Chapter 4
Conjunctivitis

Tayyeba K. Ali and Seth M. Pantanelli

Introduction

"Pink eye" is one of the most common complaints seen by doctors and a source of frequent referral to ophthalmology. Infectious conjunctivitis is one of the leading components of the pink-eye differential. Nevertheless, redness is not the only way microbial disease of the conjunctiva manifests. The conjunctiva is a mucous membrane that lines the sclera and is composed of two layers: epithelium and submucosal substantia propria. When these layers become inflamed or infected, it manifests as conjunctivitis. Physiologically speaking, conjunctivitis is a vascular dilation accompanied by cellular infiltration and exudation. Proper eyelid closure, meibomian gland function, and ocular surface health are required to keep the conjunctiva moist and healthy. Disorders that affect these parameters, such as Bell's palsy, meibomian gland dysfunction, and cicatrizing disease, can lead to compromised conjunctival health and microbial infections.

While most infectious conjunctivitis is self-limiting, sequelae of microbial disease include membrane/pseudomembrane formation, cicatrization, and extension of the disease to the cornea and lacrimal system, as the epithelium that covers the conjunctiva is contiguous with the corneal epithelium and also extends to the

The authors of this article have no financial disclosures.

T.K. Ali, MD (✉)
Department of Ophthalmology, University of Arkansas for Medical Sciences, Little Rock, AR 72205, USA

Jones Eye Institute, University of Arkansas for Medical Sciences, 4301 W. Markham Street, Little Rock, AR 72205, USA
e-mail: tkali@uams.edu

S.M. Pantanelli, MD, MS
Cornea and External Diseases, Department of Ophthalmology, Penn State College of Medicine, Penn State Health-Milton S. Hershey Medical Center, Hershey, PA 17033, USA

N.V. Laver, C.S. Specht (eds.), *The Infected Eye*,
DOI 10.1007/978-3-319-42840-6_4

lacrimal apparatus and glands [1]. Additionally, post-infectious cicatrizing conjunctivitis holds significant morbidity, and common causes include trachoma, diphtheria, and streptococcal infection [2–4]. In the United States, the leading post-infectious sources are adenovirus and herpes simplex [5, 6].

Clinicians should be aware of the various presentations of conjunctivitis, particularly the factors that are common in infectious processes. The disease can be classified by laterality, onset of activity, morphology, discharge, and associated systemic illnesses. Taking a thorough history is key, followed by a focused physical examination in order to make a quick, accurate diagnosis and provide the most appropriate therapy.

Most cases of infectious conjunctivitis can be treated conservatively; nevertheless, it is imperative not to miss visually threatening or systemic disease. Morphology that is commonly associated with infectious etiologies includes papillary or follicular reactions, secondary to bacteria or to *Chlamydia* and viruses, respectively. The substantia propria has a superficial adenoid cell layer that contains lymphoid tissue. This layer is where follicles form. The deeper fibrous layer is composed of connective tissue, where fibroblasts, macrophages, mast cells, and polymorphonuclear cells are present in healthy tissue [1]. Other factors to consider are rapidity of onset, type of discharge, history of sick contacts, and presence of systemic illness.

Epidemiology of Conjunctivitis

While the numbers are likely higher today, older studies show that 1 % of annual primary care visits in the United States are related to conjunctivitis and 70 % of patients with conjunctivitis present to general practitioner offices or urgent care facilities [7]. Despite the fact that most cases of infectious conjunctivitis are self-limiting, it imposes a significant social and financial burden. Estimates suggest that four to six million people are affected annually in the United States [8], with an average of $705 million spent on direct and indirect costs related to the illness [9]. These numbers are conservative and only take into account office visits, not cases secondary to atypical causes of disease, such as conjunctivitis neonatorum.

Host Defenses (Table 4.1)

The eye's natural defense against pathogen invasion is multitiered and listed in Table 4.1. Initially, the physical barrier of the orbital rim and eyebrows keeps foreign material away from the ocular surface. This is followed by protection from the eyelashes and blink response, which work to keep smaller particles away from the surface of the eye. An additional mechanical tool includes the tear film, which washes away pathogens. The tear film is composed of many antimicrobial components, including lysozyme, beta-lysin, lactoferrin, immunoglobulins (primarily IgA), complement, and cathelicidin [10–15], which decrease colonization of

Table 4.1 Host defenses

Orbital rim
Eyelids
Eyebrows/eyelashes
Blink reflex
Tear film
Lysozyme
Beta-lysin
Lactoferrin
Immunoglobulins (IgA)
Complement
Cathelicidin
Goblet cell mucus
Conjunctiva-associated lymphoid tissue (CALT)
Low temperature
Ocular microbiota

microbes by killing the pathogens and preventing adhesion to the ocular surface. Mucus from goblet cells traps bacteria [10]. Furthermore, the ocular microbiota, composed of inherent and indigenous bacteria, prevents more pathogenic microbes from colonizing the surface [16, 17]. Conjunctiva-associated lymphoid tissue along with Toll-like receptors that regulate the adaptive immune response provides further protection [17]. Finally, the temperature of the ocular surface is not advantageous for microbial growth [17].

Risk Factors (Table 4.2)

Intrinsic

Any specific abnormality in the series of host defenses listed above can lead to microbial infection of the conjunctiva. While exposure from eyelid dysfunction or an absent Bell's phenomenon can often lead to corneal pathology, these factors also cause conjunctival drying and secondary infection. Severe meibomian gland dysfunction, abnormal tear film, and an altered microbiota can also be underlying factors that lead to further problems.

Extrinsic

Worldwide, a leading cause of preventable blindness is trachoma, which spreads from direct contact from ocular or nasal secretions, fomites, or via flies [18]. The most common type of infectious conjunctivitis in the United States is adenoviral conjunctivitis, and this occurs secondary to direct inoculation by ocular or nasal secretions, similar to the common cold. Less commonly, infectious organisms

Table 4.2 Risk factors

Intrinsic	Extrinsic
Abnormal lid anatomy	Direct inoculation
Lid retraction	Adenoviral
Lagophthalmos	Common bacterial
Abnormal blink reflex	Trachoma
Abnormal tear film	Transvaginal
Mucin layer	Sexual contact
Vit A deficiency	HSV/VZV
Aqueous layer	Trauma
Rheumatoid	Prior ocular surgery
Sjögren	Contaminated topical medications
Lipid layer	
Rosacea	
MGD	
CCC	
Altered microbiota	
Systemic	
NLDO	
Infection	

Abbreviations: *MGD* meibomian gland dysfunction, *CCC* chronic cicatrizing conjunctivitis, *NLDO* nasolacrimal duct obstruction

similar to trachoma and also sexually transmitted diseases can spread to the conjunctiva of neonates through transvaginal or perivaginal exposure during delivery [19].

Infection with herpes-family viruses typically manifests as a keratitis or sclerokeratitis but can present as blepharoconjunctivitis and should be kept in the differential for cases that are not self-limiting or that get worse on steroid eye drops. Trauma, previous eye surgery, and contaminated topical medications can all lead to spread of pathogenic bacteria. Common risk factors are listed in Table 4.2.

History and Clinical Examination

Numerous algorithms have been constructed to help guide the diagnosis of conjunctivitis. A detailed history is imperative to make a timely and accurate diagnosis. Often the physical examination will simply confirm the leading diagnosis and allow for appropriate therapy to be implemented quickly.

Questions important to ask on a history are: time of onset (hyperacute, acute, or chronic), laterality, presence of sick contacts, previous episodes, systemic diseases, and other risk factors. Hyperacute onset is typically defined by rapidity of onset and extent of disease. In adults, this would be <48 h after inoculation and with copious, hyperpurulent discharge, which generally represents gonorrheal disease. In neonates, conjunctivitis within the first 48 h of birth is usually toxic, whereas conjunctivitis due

Table 4.3 Differential for chronic, noninfectious conjunctivitis

Vernal keratoconjunctivitis
Atopic keratoconjunctivitis
Secondary giant papillary conjunctivitis
Foreign body
Sebaceous cell carcinoma
Floppy eyelid syndrome
Superior limbic keratoconjunctivitis
Toxic keratoconjunctivitis
Mucus-fishing syndrome
Keratoconjunctivitis sicca
Ligneous conjunctivitis
Stevens–Johnson syndrome
Ocular cicatricial pemphigoid
Sarcoidosis
Lymphoma

to *Neisseria gonorrhoeae* typically presents between days 2 and 5. In the general population, if onset of symptoms is less than 2 weeks, the likely etiology will be viral or nongonococcal bacterial. Up to 75 % of acute conjunctivitis has been attributed to viral infection [20]. Chronic conjunctivitis has an extensive, noninfectious differential and is listed in Table 4.3. Infection may be secondary to local spread from a dacryocystitis or canaliculitis. Chronic infection may be secondary to *Moraxella catarrhalis*, *Chlamydia* species, *Borrelia burgdorferi* (Lyme disease), molluscum contagiosum, or Parinaud's oculoglandular syndrome. Diagnoses based on onset of symptoms and then further subdivided based on morphology are listed in Fig. 4.1.

Laterality is the next question to probe, as adenoviral conjunctivitis classically starts in one eye and spreads to the other eye within 2–3 days of onset. Bacterial conjunctivitis will likely be bilateral and may be associated with sinusitis or nasolacrimal duct obstruction. Staphylococcal marginal blepharoconjunctivitis or infection secondary to lacrimal apparatus stasis can be unilateral or asymmetric in appearance.

Herpes-related conjunctivitis is often unilateral, though bilateral disease can be seen and is more common in atopic or immunocompromised patients. These patients may also have experienced previous episodes of redness, irritation, and light sensitivity.

Systemic diseases may need to be ruled out. Viral etiologies are presumed in the presence of preauricular lymphadenopathy and the absence of other more severe signs of illness. Patients at risk or with suggestive histories should be asked if they have known sexually transmitted diseases. Other important factors would be previous trauma, surgery, long-term topical medication use, topical steroid use, and history of radiation to the face.

A focused physical examination can confirm a diagnosis or lead the astute physician to make a less likely diagnosis. Morphology focuses on the type of conjunctival

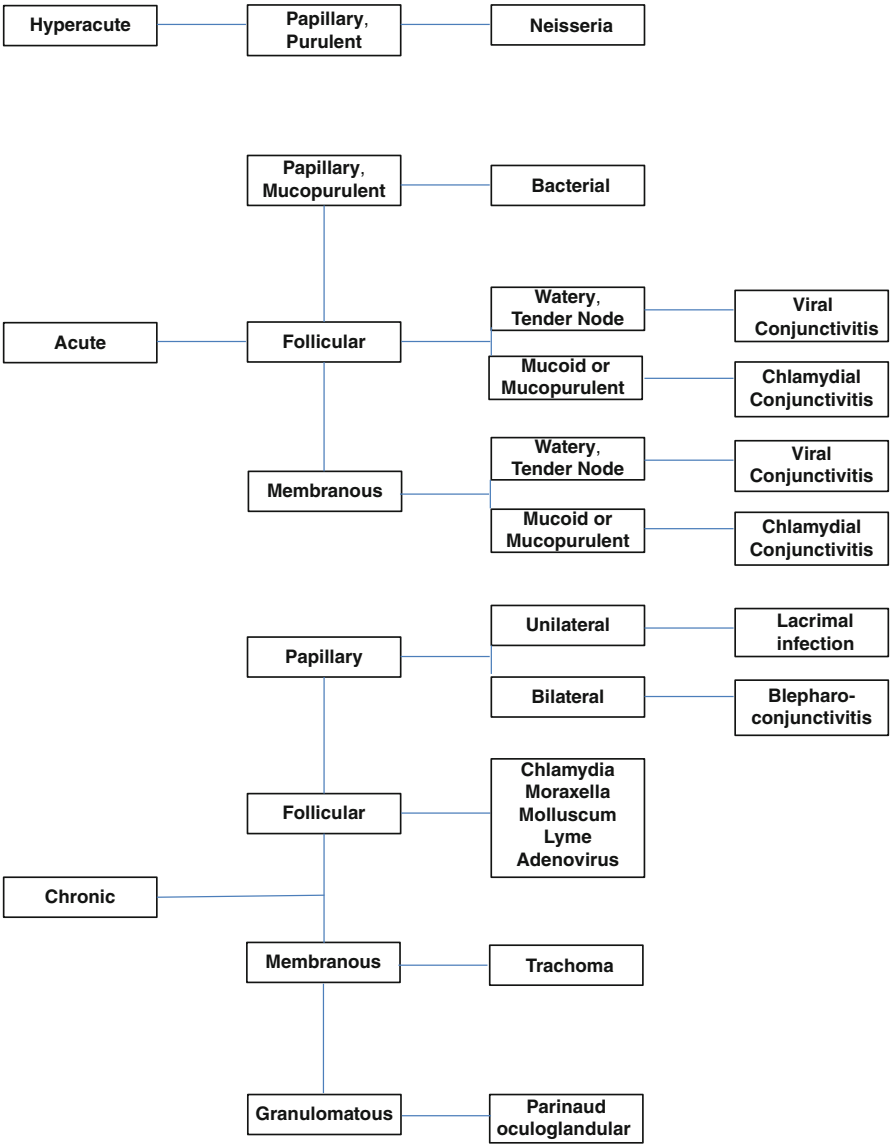

Fig. 4.1 Most likely cause of conjunctivitis based on rapidity of onset and morphological features (Adapted from Figures 42.1 and 42.2 in Lindquist [1])

reaction: papillary versus follicular. There may be a mixed response, but often one type will predominate. Classically papillary conjunctivitis is bacterial or allergic in origin. Follicles suggest a viral or chlamydial etiology. Other factors to look for are the presence of membranous or granulomatous disease.

Enumeration and Presentation of Common Pathogens

Understanding which organisms not only are the most common causes of conjunctivitis but also are most pathogenic is important in order to provide appropriate therapy. Knowing the risk factors associated with various microbes also assists in diagnosis.

Viral Conjunctivitis

Adenovirus

Adenoviral conjunctivitis (Fig. 4.2) is the most common cause of infectious conjunctivitis [20, 21] and is seen most often in the summer [22]. The virus has over 60 serotypes and seven subgroups; of the seven subgroups, group D is the most frequent source of adenoviral keratoconjunctivitis. There are four main ocular manifestations of adenoviral conjunctivitis, of which acute follicular conjunctivitis is the most benign [5]. Another frequent manifestation is epidemic keratoconjunctivitis (EKC). EKC is more aggressive and can be associated with pseudomembranes and symblepharon, as well as with corneal subepithelial infiltrates (SEIs). Pharyngoconjunctival fever (PCF) is characterized by fever, pharyngitis, follicular reaction, and preauricular adenopathy. Chronic conjunctivitis can wax and wane for months to years after the initial bout but eventually has spontaneous resolution. It can present with a mixed papillary and follicular reaction as well as with SEIs [23, 24].

Patients complain of bilateral symptoms, and classically the second eye becomes involved 2–3 days after the first. People in healthcare settings, day-cares, and other situations where there is close contact are at higher risk. The disease is biphasic and an inflammatory phase follows the initial infective phase at about 7–10 days after initial inoculation. Patients remain infected for up to 2–3 weeks after initial symptoms.

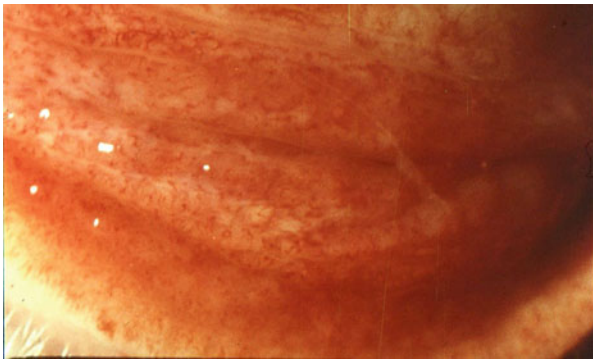

Fig. 4.2 Classic follicular response with a watery discharge, suggestive of adenoviral conjunctivitis

Herpes

Herpetic disease rarely presents as a simple follicular conjunctivitis without eyelid or corneal involvement. Nevertheless, almost 5 % of isolated follicular conjunctivitis cases that were thought to be adenovirus (due to the absence of clinical herpes) were found to be culture positive for herpes simplex virus (HSV) [25]. HSV conjunctivitis is typically unilateral and has a watery discharge. Vesicular eyelid lesions or a keratouveitis may be present [5, 26].

Primary varicella zoster virus rarely causes conjunctivitis. Infection after latency that manifests as herpes zoster ophthalmicus (HZO) can present as a conjunctivitis, scleritis, or keratouveitis and will typically be associated with the classic, dermatomal shingles rash. Involvement of the nasociliary branch of the trigeminal nerve (CN V), Hutchinson's sign, has a high correlation with ocular involvement and should be followed closely [5].

When herpetic infection is suspected, a dilated eye exam should be performed, especially if associated with a decrease in vision or worsening of symptoms, to ensure that there is no chorioretinal spread.

Atypical Viral Pathogens

Many viruses can cause conjunctivitis with a range of clinical appearances from a mild follicular reaction to significant membrane development with associated keratitis; Epstein–Barr virus [27], cytomegalovirus [28], paramyxovirus [5], or togavirus [29] may be involved. Molluscum contagiosum, secondary to poxvirus, is often associated with lid margin lesions that are raised, umbilicated, and flesh colored, as depicted in Fig. 4.3. Surgical removal [30] and other treatment options such as topical cidofovir [31] have been tried with some success for molluscum lesions.

Interest in flavivirus infection has increased since the 2015 outbreak of Zika virus in Latin America. The viruses that cause dengue, yellow fever, Japanese encephalitis, and West Nile disease are also flaviviruses. Zika virus can present with a maculopapular skin rash, fever, arthralgias, and conjunctivitis; these signs and symptoms are similar to those of dengue and chikungunya [32]. Treatment is typically supportive and conservative management is recommended for all of the abovementioned viral pathogens. Travelers to endemic areas are recommended to take proper precautions to avoid mosquito bites, as treatment is mainly preventative [33].

Bacterial Conjunctivitis

Bacterial infection is the second most common cause of conjunctivitis overall and is the source of most cases in children; it presents more frequently in winter [34]. Spread is typically through oculodigital contact or fomites [34, 35], but infection

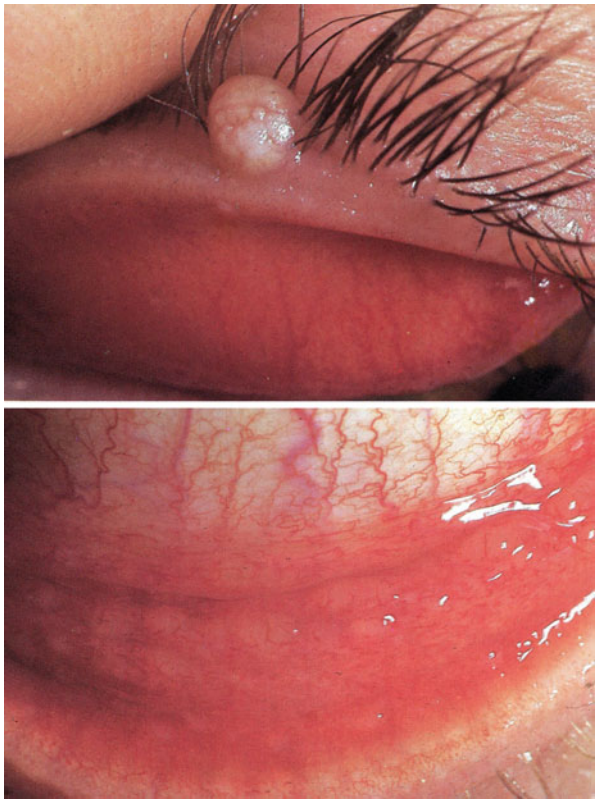

Fig. 4.3 *Upper image*: dome-shaped, waxy lesion suggestive of molluscum contagiosum, secondary to the poxvirus. *Lower image*: follicular conjunctivitis secondary to molluscum

can result from abnormal proliferation of native flora, trauma, and oculogenital or transvaginal spread as in neonatal conjunctivitis [26, 36]. Moreover, certain virulent pathogens can invade intact conjunctival and corneal epithelial surfaces, leading to deeper spread and even to perforation of the globe [17].

Staphylococcus

Staphylococcal species are the most common pathogens of adult bacterial conjunctivitis [36]. Acute bacterial conjunctivitis secondary to *Staphylococcus aureus* presents as a mucoid or mucopurulent, papillary conjunctivitis that affects the bulbar more than the palpebral conjunctiva. Typically, there is an associated matting and sticky closure of the eyelashes. It can become a chronic conjunctivitis if there is an associated blepharitis. Other normal eyelid flora includes *Staphylococcus epidermidis*, which can also become a chronic blepharoconjunctivitis [37].

Streptococcus

Although any streptococcal species can cause conjunctivitis, the second most common cause of bacterial disease is *Streptococcus pneumoniae*. It occurs more commonly in temperate climates during the winter and is observed more frequently in children [38]. Acute disease is associated with a mucopurulent discharge and a papillary reaction, as seen in other bacterial conjunctivitises.

Haemophilus

Haemophilus influenzae is the most common cause of bacterial conjunctivitis in young children [38, 39]. There is an encapsulated and a nonencapsulated form [17]. The encapsulated form often presents with mucoid or mucopurulent conjunctivitis that is highly contagious and requires treatment for resolution and prevention of recurrence [3, 17]. The nonencapsulated form is prevalent in more temperate environments and is seen in the springtime. It is often associated with upper respiratory tract infections and *H. influenza*-associated otitis media [38]; this form is self-limiting and often resolves within 1–2 weeks of onset [3, 17].

Moraxella

Moraxella catarrhalis can cause a chronic conjunctivitis and is often associated with an angular blepharitis [17].

Neisseria

Neisseria gonorrhoeae causes a hyperacute, profuse, and purulent conjunctivitis accompanied by severe chemosis, eyelid swelling, and keratitis [40]. The incubation period is typically 3 days to 3 weeks, and the urethral symptoms often precede the ocular findings by several weeks [40]. Still, cases without any urethral discharge and longer incubation periods have been reported [41]. If inadequately treated, gonococcal conjunctivitis can progress rapidly and may lead to corneal perforation within 24 h. Aggressive systemic therapy with antibiotics can reduce the risk of vision loss associated with perforation and other significant sequelae. The Centers for Disease Control recommend that patients being treated for gonococcal conjunctivitis be hospitalized and given high-dose parenteral antibiotics for 5 days [42]. Recently, there has been an increased incidence of gonococcal conjunctivitis, as well as increased levels of resistance to penicillin [40, 43]. Thus, cases that have rapid progression, that are refractory to treatment, or where there is a high suspicion for a sexually transmitted disease should have cultures and sensitivities performed in order to rule out more virulent or resistant pathogens.

Chlamydia

Chlamydia trachomatis is the primary species that causes conjunctivitis. Serovars A-C are associated with trachoma, the leading cause of preventable blindness worldwide [44]. The disease spreads via direct contact but also can be transmitted via fomites and flies; low socioeconomic status is a significant risk factor [18, 44, 45]. Trachoma manifests as a follicular conjunctivitis with mucoid discharge and hyperemia. In the later stages of the disease, classic findings include Herbert's pits along the limbus and Arlt's line along the superior tarsus. The inflammatory phase is followed by cicatricial changes; the stages of the disease are listed in Table 4.4 [44, 46].

Serovars D-K cause inclusion conjunctivitis, a sexually transmitted disease that is seen more commonly in industrialized nations [47]. It presents as a follicular reaction in adults about 1–2 weeks after inoculation, which occurs via direct contact with genital secretions and can be seen in up to 2 % of patients with urogenital *Chlamydia* infection [48]. Though less virulent, similar to gonorrheal conjunctivitis, it must be treated as a systemic disease requiring oral treatment with doxycycline or azithromycin [49]. Neonatal disease is discussed separately below.

Additionally, serovars L1–3 lead to lymphogranuloma venereum. In patients with high-risk sexual activity and a chronic follicular conjunctivitis, this rare entity should remain on the differential. *Chlamydia psittaci*, in patients who handle pigeons and certain other birds, may also present with a rare follicular conjunctivitis [50].

Atypical Bacterial Pathogens

Any number of bacteria can cause conjunctival inflammation, typically manifesting as a papillary conjunctivitis with a granulomatous component. One example is *Bartonella henselae*, which causes cat-scratch disease [51]. Cat-scratch disease can present with a nodular conjunctivitis and local lymphadenopathy and is a leading cause of Parinaud's oculoglandular syndrome. There may be history of a cat scratch, though this is not necessary [52, 53]. The list of possible pathogens

Table 4.4 Stages of trachoma [44, 46]

TF: Follicular inflammation – five or more follicles (0.5 mm) in upper tarsus
TI: Intense inflammation – significant tarsal thickening that obscures > ½ of the deep vessels
TS: Trachomatous scarring – tarsal scarring
TT: Trachomatous trichiasis – one or more eyelashes rubbing on surface
CO: corneal opacity – opacification over the pupil

Table 4.5 More frequent causes of Parinaud's oculoglandular syndrome

Cat-scratch *B. henselae*
Tularemia
Sporotrichosis
Tuberculosis
Syphilis
Coccidioidomycosis

Adapted from Gruzensky [54], which contains the complete differential

causing oculoglandular conjunctivitis is extensive [54], but *Francisella tularensis* [54], *Mycobacterium tuberculosis* [55], and *Treponema pallidum* [56] are high in the etiological differential diagnosis. Any of these organisms can cause granulomatous inflammation. If risk factors are present and the clinical picture is not that of a typical form of conjunctivitis, conjunctival scrapings should include acid fast and gram stains as well as cultures on Löwenstein–Jensen medium and chocolate agar. Giemsa stain and Sabouraud agar can be added if there is suspicion for a fungal etiology. Table 4.5 lists the most likely cause of Parinaud's oculoglandular syndrome.

Neonatal Conjunctivitis (Ophthalmia Neonatorum)

Ophthalmia neonatorum is a sight-threatening disease that manifests within the first 3–4 weeks of life and requires urgent treatment. Time to incubation and onset of disease are important factors in determining the cause of disease. Most often, neonatal conjunctivitis presents as a hyperacute papillary reaction; a follicular response is atypical before 6–8-week postpartum due to an inability to mount an immune response until that age [57].

Noninfectious conjunctivitis, or chemical conjunctivitis, often presents within the first 24–48 h of birth [58] and is generally secondary to the use of silver nitrate solution for prophylaxis against ophthalmia neonatorum. Chemical conjunctivitis is much less common in current neonatal practice, as the less toxic erythromycin ointment or povidone iodide eye drops have replaced silver nitrate solution for prophylaxis against ocular infections.

Conjunctivitis in the neonate can be secondary to infection with bacterial, viral, or rarely fungal organisms. Gonococcal conjunctivitis usually presents within 2–5 days after birth and will manifest with copious thick, purulent discharge [59] Urgent treatment is required in order to prevent scarring and corneal perforation. Other less common causes of bacterial neonatal conjunctivitis include *Haemophilus* spp., *Streptococcus pneumoniae*, and *Staphylococcus aureus* [60, 61]. Neonatal inclusion conjunctivitis is caused by *C. trachomatis* and is the most common cause of infectious neonatal conjunctivitis in the industrialized world [62]. It typically presents between 5 and 14 days after rupture of membranes. While membranes and conjunctival scarring can cause long-term sequelae, the disease is typically

Table 4.6 Neonatal conjunctivitis: diagnosis and treatment

Time to onset (postpartum)	Likely pathogen	Treatment
24–48 h	Chemical	Artificial tears and lubrication
2–5 days	*Neisseria gonorrhoeae*	Ceftriaxone 125 mg IM ×1 [60] OR Cefotaxime 25 mg/kg IM or IV BID-TID × 7 days [65] OR Penicillin G 100,000 U/kg/day IV divided QID × 7 days [58, 66] PLUS saline irrigation
5–14 days	*Chlamydia*	Erythromycin 12.5 mg/kg/day PO or IV divided QID × 14 days OR Azithromycin 20 mg/kg PO daily × 3 days PLUS erythromycin 0.5 % ointment QID [49]
>5 days	Fungal (*Candida*)	Natamycin 5 % drops Q1 hour × 14 days [6]
1–2 weeks	Herpes simplex	Acyclovir 30 mg/kg/day × 10 days OR Vidarabine 30 mg/kg/day × 10 days PLUS topical drops or ointment (trifluorothymidine 1 % Q2 hour OR ganciclovir ointment 5×/day) [59, 66, 67]

self-limiting. Systemic treatment is required because chlamydial pneumonitis is often associated with this condition [58, 63].

Herpes-related neonatal conjunctivitis typically presents 6–14 days after birth and is associated with eyelid swelling and a watery discharge. In addition to a vesicular skin rash, the cornea may be involved. Similar to chlamydial conjunctivitis, herpetic conjunctivitis needs to be treated systemically due to the mortality rate associated with disease dissemination [64].

Though infrequent, conjunctivitis due to infection by *Candida* spp. has been reported and typically will present five or more days after birth [6, 57]. Table 4.6 describes time to onset for neonatal conjunctivitis, as well as treatment options [65–67].

Diagnostic and Treatment Algorithm

Guidelines for treatment of conjunctivitis vary based on the characteristics of a given patient population (adults, neonates, the presence or absence of specific risk factors). Nevertheless, certain pathogens are seen at such a high frequency that an algorithm based on onset of disease can be used for most clinic situations (Fig. 4.1).

Meta-analysis of clinical features that would help accurately identify the type of infectious conjunctivitis shows that complete redness of the conjunctiva including tarsus, purulent discharge, and matting of both eyes in the morning increases the likelihood of a bacterial source [68]. Matting of the eyelids is the most important of

these three factors [69]. Classically, preauricular lymphadenopathy is associated with viral conjunctivitis; however, this has not been shown to be diagnostically accurate [68].

Conjunctival cultures are not performed routinely but are indicated in cases of recurrent or recalcitrant disease, high suspicion for gonococcal or chlamydial infection, or in cases of neonatal conjunctivitis. Frequently used smears and culture media are listed in Tables 4.7 and 4.8, as it is imperative to culture on media that is most likely to grow the suspected organism.

In-office rapid antigen testing for adenoviral conjunctivitis can be instituted in the primary care setting; this may lead to a reduction in inappropriate therapy and visits [8]. This testing could also be useful in the ophthalmologist's office, as it is relatively inexpensive and provides the patient with the reassurance needed to continue with conservative management when indicated [21]. The mainstay of treatment for adenoviral conjunctivitis is conservative management with cool compresses and artificial tears. Strict hand-washing and limiting the spread of the disease by using separate hand towels, pillowcases, and refraining from going to regularly scheduled crowded places like day-care and work are important factors to discuss with the patient.

Herpes-related conjunctivitis typically has additional clinical features with possible involvement of the eyelids, cornea, and sclera. If the clinical picture remains unclear, shave biopsy of eyelid lesions, viral culture of the fornix, or impression cytology of corneal epithelial lesions can be performed. Herpes-associated conjunctivitis often resolves on its own. If there is corneal involvement or if symptomatic

Table 4.7 Frequently used smears and their corresponding organisms

Stain	Organisms seen
Gram stain	Bacteria (gram positive vs. gram negative), fungi, *Acanthamoeba*
Giemsa stain	Bacteria, fungi, *Chlamydia*, *Acanthamoeba*
Acid fast	*Mycobacterium*, *Nocardia*
Calcofluor white	Fungi

Table 4.8 Frequently used culture media and the common isolates grown on them

Culture media	Common isolates	Comment
Blood agar	Aerobic and facultative anaerobic bacteria	Incubate at 35°
Chocolate agar	Primarily anaerobic bacteria and facultative anaerobic, but may also grow aerobic	Incubate at 35°
Sabouraud agar	Primarily fungi, but may also grow filamentous bacteria, i.e., *Nocardia* spp.	Incubate at room temperature
Thioglycollate broth	Aerobic, anaerobic, and facultative anaerobic bacteria	Incubate at 35°
Lowenstein–Jensen medium	*Mycobacterium* and *Nocardia* spp.	Incubate at 35°
Thayer–Martin agar	*Neisseria* spp.	Incubate at 35°

Table 4.9 Common bacterial pathogens and their treatment in adults

Pathogen	Type of conjunctivitis	Treatment
Neisseria	Hyperacute	Ceftriaxone 1 g IM PLUS saline lavage [42]
Gram-positive bacteria (*S. aureus* or *S. pneumoniae*)	Acute	Vancomycin Cefazolin Fluoroquinolones (4th generation)
Gram-negative (*H. influenza*)	Acute	Tobramycin Gentamicin Ceftazidime Fluoroquinolones

Table 4.10 Management options for acute conjunctivitis

Artificial tears during day and ointment at night for adults and school-aged children
Artificial tear ointment in infants and toddlers
Strict hand-washing
Cool compresses
Avoid direct contact with others for 1–2 weeks
Antibiotic eye drops for bacterial conjunctivitis 2–4×/day
Steroid eye drops if associated subepithelial corneal infiltrates with VA < 20/40
Steroid eye drops for membranous conjunctivitis
Membrane peeling
Symblepharon ring +/− amniotic membrane to prevent aggressive membranes from forming a symblepharon
Rapid antigen testing or cultures to verify etiology or when conjunctivitis persists > 4 weeks

relief is needed, a 10-day course of antivirals should be used. Conjunctivitis secondary to atypical viruses is treated conservatively. Common causes of bacterial conjunctivitis and useful topical medications are listed in Table 4.9.

For many cases of viral or bacterial conjunctivitis, follow-up can be scheduled for 7–14 days after initial symptoms or first clinic visit based on the extent of disease. Typically, if patients are asymptomatic and have no visual complaints, they do not require a repeat ophthalmic examination. The authors leave follow-up for simple conjunctivitis up to the patient. In cases where there are pseudomembranes, risk for symblepharon formation, and visually significant subepithelial infiltrates, visits should be scheduled more frequently and compliance stressed. Membranes should be peeled every 3–5 days, if not more frequently, and sequelae of aggressive disease monitored closely. Therapy should be tailored based on etiology. Common treatment options are listed in Table 4.10.

Conjunctival infection that arises as a complication of surgical or nonsurgical trauma rarely remains limited to the conjunctiva. If there is significant pain, decrease in vision, or conjunctival injection that does not blanch with a drop of phenylephrine, a full dilated eye examination should be performed so that conjunctival epithelial defects, lacerations, foreign bodies, uveitis, or any posterior segment involvement can be identified.

Neonatal conjunctivitis requires rapid, accurate diagnosis and treatment. The time of onset, mother's medical history, and cultures are key factors to determine the underlying cause. Table 4.6 lists the most likely causes of neonatal conjunctivitis based on onset of disease and describes available treatments.

Additional Treatment Options

Steroids are rarely required when treating conjunctivitis and may prolong the disease course by increasing viral shedding. They may also exacerbate the disease if the conjunctivitis is accompanied by herpetic epithelial keratitis or a fungal infection.

Still, judicious use is indicated in cases that are associated with a strong inflammatory component, such as pseudomembranes or corneal subepithelial infiltrates causing vision less than 20/40 on the Snellen chart. For patients with recurrent, aggressive membranes, especially those who cannot be seen for frequent visits, symblepharon rings may be an option (Fig. 4.4), as well as amniotic membrane on a ring or sutured to the conjunctiva and positioned in the fornix.

Prognosis

Most cases of conjunctivitis, whether viral or bacterial, are self-limiting and resolve without any visually significant sequelae [26]. Infection with an aggressive viral strain or resistant bacteria may lead to symblepharon formation and post-infectious

Fig. 4.4 Plastic ring placed within the fornices to prevent further cicatrization and symblepharon formation. Amniotic membrane attached to the ring (ProKera) or sutured in place to cover the fornices can be used for additional treatment

cicatrization. If treated appropriately and aggressively early in the disease course with judicious use of steroids or physical removal, permanent damage may be avoided. When dealing with virulent pathogens like *N. gonorrhoeae* or potentially chronic, progressive conditions like chlamydial conjunctivitis, early diagnosis and aggressive treatment that includes systemic therapy can limit damage to the ocular surface and prevent visual compromise. Ultimately, preventing spread of disease is critical and remains the mainstay of treatment, as most conjunctivitis is secondary to direct inoculation via hand–eye touch or fomites.

References

1. Lindquist T. Conjunctivitis: an overview and classification. In: Krachmer JH, Mannis MJ, Holland EJ, editors. Cornea. China: Mosby; 2011. p. 509–20.
2. Faraj HG, Hoang-Xuan T. Chronic cicatrizing conjunctivitis. Curr Opin Ophthalmol. 2001;12:250–7.
3. Duke-Elder S. System of ophthalmology. St. Louis: Mosby; 1965. p. 159–61.
4. Landers J, Kleinschmidt A, Wu J, Burt B, Ewald D, Henderson T. Prevalence of cicatricial trachoma in an indigenous population of Central Australia: the Central Australian Trachomatous Trichiasis Study (CATTS). Clin Experiment Ophthalmol. 2005;33:142–6.
5. Alvarenga L, Scaarpi M, Mannis M. Viral conjunctivitis. In: Krachmer JH, Mannis MJ, Holland EJ, editors. Cornea. China: Mosby; 2011. p. 535–44.
6. Arffa RC, Grayson M. Grayson's diseases of the cornea. 4th ed. St. Louis: Mosby; 1997. p. 125–56.
7. Kaufman HE. Adenovirus advances: new diagnostic and therapeutic options. Curr Opin Ophthalmol. 2011;22:290–3.
8. Udeh BL, Schneider JE, Ohsfeldt RL. Cost effectiveness of a point-of-care test for adenoviral conjunctivitis. Am J Med Sci. 2008;336:254–64.
9. Smith AF, Waycaster C. Estimate of the direct and indirect annual cost of bacterial conjunctivitis in the United States. BMC Ophthalmol. 2009;9:13.
10. Gilger BC. Immunology of the ocular surface. Vet Clin North Am Small Anim Pract. 2008;38:223–31, v.
11. Dawson CR. How does the external eye resist infection. Invest Ophthalmol. 1976;15:971–4.
12. Selinger DS, Selinger RC, Reed WP. Resistance to infection of the external eye: the role of tears. Surv Ophthalmol. 1979;24:33–8.
13. Williams RC, Gibbons RJ. Inhibition of bacterial adherence by secretory immunoglobulin A: a mechanism of antigen disposal. Science. 1972;177:697–9.
14. Stuchell RN, Farris RL, Mandel ID. Basal and reflex human tear analysis. II. Chemical analysis: lactoferrin and lysozyme. Ophthalmology. 1981;88:858–61.
15. Ford LC, DeLange RJ, Petty RW. Identification of a nonlysozymal bactericidal factor (beta lysin) in human tears and aqueous humor. Am J Ophthalmol. 1976;81:30–3.
16. Chandler JW, Gillette TE. Immunologic defense mechanisms of the ocular surface. Ophthalmology. 1983;90:585–91.
17. Soukiasian SaB J. Bacterial conjunctivitis. In: Krachmer JH, Mannis MJ, Holland EJ, editors. Cornea. China: Mosby; 2011. p. 521–34.
18. Schemann JF, Sacko D, Malvy D, Momo G, Traore L, Bore O, et al. Risk factors for trachoma in Mali. Int J Epidemiol. 2002;31:194–201.
19. Givner LB, Rennels MB, Woodward CL, Huang SW. Chlamydia trachomatis infection in infant delivered by cesarean section. Pediatrics. 1981;68:420–1.
20. Woodland RM, Darougar S, Thaker U, Cornell L, Siddique M, Wania J, et al. Causes of conjunctivitis and keratoconjunctivitis in Karachi, Pakistan. Trans R Soc Trop Med Hyg. 1992;86:317–20.

21. Jhanji V, Chan TC, Li EY, Agarwal K, Vajpayee RB. Adenoviral keratoconjunctivitis. Surv Ophthalmol. 2015;60:435–43.
22. Ariga T, Shimada Y, Shiratori K, Ohgami K, Yamazaki S, Tagawa Y, et al. Five new genome types of adenovirus type 37 caused epidemic keratoconjunctivitis in Sapporo, Japan, for more than 10 years. J Clin Microbiol. 2005;43:726–32.
23. Darougar S, Grey RH, Thaker U, McSwiggan DA. Clinical and epidemiological features of adenovirus keratoconjunctivitis in London. Br J Ophthalmol. 1983;67:1–7.
24. Pettit TH, Holland GN. Chronic keratoconjunctivitis associated with ocular adenovirus infection. Am J Ophthalmol. 1979;88:748–51.
25. Uchio E, Takeuchi S, Itoh N, Matsuura N, Ohno S, Aoki K. Clinical and epidemiological features of acute follicular conjunctivitis with special reference to that caused by herpes simplex virus type 1. Br J Ophthalmol. 2000;84:968–72.
26. Azari AA, Barney NP. Conjunctivitis: a systematic review of diagnosis and treatment. JAMA. 2013;310:1721–9.
27. Slobod KS, Sandlund JT, Spiegel PH, Haik B, Hurwitz JL, Conley ME, et al. Molecular evidence of ocular Epstein-Barr virus infection. Clin Infect Dis. 2000;31:184–8.
28. Brown HH, Glasgow BJ, Holland GN, Foos RY. Cytomegalovirus infection of the conjunctiva in AIDS. Am J Ophthalmol. 1988;106:102–4.
29. Hara J, Fujimoto F, Ishibashi T, Seguchi T, Nishimura K. Ocular manifestations of the 1976 rubella epidemic in Japan. Am J Ophthalmol. 1979;87:642–5.
30. Wheaton AF, Timothy NH, Dossett JH, Manders EK. The surgical treatment of Molluscum contagiosum in a pediatric AIDS patient. Ann Plast Surg. 2000;44:651–5.
31. Zabawski Jr EJ, Cockerell CJ. Topical and intralesional cidofovir: a review of pharmacology and therapeutic effects. J Am Acad Dermatol. 1998;39:741–5.
32. Musso D, Nilles EJ, Cao-Lormeau VM. Rapid spread of emerging Zika virus in the Pacific area. Clin Microbiol Infect. 2014;20:O595–6.
33. Summers DJ, Acosta RW, Acosta AM. Zika virus in an American recreational traveler. J Travel Med. 2015;22:338–40.
34. Hovding G. Acute bacterial conjunctivitis. Acta Ophthalmol. 2008;86:5–17.
35. Sattar SA, Dimock KD, Ansari SA, Springthorpe VS. Spread of acute hemorrhagic conjunctivitis due to enterovirus-70: effect of air temperature and relative humidity on virus survival on fomites. J Med Virol. 1988;25:289–96.
36. Mannis MJ. Bacterial conjunctivitis. In: Tasman W, Jaeger E, editors. Duane's clinical ophthalmology, vol. 4. Philadelphia: JB Lippincott; 1990. p. 1–8.
37. Valenton MJ, Okumoto M. Toxin-producing strains of Staphylococcus epidermidis (albus). Isolates from patients with staphylococcic blepharoconjunctivitis. Arch Ophthalmol. 1973;89:186–9.
38. Gigliotti F, Williams WT, Hayden FG, Hendley JO, Benjamin J, Dickens M, et al. Etiology of acute conjunctivitis in children. J Pediatr. 1981;98:531–6.
39. Brook I. Anaerobic and aerobic bacterial flora of acute conjunctivitis in children. Arch Ophthalmol. 1980;98:833–5.
40. Kestelyn P, Bogaerts J, Stevens AM, Piot P, Meheus A. Treatment of adult gonococcal keratoconjunctivitis with oral norfloxacin. Am J Ophthalmol. 1989;108:516–23.
41. Lee JS, Choi HY, Lee JE, Lee SH, Oum BS. Gonococcal keratoconjunctivitis in adults. Eye (Lond). 2002;16:646–9.
42. Control CfD. Antibiotic-resistant strains of Neisseria gonorrhoeae. Policy guidelines for detection, management, and control. MMWR. 1987:244.
43. Rothenberg R, Voigt R. Epidemiologic aspects of control of penicillinase-producing Neisseria gonorrhoeae. Sex Transm Dis. 1988;15:211–6.
44. Wright HR, Turner A, Taylor HR. Trachoma. Lancet. 2008;371:1945–54.
45. Lietman T, Porco T, Dawson C, Blower S. Global elimination of trachoma: how frequently should we administer mass chemotherapy? Nat Med. 1999;5:572–6.

46. Bowman RJ, Jatta B, Cham B, Bailey RL, Faal H, Myatt M, et al. Natural history of trachomatous scarring in The Gambia: results of a 12-year longitudinal follow-up. Ophthalmology. 2001;108:2219–24.
47. Prevention CfDCa. Recommendations for the prevention and management of Chlamydia trachomatis infections. MMWR. 1993:RR-12.
48. Stenberg K, Mardh PA. Genital infection with Chlamydia trachomatis in patients with chlamydial conjunctivitis: unexplained results. Sex Transm Dis. 1991;18:1–4.
49. Hammerschlag MR. Chlamydial infections. J Pediatr. 1989;114:727–34.
50. Singal N, Rootman D. Chlamydial infections. In: Krachmer JH, Mannis MJ, Holland EJ, editors. Cornea. China: Mosby; 2011. p. 545–52.
51. Carithers HA. Cat-scratch disease. An overview based on a study of 1,200 patients. Am J Dis Child. 1985;139:1124–33.
52. Tobin EH, McDaniel H. Oculoglandular syndrome. Cat-scratch disease without the cat scratch. Postgrad Med. 1992;91:207–8, 10.
53. Ridder GJ, Boedeker CC, Technau-Ihling K, Sander A. Cat-scratch disease: otolaryngologic manifestations and management. Otolaryngol Head Neck Surg. 2005;132:353–8.
54. Gruzensky W. Parinaud's oculoglandular syndrome. In: Krachmer JH, Mannis MJ, Holland EJ, editors. Cornea. China: Mosby; 2011. p. 559–66.
55. Archer D, Bird A. Primary tuberculosis of the conjunctiva. Br J Ophthalmol. 1967;51: 679–84.
56. Spektor FE, Eagle Jr RC, Nichols CW. Granulomatous conjunctivitis secondary to Treponema pallidum. Ophthalmology. 1981;88:863–5.
57. Lindquist T. Ophthalmia neonatorum. In: Krachmer JH, Mannis MJ, Holland EJ, editors. Cornea. China: Mosby; 2011. p. 553–8.
58. Grosskreutz C, Smith LB. Neonatal conjunctivitis. Int Ophthalmol Clin. 1992;32:71–9.
59. Overall Jr JC, Glasgow LA. Virus infections of the fetus and newborn infant. J Pediatr. 1970;77:315–33.
60. Laga M, Plummer FA, Nzanze H, Namaara W, Brunham RC, Ndinya-Achola JO, et al. Epidemiology of ophthalmia neonatorum in Kenya. Lancet. 1986;2:1145–9.
61. Chandler JW, Rapoza PA. Ophthalmia neonatorum. Int Ophthalmol Clin. 1990;30:36–8.
62. Rours IG, Hammerschlag MR, Ott A, De Faber TJ, Verbrugh HA, de Groot R, et al. Chlamydia trachomatis as a cause of neonatal conjunctivitis in Dutch infants. Pediatrics. 2008;121: e321–6.
63. McCormack WM, Evrard JR, Laughlin CF, Rosner B, Alpert S, Crockett VA, et al. Sexually transmitted conditions among women college students. Am J Obstet Gynecol. 1981;139:130–3.
64. Gutierrez KM, Falkovitz Halpern MS, Maldonado Y, Arvin AM. The epidemiology of neonatal herpes simplex virus infections in California from 1985 to 1995. J Infect Dis. 1999;180:199–202.
65. Lepage P, Bogaerts J, Kestelyn P, Meheus A. Single-dose cefotaxime intramuscularly cures gonococcal ophthalmia neonatorum. Br J Ophthalmol. 1988;72:518–20.
66. de Toledo AR, Chandler JW. Conjunctivitis of the newborn. Infect Dis Clin North Am. 1992;6:807–13.
67. Whitley RJ. Herpes simplex virus infections of women and their offspring: implications for a developed society. Proc Natl Acad Sci U S A. 1994;91:2441–7.
68. Narayana S, McGee S. Bedside diagnosis of the 'red eye': a systematic review. Am J Med. 2015;128:1220–4.e1.
69. Rietveld RP, ter Riet G, Bindels PJ, Sloos JH, van Weert HC. Predicting bacterial cause in infectious conjunctivitis: cohort study on informativeness of combinations of signs and symptoms. BMJ. 2004;329:206–10.