chain reaction, direct fluorescent antibody staining, and enzyme immunoassay is also available to identify the organism.

Conjunctivitis

Conjunctivitis – red or pink eye – has a number of causative agents including bacterial, viral, allergic, and chlamydial. Common clinical features and symptoms in addition to redness include pain, burning, and stinging. Often they can be differentiated by other features including type of discharge, degree of itching, involvement of the lashes, and associated conjunctival response [23]. Five morphological conjunctival forms can occur: papillary, follicular, membranous/pseudomembranous, cicatrizing, and granulomatous. Papillae are characterized by a central fibrovascular core that arborizes on the conjunctival surface. They are a nonspecific finding of polymorphonuclear cell infiltration, but classically occur in bacterial conjunctivitis. Follicular conjunctivitis is most commonly caused by viral infections. Follicles are discrete round elevations of the conjunctiva from a lymphocytic response. The central portion is avascular with blood vessels sweeping up and over from the base. In membranous bacterial conjunctivitis, a fibrinous adherent exudate forms that bleeds with attempted removal. It occurs with *Corynebacterium diphtheria* and *Streptococcus pyogenes* infections. Pseudomembranous conjunctivitis has a less severe inflammatory response without necrosis where the thick exudate can be removed. It is somewhat nonspecific and can occur in conjunctivitis caused by *Neisseria gonorrhoeae*, *Haemophilus influenzae*, *Streptococcus pyogenes*, *Staphylococcus aureus*, *Candida*, adenovirus, and herpes simplex virus. Cicatrizing conjunctivitis is primarily an autoimmune process that develops in mucus membrane pemphigoid and Stevens-Johnson syndrome. Conjunctival scarring develops from progressive subepithelial fibrosis leading to severe dry eye from loss of goblet cells and obliteration of lacrimal gland ductules along with forniceal foreshortening and symblepharon formation. Granulomatous conjunctivitis describes nodular conjunctival elevations that are typically associated with preauricular adenopathy. Infectious causes include *Bartonella henselae* (cat scratch), *Francisella tularensis* (tularemia), *Mycobacterium tuberculosis*, and *Treponema pallidum* (syphilis). Biopsy of the conjunctival nodules demonstrates central caseation. This is in contrast to noncaseating causes for granulomatous conjunctivitis which include sarcoidosis and a foreign body reaction. Types of discharge include serous, mucopurulent, or purulent. Purulent discharge occurs more with bacterial infection while watery or serous in viral conjunctivitis.

Bacterial Conjunctivitis

Acute bacterial conjunctivitis occurs in school-age children and is most often caused by *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella* spp. [24, 25]. Most cases are self-limited with symptoms subsiding in around 14 days even without

treatment. However, because of the morbidity involved and its contagious nature, topical antibiotics are recommended. Treatment shortens the course to a few days and decreases the contagion. The recent widespread immunization against some subspecies of *Streptococcus* and *Haemophilus* has decreased the incidence of these causative agents. Clinically children with bacterial conjunctivitis present with hyperemia of the bulbar conjunctiva, matting of the lashes, and discharge. It can be unilateral or bilateral. Concomitant otitis media can occur with associated low-grade fever, cough, sore throat, and nasal discharge. In these instances systemic antibiotics are warranted.

Membranous bacterial conjunctivitis is primarily caused by *Corynebacterium diphtheria* and *Streptococcus pyogenes*. It is seen uncommonly in developed countries because of vaccination programs. Adherent membranes are formed primarily to the palpebral conjunctiva because of a necrotic inflammatory response leading to a fibrinous adherent exudate. The membrane is thick and gray yellow in color. It bleeds on attempted removal. The membrane ultimately sloughs and is replaced by granulation tissue. Cicatrization may develop leading to trichiasis and xerosis. In the acute phase, corneal ulceration can occur and the bacterial can penetrate intact epithelium

Viral Conjunctivitis

Adenovirus is the most common pathogen in viral conjunctivitis. The severity of the disease can be mild to severe and is often associated with upper respiratory tract infection. Mild symptoms include a clear watery discharge. Preauricular adenopathy is often present. The usual source of the infection is via droplet and person to person. Thus viral conjunctivitis can be highly contagious. More severe forms include epidemic keratoconjunctivitis (EKC) and pharyngoconjunctival fever.

Epidemic keratoconjunctivitis tends to occur in outbreaks. It is most often caused by adenovirus serotypes 8, 19, and 37. Presenting symptoms include discomfort, photophobia, conjunctival chemosis, small subconjunctival hemorrhages, and preauricular adenopathy. A focal corneal epithelial keratitis ensues within 3–5 days followed by subepithelial focal infiltrates. Although the epithelial component is self-limited, the subepithelial opacities may persist for years. In severe infections there is marked swelling of the eyelids that is often confused with primary preseptal or orbital cellulitis. Conjunctival membranes can also develop, especially in infants.

Pharyngoconjunctival fever is associated with type 3 and 7 adenovirus. The presenting symptoms are similar to EKC, but without the subepithelial infiltrates or membrane formation. Corneal involvement is usually limited to punctate keratitis.

Herpes simplex virus conjunctivitis presents with similar viral symptoms of discomfort, redness, watery discharge, and preauricular adenopathy. Periocular and eyelid vesicles develop and help identify the disease. It is commonly unilateral and caused by both HSV-1 and HSV-2. There often is a history of recurrent cold sores. 50 % of patients with HSV conjunctivitis develop corneal epithelial manifestations

Table 8.4 Infectious conjunctivitis

Infectious conjunctivitis Causative agent	Ophthalmic findings	Systemic findings
Bacterial conjunctivitis *Streptococcus pneumoniae* *Haemophilus influenzae* *Moraxella*	Bulbar conjunctival hyperemia Matting of the lashes Mucopurulent discharge	Otitis media Low-grade fever Cough Sore throat Nasal discharge
Viral conjunctivitis Adenovirus	Clear watery discharge	Preauricular adenopathy

that range from fine punctate epithelial staining to the classic dendrites. Anterior uveitis can be present, but is usually mild (Table 8.4).

Blepharitis

Blepharitis is a common cause of chronic conjunctivitis in children. Disease anterior to the gray line of the lid margin is often caused by *Staphylococcus aureus* and *Staphylococcus epidermidis*. Symptoms include irritation, crusting, erythema, photophobia, and rubbing. It can be associated with atopic eczema and styes. Collarettes can be present. These are fibrinous scales centered on a lash. Tear film instability and inferior keratitis may develop. This can be severe with resultant peripheral corneal scarring and phlyctenules [26]. Involvement posterior to the gray line of the lid margin is more consistent with Meibomian dysfunction. Inspissated secretions are present with the development of chalazion [27].

Orbital and Adnexal Infections

Preseptal Cellulitis

Preseptal cellulitis is an inflammation or infection that is confined to the tissues anterior to the orbital septum. It primarily involves the eyelid, but can extend to surrounding areas such as the brow and forehead. Symptoms include redness, swelling, and pain. Preseptal cellulitis must be differentiated from secondary involvement of the orbit. In these cases, pain on eye movements, proptosis, and optic neuropathy would be consistent with orbital cellulitis [28]. Causes of preseptal cellulitis are multiple and historical data can help in its elucidation. Secondary infection of a chalazion can spread to involve the whole lid. In this case the child may have a history of prior chalazion or have noticed a small bump prior to the more severe lid swelling. Trauma with a small puncture wound or laceration is not uncommon with secondary staphylococcal infection. Insect bites can cause a significant allergic reaction with lid swelling or become secondarily infected. Association with a severe conjunctivitis can also develop from herpes zoster or impetigo. If bilateral,

adenoviral infection leading to epidemic keratoconjunctivitis or pharyngoconjunctival fever should be suspected. This is a not uncommon scenario where a younger child might get admitted to the hospital for presumed bilateral orbital cellulitis because of difficulty in examination for orbital signs from severe conjunctival chemosis and lid swelling, only to discover that there is no sinus involvement on imaging and the causative agent is severe adenoviral conjunctivitis [29]. Clues to the diagnosis include other family members with conjunctivitis, large preauricular nodes, and whitish membranes on the palpebral conjunctiva. Finally, preseptal cellulitis can occur in association with an upper respiratory tract infection from *Haemophilus influenzae* especially in children under age 2 where the sinuses are not developed. This incidence has diminished, however, with the widespread use of Hib vaccine.

Orbital Cellulitis

The vast majority of orbital cellulitis occurs in children over age 5 (average 7 years) from contiguous spread of infection from the ethmoid or frontal sinuses [28]. This is because the bones separating the orbit and sinuses are thin at this age allowing for easy spread of infection. Less commonly it develops with associated penetrating orbital trauma or dental infections. Signs and symptoms of orbital cellulitis include progressive ocular pain, fever, lid edema, rhinorrhea, lethargy, and headache. Progressive proptosis and limited extraocular movement are of concern since this can lead to increased intraocular pressure and a compressive or infiltrative optic neuropathy (Fig. 8.5). Delay in treatment can also allow intracranial spread of the infection, especially via the venous drainage system of the orbit. This can cause septic cavernous sinus thrombosis, subdural empyema, and intracranial abscesses. Orbital cellulitis is therefore sight and life threatening. These patients should be admitted to the hospital for workup to include imaging of the sinuses. Identification of the extent of sinus involvement is important as well as the possible presence of a subperiosteal abscess or foreign body. Blood, nasal, and throat cultures can help with identifying the causative agent. Consultation with otolaryngology and infectious disease is important as a multidisciplinary approach to treatment is often needed.

The most common etiologic agents causing orbital cellulitis vary with age. *Staphylococcus aureus* and gram-negative bacilli are more common in the neonate. In children under age 9, a single aerobic pathogen such as *Streptococcus pneumoniae*, *Moraxella catarrhalis*, and *Haemophilus influenzae* is more common. This mirrors the microbiology of sinusitis. Older children have more complex infections with multiple pathogens both aerobic and anaerobic. Anaerobic organisms include *Fusobacterium* and *Bacteroides. Streptococcus pyogenes* may cause erysipelas, necrotizing fasciitis, or toxic shock, which requires aggressive treatment. Fungal infections are rare, but must be excluded in diabetic or immunocompromised patients (Table 8.5).

Fig. 8.5 Orbital cellulitis left eye with associated elevation deficit

Table 8.5 Preseptal vs. orbital sinusitis

Cellulitis	Site of infection	Signs and symptoms	Causative agents
Preseptal	Tissue anterior to the orbital septum, eyelid, brow, forehead	Redness, pain, and swelling of preseptal tissues	Chalazion, trauma, insect bite, viral
Orbital	Orbit and preseptum	Lid edema, proptosis, pain, and limitation of eye movements, optic neuropathy	Spread of infection from ethmoid, maxillary, or frontal sinus

Recommended Therapy for Common Clinical Conditions

Treatment of infectious ocular disorders in children in most cases is antibiotic driven, but the choice of therapeutic approach is dependent on the age of the patient, the site of the disorder, and the underlying natural history. Thus with some congenital or acquired infections, there may be no specific treatment, or the disorder may resolve without intervention.

Intrauterine or Perinatal Infections

Intrauterine infections that cause ocular anomalies typically do so by disturbing embryogenesis with associated organ damage that can extend into postnatal life. Most common ocular anomalies occur during the first trimester of gestation. However, ocular damage can also occur due to infection with varicella or CMV

during the second trimester or with postnatal syphilitic infection. Thus the treatment of these disorders includes (1) primary prevention by eliminating exposure or through maternal vaccination, (2) treatment of the mother or the neonate with appropriate antibiotics or antivirals, and (3) treatment of the underlying ocular damage, i.e., cataract extraction, refractive error, and visual rehabilitation.

Rubella

Treatment of rubella has primarily been directed toward its prevention with the introduction of the attenuated vaccine in 1969 [30]. Since that time its incidence has been dramatically reduced; however it is still prevalent in those areas of the world that do not have robust vaccination programs. Thus the primary intervention in these children is lensectomy for cataractous changes which most often occur bilaterally [31]. An intense postoperative inflammatory process can develop that is thought to be due to sequestered virus [4]. Unfortunately there is no specific treatment for the pigmentary retinopathy and it may be slowly progressive. The rare development of subretinal neovascularization is an additional concern with these patients.

Herpes Virus Family

Cytomegalovirus

The mainstay of treatment of infants with cytomegalovirus causing systemic or ocular disease is ganciclovir. Administration may reduce the severity of sensorineural hearing loss although its effect on neurodevelopmental outcomes is still to be determined [32]. Treatment in older immunocompromised children includes ganciclovir, valganciclovir, foscarnet, cidofovir, and fomivirsen. The use of intraocular ganciclovir implants in children has been reported [33].

Herpes Simplex

Neonatal herpes simplex viral infections are often initially detected by a vesicular eruption. Dissemination leads to multisystemic involvement and a high mortality rate. Treatment is with systemic acyclovir [34].

Varicella Zoster

Maternal vaccination is the mainstay of prevention of chicken pox. It also has been shown to be effective following exposure if given within 3 days of maternal exposure [35]. Maternal treatment includes the antivirals, acyclovir, valacyclovir, and famciclovir. They can also be combined with VZIG. Despite a theoretical risk of teratogenesis

with fetal exposure to acyclovir especially in the first trimester, this has not been demonstrated. Neonates with chicken pox may benefit from the use of intravenous acyclovir. VZIG may also reduce the severity of infection if given to neonates whose mothers develop chicken pox from 5 days before delivery to 2 days after delivery.

Toxoplasmosis

Treatment of toxoplasmosis is to some extent dependent on the age of detection. In those neonates who develop intrauterine infection detected serologically with or without systemic findings, it is recommended that they be treated with pyrimethamine and sulfadiazine. Folic acid should be given with this regimen to prevent leukopenia and thrombocytopenia associated with the use of pyrimethamine [36]. From the ophthalmic standpoint, treatment in cases of reactivation is determined by the degree of vision-threatening ocular involvement. Reactivation or acute chorioretinitis is typically self-limited. Thus peripheral lesions can be observed without treatment. However in cases of severe visual loss or with lesions that threaten the optic nerve or macula, treatment is indicated. Regimens include pyrimethamine and sulfadiazine with folic acid, sulfonamides, clindamycin, Bactrim, or doxycycline. With severe inflammation corticosteroids are used cautiously with antibiotics [37].

Syphilis

Treatment of congenital syphilis is with intravenous aqueous crystalline penicillin G. In order to ensure adequate treatment, serologic tests are repeated. Persistent positive titers require retreatment [38].

Lymphocytic Choriomeningitis Virus

Unfortunately there is no effective antiviral treatment for LCMV at this time and no vaccine exists. Since the manifestations are developmental anomalies including the peripheral chorioretinitis, the primary intervention is in prevention. Since a significant number of women who contract LCMV do so because of exposure to rodents, this contact should be minimized [39].

Ophthalmia Neonatorum

Treatment of ophthalmia neonatorum is dependent on early recognition, the time course of presentation, and isolation or detection of the offending organisms. The two most common organisms are *Neisseria* and *Chlamydia*. Prophylaxis for gonorrheal ophthalmia neonatorum was introduced in the 1880s with the use of 2 % silver nitrate.

With the increased incidence of *Chlamydia*, erythromycin ointment became the agent of choice. In the last decade, povidone-iodine drops have been shown to be equally effective, less toxic, and less costly. Now povidone-iodine is playing an important role in developing countries [40]. Treatment of *Neisseria* and *Chlamydia* conjunctivitis is with a directed appropriate antibiotic regimen. In addition to treatment of the neonates, it is equally important to treat their mothers and all of their contacts.

Neisseria gonorrhoeae

The mainstay of treatment for *Neisseria gonorrhoeae* conjunctivitis is intravenous penicillin G. However because of widespread resistance in many urban areas, a third-generation cephalosporin is recommended. Both intramuscular and intravenous administration appears to be equally effective. In addition frequent ocular irrigation with saline as well as the addition of topical antibiotics is typically recommended. Because concomitant infection with *Chlamydia* often occurs, treatment for inclusion conjunctivitis should be instituted until ruled out [41].

Chlamydia trachomatis

Treatment of neonatal conjunctivitis due to *Chlamydia trachomatis* is with oral erythromycin. This is because of the high incidence of pneumonitis and nasopharyngeal colonization. Although there is no evidence that it is necessary, supplemental topical erythromycin ophthalmic ointment is often recommended [22, 41].

Conjunctivitis

Treatment of conjunctivitis truly depends upon the offending agent, whether bacterial, viral, allergic, or associated with blepharitis. The diagnosis is often made on the clinical signs and symptoms, as well as findings of papillae, follicles, membranes, or granuloma to support a diagnosis. Gram stain and culture are needed to definitively confirm the offending agent, but this is often impractical. Thus broad-spectrum treatment directed at the most likely pathogens is typically employed.

Bacterial Conjunctivitis

Treatment of bacterial conjunctivitis is directed toward the most likely offending organisms, that being *Streptococcus*, *Staphylococcus*, *Haemophilus*, and *Moraxella* [25]. Because in many instances the infection is self-limited, especially if the child is being treated with systemic antibiotics for concomitant otitis, there is great debate about the efficacy of any particular antibiotic agent. Issues to take into consideration include whether the antibiotic is bacteriostatic vs. bactericidal, parental compliance

regarding the dosage regimen, the contagiousness, and the overall cost. Most clinicians do recommend treatment because it leads to a more rapid clinical resolution and a higher eradication rate of bacteria [42]. Systemic treatment is necessary for membranous conjunctivitis and in immunocompromised patients. This often requires hospital admission as the majority of these patients are often toxic and febrile. In addition prevention of symblepharon by sweeping the fornices with a lubricated glass rod or the placement of contact shell is required.

Viral Conjunctivitis

Unfortunately there are no antiviral treatments directed toward the adenoviruses that cause viral conjunctivitis, epidemic keratoconjunctivitis, or pharyngoconjunctival fever. Intervention is primarily supportive with ocular lubricants, cool compresses, and occasionally topical antihistamines. Since viral conjunctivitis is very contagious, discussion with patients regarding proper hygiene is important to eradicate spread to others. Topical steroids potentiate viral replication. However in cases where the keratopathy is symptomatic and vision threatening, topical steroids can rapidly improve the keratopathy at the risk of difficulty in its taper with reactivation.
In contrast to adenoviral infections, treatment is available for conjunctivitis or keratitis secondary to herpes simplex. Although treatment of the conjunctivitis does not seem to alter the course of the disease, if the cornea is involved, intervention is warranted. Oral acyclovir has been shown to be effective for treating herpetic epithelial keratitis and for reducing the rate of recurrence when used prophylactically [43]. However, more recently the introduction of topical ganciclovir gel 0.15 % is increasingly being shown to be equally effective for the acute keratitis [44].

Blepharitis

Treatment of blepharitis is multifactorial. The primary goals are to treat any acute infection, reduce bacterial load at the lid margin, and manage the hypersensitivity response that can cause keratopathy. Thus the mainstays of therapy include topical antibiotics, lid hygiene with warm compresses and eyelid scrubs, flaxseed oil supplementation, and topical steroids. Persistent cases may benefit from oral antibiotics. Because tetracyclines can lead to dental staining, erythromycin is the preferred agent [45, 46].

Orbital and Adnexal Infections

Preseptal Cellulitis

Preseptal cellulitis is most often caused by *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Streptococcus epidermidis*. Thus treatment consists of intravenous or oral antibiotics directed toward the suspected

organism. Typically intravenous antibiotics are used in cases where the infection is severe and could spread into the orbit. Oral antibiotics on the other hand are reserved for more local infections. If the preseptal cellulitis is associated with a chalazion, incision and drainage might be required. Suspicion should also be high for occult trauma. If so, any retained foreign body must be identified and removed. Also any wound discharge should be cultured and tetanus prophylaxis provided. Of concern would be the development of necrotizing fasciitis and septic shock from beta-hemolytic *Streptococcus* [47].

Orbital Cellulitis

All patients with orbital cellulitis require immediate hospitalization for intravenous antibiotics and imaging to evaluate the extent of sinusitis and subperiosteal abscess [48]. In most instances pediatric otolaryngological consultation should be considered. Although many subperiosteal abscesses will resolve with intravenous antibiotics, drainage should be undertaken if there is progressive enlargement, optic nerve involvement, or risk of cavernous sinus thrombosis [49]. In addition, drainage of the offending sinus is often required.

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