



# A Comprehensive Review of Conjunctivitis: Causes, Symptoms, and Treatment

Keerthana N<sup>1</sup>, Natarajan P<sup>2</sup>, Koteeswaran K<sup>3</sup>, Jeyasheely J<sup>3</sup>

M. Pharm, Department of Pharmacology

Sankaralingam Bhuvaneshwari College of Pharmacy, Sivakasi<sup>1</sup>

M.Pharm, Ph.D., Department of Pharmacology

Sankaralingam Bhuvaneshwari College of Pharmacy, Sivakasi<sup>2</sup>

M. Pharm, Department of Pharmacology

Sankaralingam Bhuvaneshwari College of Pharmacy, Sivakasi<sup>3</sup>

## ABSTRACT

Conjunctivitis is a more common problem. Conjunctivitis is also called inflammation or infection of the conjunctiva. Start by providing a more detailed definition of conjunctivitis and its common symptoms. Viral conjunctivitis is the most common overall cause of infectious conjunctivitis, and to clarify, while viral conjunctivitis does not require treatment, other forms of conjunctivitis do. Most simple instances of bacterial conjunctivitis resolve in 1–2 weeks, making it the second most prevalent cause of infectious conjunctivitis. Provide more information about the specific signs and symptoms associated with bacterial conjunctivitis, such as mattering and eyelid adhesion. Explain that, while topical antibiotics can shorten the duration of bacterial conjunctivitis, treatment for other types of conjunctivitis is different. Emphasize the importance of seeking medical help for allergic conjunctivitis and provide more details about the treatments available. Itching is the most consistent sign of allergic conjunctivitis, and treatment consists of topical mast cell inhibitors and antihistamines. This review article will teach the reader about the etiology, pathophysiology, diagnosis, management, and treatment of conjunctivitis, as well as the use of antihistamines and mast cell stabilizers in allergic conjunctivitis, various antibiotics, and different antibiotics in infectious conjunctivitis.

**Keywords:** conjunctivitis, viral conjunctivitis, bacterial conjunctivitis, allergic conjunctivitis, mast cell inhibitors.

## 1. INTRODUCTION

The prevalence of conjunctivitis, popularly known as “Madras Eye” is rising rapidly, mostly among children, in Chennai [1]. affects patients of all ages [2], demographics [3], and socioeconomic classes [2]. The conjunctiva is the transparent, lubricating mucous membrane covering the outer surface of the eye [4]. There are several ways to categorise conjunctivitis; it may be classified based on severity, etiology, or extent of involvement of the surrounding tissue. The examination of conjunctivitis may reveal that it is infectious or non-infectious. Viral conjunctivitis, followed by bacterial conjunctivitis, is the most common cause of infectious conjunctivitis, while allergic and toxin-induced conjunctivitis are among the most common non-infectious aetiologies [5]. It is composed

of two parts: the "bulbar conjunctiva," which covers the globe, and the "tarsal conjunctiva," which lines the eyelid's inner surface. Conjunctivitis refers to the inflammation of the conjunctival tissue, pain, engorgement of the blood vessels, and ocular discharge. Acute conjunctivitis refers to a symptom duration of 3–4 weeks from presentation (usually only lasting 1-2 weeks), whereas chronic is defined as lasting more than four weeks [6] [7]. Viral conjunctivitis is responsible for the majority of infectious conjunctivitis, accounting for up to 75% of cases [2]. Adenovirus is the most common cause of this highly contagious acute conjunctival infection [2]. More than 80% of all acute cases are generally diagnosed by non-ophthalmologists, such as primary care providers, internists, pediatricians, and nurse practitioners [3]. This imparts an enormous economic burden on the health care system, causing a large portion of clinic visits in several medical specialties. The amount to be spent managing bacterial conjunctivitis in the United States is 857 million US dollars annually [8].

## 2. ETIOLOGY

Conjunctivitis is the more prevalent etiology of eye redness and discharge. The etiology of conjunctivitis could be infectious or non-infectious. The commonest causes of conjunctivitis are viral and bacterial conjunctivitis, and among non-infectious etiologies, the most common are allergic and toxin-induced conjunctivitis. The presence of bacteria, fungi, viruses, and parasites can all cause infectious conjunctivitis. Nonetheless, 80% of acute episodes of conjunctivitis are caused by viruses, with adenovirus being the most prevalent culprit. Adenoviruses are responsible for 65–90% of cases of viral conjunctivitis [9]. Other common viral pathogens are herpes zoster, herpes simplex, and enterovirus. Children get bacterial conjunctivitis far more frequently than adults do, and the germs that cause it change depending on the age group. Staphylococcal species, specifically *Staphylococcus aureus*, followed by *Haemophilus influenzae* and *Streptococcus pneumoniae*, are the most common causes in adults [10]. Though, in children, the disease is more often caused by *H. influenzae*, *S. pneumoniae*, and *Moraxella catarrhalis* [9]. Other bacterial causes include *N. gonorrhoeae*, *Corynebacterium diphtheriae*, and *Chlamydia trachomatis*. The most common cause of bacterial conjunctivitis in sexually active adults and neonates is *N. gonorrhoeae* [4, 11]. Allergens, local irritants, and toxins are responsible for non-infectious conjunctivitis.

## 3. PATHOPHYSIOLOGY

Conjunctivitis results from inflammation of the conjunctiva. Inflammation can be caused by infectious pathogens or non-infectious irritants. The result of this infection or irritation is injection or dilation of the conjunctival vessels, which results in edoema of the conjunctiva and classic redness, or hyperemia. The entire conjunctiva is commonly involved, and there is often discharge as well. The quality of the discharge varies depending on the causative agent. In bacterial conjunctivitis, the surface tissues of the eye are colonised by normal flora such as *Corynebacterium*, *Staphylococci*, and *Streptococci*. The primary defence mechanism against infection is the epithelial cover of the conjunctiva. Any breach in this barrier can cause infection [12]. Secondary defence mechanisms include immune reactions carried out by the tear film immunoglobulin and lysozyme, the conjunctival vasculature, and the rinsing actions of blinking and lacrimation [13].

## 4. HOW TO DIFFERENTIATE CONJUNCTIVITIS OF DIFFERENT ORIGINS

### 4.1 History and Physical Examination

"Madras eye" is an idiomatic term that has been used in India for the disease. A focused ocular examination and history are crucial for making relevant decisions about the treatment and management of any eye condition, including conjunctivitis. Eye discharge type and ocular symptoms can be used to estimate the cause of the conjunctivitis [14, 15]. A purulent or mucopurulent discharge, for example, is frequently caused by bacterial conjunctivitis, whereas a watery discharge is most often caused by viral conjunctivitis [14, 15]. Itching is also associated with allergic conjunctivitis [16, 17]. Although the clinical presentation is often nonspecific, patient symptoms and relying on the type of discharge do not always lead to an accurate diagnosis. Moreover, there is sometimes a dearth of scientific data connecting conjunctivitis signs and symptoms with the underlying cause [14]. For instance, 65% of patients in a study of those with culture-positive bacterial conjunctivitis reported burning, 58% reported itching, and 35% reported severe or no discharge at all [18], demonstrating the nonspecificity of the disease's signs and symptoms. In 2003, a large meta-analysis failed to find any clinical studies correlating the signs and symptoms of conjunctivitis with an underlying cause [14]. Later, when the same authors [14] carried out prospective research, they found that a combination of three signs—bilateral matting of the eyelids, absence of itching, and no previous conjunctivitis—strongly indicated bacterial conjunctivitis. Having both eyes matter and the lids be stuck in the morning was a stronger predictor for a positive bacterial culture result, and either itching or a previous episode of conjunctivitis made a positive bacterial culture result less likely [18]. Furthermore, the type of discharge (purulent, mucus, or watery) or other symptoms were not specific to any one type of conjunctivitis

[18, 19]. Although an ocular examination in primary care is frequently limited due to a lack of a slit lamp, useful information can be obtained with a simple penlight. The eye examination should focus on the assessment of the visual acuity, type of discharge, corneal opacity, shape and size of the pupil, eyelid swelling, and presence of proptosis [20].

## 4.2 Differential Diagnosis

Conjunctivitis is often diagnosed through laboratory testing, and clinical examinations are not always necessary unless the symptoms are severe [21, 22, 23]. Eye redness can be caused by a variety of emergent and non-emergent conditions. Potential causes of vision loss must be ruled out before accepting a conjunctivitis diagnosis. The differentials for conjunctivitis include: iritis, glaucoma, keratitis, scleritis, pterygium, episcleritis, corneal ulcers, foreign bodies, subconjunctival hemorrhage, blepharitis, hordeolum chalazion, overuse of contact lenses, and dry eyes. Localized redness (redness that does not involve the entire conjunctiva), ciliary flush, vision loss, increased intraocular pressure, moderate to severe pain, hypopyon, pupil asymmetry, hyphema, decreased pupil response, and difficulty opening or maintaining the eye open are a few signs and symptoms that suggest a diagnosis other than conjunctivitis. The clinician must not miss angle-closure glaucoma, iritis, foreign bodies, infectious keratitis, corneal ulcers, and scleritis, as they are sight-threatening and must have ophthalmologist management [24]. Typically, the redness in keratitis, angle closure glaucoma, and iritis will involve the entire bulbar conjunctiva but spare the tarsal conjunctiva. Moreover, patients presenting with glaucoma may have a ciliary flush, corneal opacity, a semi-dilated pupil, and increased intraocular pressure. In contrast, the symptoms of iritis, also known as anterior uveitis, include discomfort, photophobia, impaired vision, hypopyon, and a ciliary flush. The anterior chamber contains an inflammatory cell mass called the hypopyon, which is whitish-yellow in color. Even though hypopyon is frequently linked to iritis, it can also be caused by other diseases such as infected keratitis or a corneal ulcer.

In contrast to iritis, individuals with infective keratitis frequently report feeling like a foreign body and having difficulty opening or maintaining the eye. These symptoms are consistent with corneal attachment and can coexist with other corneal disorders such as abrasion, corneal ulcer, or foreign body [25]. Foreign body and orbital trauma can both result in hyphema, which refers to the collection of blood in the anterior chamber, which results in acute and permanent vision loss. The final emergent stipulation not to miss is scleritis. Scleritis typically presents with serious pain radiating to the face that is worse in the morning and/or at night and is related to photophobia, pain with extraocular movement, scleral edema, and tenderness to palpation [26]. Within 12 to 24 hours after presentation, an ophthalmologist should evaluate the patients with hypopyon, hyphema, suspected iritis, scleritis, keratitis, corneal ulcers, or corneal foreign bodies. Patients with suspected angle-closure glaucoma should visit an ophthalmologist as soon as feasible.

The remaining diagnoses are non-emergent. Episcleritis and pterygium are typically associated with localised redness, which differs from the diffuse redness seen in conjunctivitis. Blepharitis, dry eyes, and contact lens overuse are similar in presentation to allergic conjunctivitis. All commonly present with itching, a foreign body sensation, or burning. History of contact lens use, lack of blinking, allergies, and atopy are important in differentiating allergic conjunctivitis, contact lens overwear, and dry eyes, respectively. Crusting of the eyelids and marked edema and erythema of the eyelid margins are most consistent with blepharitis. Finally, a subconjunctival haemorrhage is due to bleeding of conjunctival vessels and appears as blood in the subconjunctival space rather than the typical injection or vessel dilation seen in conjunctivitis [24, 27, 28].

## 4.3 Infectious conjunctivitis

### 4.3.1 Viral conjunctivitis

#### 4.3.1.1 Epidemiology, cause, and presentation

These viruses cause up to 80% of all cases of acute conjunctivitis [29, 30, 31, 32, 33, 34] and [35]. The rate of clinical precision in diagnosing viral conjunctivitis is less than 50% compared with laboratory confirmation [16]. Numerous cases are misdiagnosed as bacterial conjunctivitis [16]. Adenoviruses are responsible for between 65% and 90% of cases of viral conjunctivitis [16]. They produce two of the common clinical entities associated with viral conjunctivitis: epidemic keratoconjunctivitis and pharyngoconjunctival fever [15]. Epidemic keratoconjunctivitis is more severe and presents with watery discharge, hyperemia, chemosis, and ipsilateral lymphadenopathy [36], whereas pharyngoconjunctival fever is characterised by the abrupt onset of pharyngitis, a high fever, bilateral conjunctivitis, and periauricular lymph node expansion [36]. Lymphadenopathy is distinguishable in up to 50% of viral conjunctivitis cases and is more prevalent in viral conjunctivitis compared with bacterial conjunctivitis [16].

### 4.3.1.2 Symptoms

Symptoms include tearing and itching, a recent upper respiratory tract infection, inferior palpebral conjunctival follicles, watery discharge, and tender periauricular lymphadenopathy [37, 38, 39, 40].

### 4.3.1.3 Prevention and treatment

Viral conjunctivitis secondary to adenoviruses is sorely contagious, and the prospect of transmission has been estimated to be 10% to 50% [41, 42]. The virus spreads through direct contact with medical instruments, contaminated fingers, swimming pool water, or personal items. In a single study, 46% of infected people had positive cultures grown from swabs of their hands [43]. Because of the high rates of transmission, strict instrument disinfection, hand washing, and isolation of the infected patients from the rest of the clinic have been commended [44]. Communicability and incubation are estimated to be five to twelve days and ten to fourteen days, respectively [42].

Although there is no cure, there are some symptoms that may be relieved by topical antihistamines, artificial tears, or cold compresses [20, 45]. Povidone-iodine 0.8% may be a potential option to diminish contagiousness in patients with adenoviral infections [46]. Possible antiviral medications are not useful [20, 45], and topical antibiotics are not indicated [47]. Topical antibiotics do not rescue against secondary infections, and their use may complicate the clinical presentation by causing toxicity and allergy, leading to delays in the diagnosis of other possible ocular diseases [16]. The use of antibiotic eye drops can increase the risk of infection spreading to the other eye due to contaminated droppers [16]. Antibiotic overuse also contributes to increased resistance [41]. Patients should be referred to an eye specialist if symptoms do not resolve after 7 to 10 days because of the risk of complications [48].

### 4.3.2 Herpes conjunctivitis

Herpes simplex virus comprises 1.3% to 4.8% of all cases of acute conjunctivitis [30, 31, 32, 33]. Herpes conjunctivitis caused by the virus is usually unilateral. The discharge is watery and thin, and multiple vesicular eyelid lesions may be present. Oral and topical antivirals are recommended to condense the course of the disease [20]. Topical corticosteroids should be avoided since they potentiate the virus and may cause harm [20, 49]. Herpes zoster virus, which causes shingles, can involve ocular tissue, specifically if the first and second branches of the trigeminal nerve are involved. The most frequently site of ocular involvement is the eyelids (45.8%), followed by the conjunctiva (41.1%) [50]. Uveitis and corneal complications may be present in 38.2% and 19.1% of cases, respectively [50]. Patients with suspected eyelid or eye involvement or those presenting with the Hutchinson sign (vesicles at the tip of the nose, which have high correlations with corneal involvement) should be referred for a thoroughgoing ophthalmic evaluation. Treatment usually consists of a combination of topical steroids and oral antivirals [51].

### 4.3.3 Bacterial Conjunctivitis

#### 4.3.3.1 Epidemiology, cause, and prevention

According to one study, the prevalence of bacterial conjunctivitis is 135 per 10,000 people [52]. Bacterial conjunctivitis can be contracted directly from infected people or through the abnormal proliferation of the native conjunctival flora [53]. Contaminated fingers [42] and contaminated fomites [54] are common routes of transmission. In addition, certain conditions, such as disruption of the natural epithelial barrier, compromised tear production, trauma, abnormalities of adnexal structures, and an immunosuppressed status, predispose to bacterial conjunctivitis [20]. The more common pathogens for bacterial conjunctivitis in adults are staphylococcal species, followed by *Haemophilus influenzae* and *Streptococcus pneumoniae* [55]. In children, the disease is often caused by *S pneumoniae*, *H influenzae*, and *Moraxella catarrhalis* [55]. The course of the disease commonly lasts 7–10 days [15].

Hyperacute bacterial conjunctivitis presents with an intense, copious purulent discharge and decreased vision. There is often accompanying eye pain on palpation, eyelid swelling, and periauricular adenopathy. It is often caused by *Neisseria gonorrhoeae* and carries a high risk for corneal involvement and subsequent corneal perforation [53]. Intramuscular ceftriaxone is used to treat *N. gonorrhoeae* caused acute conjunctivitis, and concurrent chlamydial infection should be managed accordingly [56]. can spread quickly, especially in certain

environments and with certain microorganisms. Children with conjunctivitis who do not have a fever or behavioural changes can usually return to school. More common in children than adults; more frequently observed between December and April [57].

Chronic bacterial conjunctivitis is used to describe any conjunctivitis lasting more than 4 weeks, with *Moraxella lacunata*, *Staphylococcus aureus*, and enteric bacteria being the more common causes in this setting [15]. Ophthalmologic consultation should be sought for management.

Signs and symptoms include purulent or mucopurulent discharge, red eyes, and chemosis [53]. The periods of communicability and incubation are estimated to be 1–7 days and 2–7 days, respectively [42]. Bilateral matting of the eyelids, lack of itching, adherence of the eyelids, and no history of conjunctivitis are strong positive predictors of bacterial conjunctivitis [18]. Serious purulent discharge should always be cultured, and gonococcal conjunctivitis should be considered [20]. Conjunctivitis not responding to standard antibiotic therapy in sexually active patients authorises a chlamydial evaluation [47]. The prospect of bacterial keratitis is high in contact lens wearers, who should be treated with topical antibiotics [42] and referred to an ophthalmologist [19]. A patient wearing contact lenses should be asked to quickly remove them [19]. Sporadically, this occurs with an ear infection [1].

#### 4.3.3.2 Usage of antibiotics in bacterial conjunctivitis

At least 60% of cases of culture-proven or suspected acute bacterial conjunctivitis are self-limiting within 1-2 weeks of presentation [42]. Even though topical antibiotics reduce the duration of the disease, no differences have been observed in outcomes between placebo groups and treatment. In a vast meta-analysis [58], consisting of an assessment of 3673 patients in 11 randomised clinical trials, there was an approximately 10% multiplier in the rate of clinical improvement compared with that of the placebo for patients who received either 2 to 5 days or 6 to 10 days of antibiotic treatment. No consequential sight-threatening outcomes were reported in any of the placebo groups [59]. Some highly virulent bacteria, such as *N gonorrhoeae*, *S pneumoniae*, and *H influenzae*, can penetrate an intact host defence more easily and cause the most serious damage [53]. Topical antibiotics appear to be more effective in patients who have positive bacterial culture results. In a large systemic review, they were found to be effective at plenty both the clinical and microbiological cure rate in the group of patients with culture-proven bacterial conjunctivitis; therefore, only an improved microbial cure rate was observed in the group of patients with clinically suspected bacterial conjunctivitis [35]. Other studies found no notable difference in the clinical cure rate when the frequencies of the administered antibiotics were moderately changed [55, 60].

##### 4.3.3.2.1 Antibiotics options:

All broad-spectrum antibiotic eye drops appear, in general, to be effective in treating bacterial conjunctivitis. There are no notable differences in achieving clinical cure between any of the broad-spectrum topical antibiotics. Factors that influence antibiotic choice are patient allergies, local availability, resistance patterns, and cost.

##### 4.3.3.2.2 Alternatives to Immediate Antibiotic Therapy:

To our knowledge, no studies have been conducted to evaluate the efficacy of ocular decongestants, warm compresses, or topical saline for treating bacterial conjunctivitis [55]. Topical steroids should be avoided. Because of the risk of potentially prolonging the course of the disease and amplifying the infection [20].

##### 4.3.3.2.3 Summary of Recommendations for Managing Bacterial Conjunctivitis

In conclusion, benefits of antibiotic treatment involve quicker recovery, a decrease in transmissibility [16], and an early return to school [61]. Antibiotics are not used in simple cases of bacterial conjunctivitis due to their side effects. So, in cases of simple conjunctivitis, a wait-and-see policy, no therapy, and rapid treatment all seem to be viable options. Purulent or mucopurulent bacterial conjunctivitis is effectively treated by antibiotic therapy in patients who have a distinct indisposition, who wear contact lenses [42, 47], who are immunocompromised, and who have suspected gonococcal and chlamydial conjunctivitis.

### 4.3.3.3 BACTERIAL CONJUNCTIVITIS: A SPECIAL TOPIC

#### 4.3.3.3.1 Methicillin-Resistant *S. Aureus* Conjunctivitis

It is estimated that 3%–64% of ocular staphylococcal infections are methicillin-resistant due to *S. aureus* conjunctivitis. This condition is becoming more common, and the organisms are resistant to many antibiotics [62]. Patients with suspected cases must be referred to an ophthalmologist and treated with fortified vancomycin [63].

#### 4.3.3.3.2 Chlamydial Conjunctivitis

It is estimated that chlamydial conjunctivitis accounts for 1.8%–5.6% of all acute conjunctivitis [29, 30, 31, 32, 64]. The majority of cases are unilateral, with genital infection present [48]. Conjunctival hyperemia, lymphoid follicles, and mucopurulent discharge formation [65] are hallmarks of this condition. Discharge is frequently purulent or mucopurulent [47]. Despite the fact that patients frequently present with mild symptoms for weeks to months, concurrent genital chlamydial infection occurs in upto 54% of men and 74% of women [66]. The disease is frequently acquired via oculogenital spread or other intimate contact with infected individuals; in newborns, the eyes can be infected after vaginal delivery by infected mothers [20]. Treatment with systemic antibiotics such as oral doxycycline and azithromycin is efficacious; patients and their sexual partners must be treated, and a co-infection with gonorrhoea must be explored. No information supports the use of topical antibiotic therapy in addition to systemic treatment [20]. Infants with chlamydial conjunctivitis need systemic therapy because more than 50% can have concurrent lung, nasopharynx, and genital tract infections [20].

#### 4.3.3.3.3 Gonococcal conjunctivitis

Conjunctivitis caused by *N. gonorrhoeae* is a frequent source of hyperacute conjunctivitis in neonates, sexually active young adolescents, and adults [53]. Treatment consists of both oral and topical antibiotics. An increased risk of corneal perforation is linked to *Neisseria gonorrhoeae* [19]. The recommended treatment for gonococcal conjunctivitis is ceftriaxone 1 gramme intramuscularly (IM) [46].

#### 4.3.3.3.4 Conjunctivitis is secondary to trachoma

It is caused by *Chlamydia trachomatis* subtypes A through C and is the main cause of blindness, affecting 40 million people worldwide in areas accompanied by poor hygiene [67, 68]. Ocular discomfort and mucopurulent discharge may be the presenting signs and symptoms of this condition. Late complications such as scarring of the eyelid, cornea, and conjunctiva may lead to loss of vision. A single oral azithromycin dose of 20 mg/kg is effective. Patients may also be treated with topical antibiotic ointments for 6 weeks (i.e., erythromycin or tetracycline). Systemic antibiotics other than azithromycin, such as erythromycin or tetracycline for 3 weeks, may be used alternatively [67, 68].

### 4.4 Non-infectious Conjunctivitis

#### 4.4.1 Allergic conjunctivitis

##### 4.4.1.1 Prevalence and causes:

Allergic conjunctivitis is the inflammatory response of the conjunctiva to allergens such as animal dander, pollen, and other environmental antigens [69] and affects up to 40 percent of the population in the United States [69]. Only about 10 percent of individuals with allergic conjunctivitis seek medical attention, and the condition is often underdiagnosed [70]. Itching and redness are the most consistent symptoms [69]. Seasonal allergies are to blame for the majority of allergic conjunctivitis cases, which typically have bilateral symptoms, which can be presented with a watery or mucoid discharge [71], and allergic conjunctivitis, which comprises 90 percent of all allergic conjunctivitis in the United States [72].

Ocular allergies can affect the entire ocular surface, including the conjunctiva, eyelids, and cornea. Ocular allergic conditions have been divided into three main categories by Leonardi et al. based on the immunological mechanism that leads to the final clinical picture: [73] IgE-mediated reactions, such as seasonal allergic conjunctivitis (SAC) and perennial allergic conjunctivitis (PAC); combined IgE and non-IgE-mediated reactions, such as AKC and VKC; and non-IgE-mediated reactions, including giant papillary conjunctivitis (GPC) and contact dermatitis conjunctivitis (CDC) [74].

#### 4.4.1.2 Symptoms

Allergic: symptoms of itching or burning; history of allergies or atopy; watery discharge; edematous eyelids; conjunctival papillae; no periauricular lymphadenopathy [37, 38, 39, 40].

#### 4.4.1.3 Treatment

Treatment consists of avoidance of the allergen [75] and the use of artificial tears or saline solution to physically dilute and remove the allergens [69]. Antihistamines, topical decongestants [75], mast cell stabilisers [75], corticosteroids [72], non-steroidal anti-inflammatory drugs [76, 77] and others may be indicated. In a large systemic review, both antihistamines and mast cell stabilisers were superior to placebo in diminishing the symptoms of allergic conjunctivitis; researchers also found that antihistamines were better than mast cell stabilisers in providing short-term benefits [75]. The vasoconstrictor naphazoline and antihistamine antazoline should be avoided because they both can cause rebound hyperemia [75]. Steroids should be used with discretion and judiciously. Topical steroids are related to the formation of cataracts and can cause a surge in eye pressure, leading to glaucoma.

#### 4.5 Drug, chemical, and toxin-induced conjunctivitis

A variety of topical medications, such as topical antiviral medications, antibiotic eye drops, and lubricating eye drops, can induce allergic conjunctival responses, mostly because of the presence of benzalkonium chloride in eye drop preparations [78]. The cessation of receiving the offending agent results in symptoms of resolution [20].

#### 4.6 Systemic diseases associated with conjunctivitis

A variety of systemic diseases, including mucous membrane pemphigoid, Kawasaki disease, Sjögren syndrome [79], Stevens-Johnson syndrome [80], and carotid cavernous fistula [81], can present with signs and symptoms of conjunctivitis, such as conjunctival discharge and redness. Therefore, other causes should be considered in patients presenting with conjunctivitis. For example, patients with a low-grade carotid cavernous fistula of systemic disease can present with chronic conjunctivitis recalcitrant to medical therapy, which, if left untreated, can lead to death.

### 5. OMNIOUS SIGNS

As recommended by the American Academy of Ophthalmology [20], patients with conjunctivitis who are evaluated by non-ophthalmologist health care practitioners should be referred quickly to an ophthalmologist if any of the following develops: visual loss, severe purulent discharge, moderate or severe pain, corneal involvement, conjunctival scarring, recurrent episodes of conjunctivitis, lack of response to therapy, or history of herpes simplex virus eye disease. In addition, the following patients should be considered for referral: patients requiring steroids, contact lens wearers, and those with photophobia. Patients should be referred to an ophthalmologist if there is no improvement after one week [48].

### 6. THE SIGNIFICANCE OF AVOIDING ANTI-BIOTIC/STEROIDAL COMBINATION DROPS

Combination drops containing steroids or steroid drops should not be used routinely. Steroids can increase the latency of the adenoviruses, prolonging the course of viral conjunctivitis. In addition, if an undiagnosed corneal ulcer secondary to herpes, fungus, or bacteria is present, steroids can worsen the condition, leading to blindness and corneal melt [52, 64].

### 7. CONCLUSION

Most viral conjunctivitis cases are caused by adenoviruses. In viral conjunctivitis, there is no role for the use of topical antibiotics, and they should be avoided owing to the fact that they have adverse treatment effects. Viral conjunctivitis is diagnosed by using a rapid antigen test, and abstaining from the inappropriate use of antibiotics is an appropriate strategy. Nonherpetic viral conjunctivitis, followed by bacterial conjunctivitis, is the more common cause of infectious conjunctivitis. Bacterial pathogens are isolated in only 50% of cases of suspected conjunctivitis, and 60% of bacterial conjunctivitis is self-limited and does not require medical treatment, as clinically proved. Cultures are beneficial in some cases, but they do not respond to therapy, such as in cases of

hyperacute conjunctivitis and suspected chlamydial conjunctivitis. People who wear contact lenses, have eye pain and mucopurulent discharge, have uncertain cases of chlamydial and gonococcal conjunctivitis, or have preexisting ocular surface disease are commonly advised to use topical antibiotics. The advantages of antibiotics are quick resolution of the disease, quick return to jobs and school, and the possibility of diminished complications from conjunctivitis. Approximately 40% of the population is affected by allergic conjunctivitis, but only small proportions require medical care. The majority of cases of allergic conjunctivitis are caused by seasonal allergies, and allergic conjunctivitis is treated with mast cell inhibitors, antihistamines, and, in some cases, topical steroids. Steroids must be used prudently and only after a thorough ophthalmologic examination has been performed to rule out corneal involvement or herpetic infection, both of which can worsen with steroids. Approximately 1% of all patient visits to a primary care clinician are conjunctivitis-related, and the estimated cost of bacterial conjunctivitis alone is \$377 million to \$857 million annually. Relying on the signs and symptoms alone frequently leads to an inaccurate diagnosis. Physicians must be alert and not overlook sight-threatening conditions with similarities to conjunctivitis.

## REFERENCES

- [1] San Francisco, CA: American Academy of Ophthalmology Preferred Practice Pattern Cornea/External Diseases Committee. Conjunctivitis\_PPP\_2018external\_icon. American Academy of Ophthalmology. 2018; P95-169
- [2] Solano D, Fu L, Czyz CN. Viral conjunctivitis. In: *Stat Pearls*. Treasure Island, FL: Stat Pearls Publishing (2021). Available online at: <https://www.ncbi.nlm.nih.gov/book>
- [3] Shekhawat NS, Shtein RM, Blachley TS, Stein JD, Antibiotic Prescription Fills for Acute Conjunctivitis among Enrollees in a Large United States Managed Care Network. *Ophthalmology*. 2017 Aug; [PubMed PMID: 28624168]
- [4] Alfonso SA, Fawley JD, Alexa Lu X, Conjunctivitis. Primary care. 2015 Sep; [PubMed PMID: 26319341]
- [5] Ryder EC, Benson S. Conjunctivitis. In: *Stat Pearls*. Treasure Island (FL): Stat Pearls Publishing LLC; 2020.
- [6] de Laet C, Dionisi-Vici C, Leonard JV, McKiernan P, Mitchell G, Monti L, de Baulny HO, Pintos-Morell G, Spiekerkötter U, Recommendations for the management of tyrosinaemia type 1. *Orphanet journal of rare diseases*. 2013 Jan 11; [PubMed PMID: 23311542]
- [7] Sati A, Sang wan VS, Basu S, Porphyria: varied ocular manifestations and management. *BMJ case reports*. 2013 May 22; [PubMed PMID: 23704443]
- [8] Smith AF, Waycaster C, Estimate of the direct and indirect annual cost of bacterial conjunctivitis in the United States. *BMC ophthalmology*. 2009 Nov 25; [PubMed PMID: 19939250]
- [9] Azari AA, Barney NP, Conjunctivitis: a systematic review of diagnosis and treatment. *JAMA*. 2013 Oct 23 [PubMed PMID: 24150468]
- [10] Høvdig G, Acute bacterial conjunctivitis. *Acta ophthalmologica*. 2008 Feb; [PubMed PMID: 17970823]
- [11] Shields T, Sloane PD, A comparison of eye problems in primary care and ophthalmology practices. *Family medicine*. 1991 Sep-Oct; [PubMed PMID: 1936738]
- [12] O'Callaghan RJ, The Pathogenesis of Staphylococcus aureus Eye Infections. *Pathogens (Basel, Switzerland)*. 2018 Jan 10; [PubMed PMID: 29320451]
- [13] Chu WK, Choi HL, Bhat AK, Jhanji V, Pterygium: new insights. *Eye (London, England)*. 2020 Jun [PubMed PMID: 32029918]
- [14] Rietveld RP, van Weert HC, ter Riet G, Bindels PJ. Diagnostic impact of signs and symptoms in acute infectious conjunctivitis: systematic literature search. *BMJ*. 2003; 327(7418):789. [PubMed: 14525879]
- [15] Yannof, J.; Duker, JS. Editors. *Ophthalmology*. 2nd ed. Mosby; Spain: 2004. Disorders of the conjunctiva and limbus; p. 397-412.
- [16] O'Brien TP, Jeng BH, McDonald M, Raizman MB. Acute conjunctivitis: truth and misconceptions. *Curr Med Res Opin*. 2009; 25(8):1953–1961. [PubMed: 19552618]
- [17] Morrow GL, Abbott RL. Conjunctivitis. *Am Fam Physician*. 1998; 57(4):735746. [PubMed: 9490996]
- [18] Rietveld RP, ter Riet G, Bindels PJ, Sloos JH, van Weert HC. Predicting bacterial cause in infectious conjunctivitis. *BMJ*. 2004; 329(7459):206 210. [PubMed: 15201195]
- [19] Tarabishy AB, Jeng BH. Bacterial conjunctivitis: a review for internists. *Cleve Clin J Med*. 2008; 75(7):507–512. [PubMed: 18646586]



- [20] American Academy of Ophthalmology. Cornea/External Disease Panel. Preferred Practice Pattern Guidelines: Conjunctivitis-Limited Revision. American Academy of Ophthalmology; San Francisco, CA: 2011.
- [21] Martin M, Turco JH, Zegans ME, Facklam RR, Sodha S, Elliott JA, et al. An outbreak of conjunctivitis due to atypical streptococcus pneumoniae. *N Engl J Med.* (2003) 348:1112–21. doi: 10.1056/NEJMoa022521
- [22] Crum NF, Barrozo CP, Chapman FA, Ryan MAK, Russell KL. An outbreak of conjunctivitis due to a novel unencapsulated *Streptococcus pneumoniae* among military trainees. *Clin Infect Dis.* (2004) 39:1148–54. Doi: 10.1086/424522
- [23] Outbreak of Bacterial Conjunctivitis at a College — New Hampshire, January–March, 2002. Available online at: <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5110a1.htm> (accessed April 25, 2021).
- [24] Wright C, Tawfik MA, Waisbourd M, Katz LJ, Primary angle-closure glaucoma: an update. *Acta ophthalmologica.* 2016 May; [PubMed PMID: 26119516]
- [25] Austin A, Lietman T, Rose-Nussbaumer J, Update on the Management of Infectious Keratitis. *Ophthalmology.* 2017 Nov [PubMed PMID: 28942073]
- [26] Sainz de la Maza M, Molina N, Gonzalez-Gonzalez LA, Doctor PP, Tauber J, Foster CS, Clinical characteristics of a large cohort of patients with scleritis and Episcleritis. *Ophthalmology.* 2012 Jan [PubMed PMID: 21963265]
- [27] Mahmood AR, Narang AT, Diagnosis and management of the acute red eye. *Emergency medicine clinics of North America.* 2008 Feb; [PubMed PMID: 18249256]
- [28] Brandt MT, Haug RH, Traumatic hyphema: a comprehensive review. *Journal of oral and maxillofacial surgery: official journal of the American Association of Oral and Maxillofacial Surgeons.* 2001 Dec; [PubMed PMID: 11732035]
- [29] Stenson S, Newman R, Fedukowicz H. Laboratory studies in acute conjunctivitis. *Arch Ophthalmol.* 1982; 100(8):1275–1277. [PubMed: 7049134]
- [30] Rönnerstam R, Persson K, Hansson H, Renmarker K. Prevalence of chlamydial eye infection in patients attending an eye clinic, a VD clinic, and in healthy persons. *Br J Ophthalmol.* 1985; 69(5): 385–388. [PubMed: 3838901]
- [31] Harding SP, Mallinson H, Smith JL, Clearkin LG. Adult follicular conjunctivitis and neonatal ophthalmia in a Liverpool eye hospital, 1980-1984. *Eye (Lond).* 1987; 1(pt 4):512–521. [PubMed: 2832220]
- [32] Uchio E, Takeuchi S, Itoh N, et al. 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(9):968–972. [PubMed: 10966946]
- [33] Woodland RM, Darougar S, Thaker U, et al. Causes of conjunctivitis and keratoconjunctivitis in Karachi, Pakistan. *Trans R Soc Trop Med Hyg.* 1992; 86(3):317–320. [PubMed: 1412664]
- [34] Fitch CP, Rapoza PA, Owens S, et al. Epidemiology and diagnosis of acute conjunctivitis at an inner-city hospital. *Ophthalmology.* 1989; 96(8):1215–1220. [PubMed: 2797725]
- [35] Epling J. Bacterial conjunctivitis. *Clin Evid (Online).* 2010; 2010
- [36] Mahmood AR, Narang AT. Diagnosis and management of the acute red eye. *Emerg Med Clin North Am.* 2008; 26(1):35–55. vi. [PubMed: 18249256]
- [37] Leibowitz HM, The red eye. *The New England journal of medicine.* 2000 Aug 3; [PubMed PMID: 10922425]
- [38] Mahmood AR, Narang AT, Diagnosis and management of the acute red eye. *Emergency medicine clinics of North America.* 2008 Feb; [PubMed PMID: 18249256]
- [39] Puri LR, Shrestha GB, Shah DN, Chaudhary M, Thakur A, Ocular manifestations in herpes zoster ophthalmicus. *Nepalese journal of ophthalmology: a biannual peer-reviewed academic journal of the Nepal Ophthalmic Society: NEPJOPH.* 2011 Jul-Dec [PubMed PMID: 21876592]
- [40] Liesegang TJ, Herpes zoster ophthalmicus natural history, risk factors, clinical presentation, and morbidity. *Ophthalmology.* 2008 Feb [PubMed PMID: 18243930]
- [41] Kaufman HE. Adenovirus advances: new diagnostic and therapeutic options. *Curr Opin Ophthalmol.* 2011; 22(4):290–293. [PubMed: 21537185]
- [42] Høvdig G. Acute bacterial conjunctivitis. *Acta Ophthalmol.* 2008; 86(1):5–17. [PubMed: 17970823]
- [43] Azar MJ, Dhaliwal DK, Bower KS, et al. Possible consequences of shaking hands with your patients with epidemic keratoconjunctivitis. *Am J Ophthalmol.* 1996; 121(6):711–712. [PubMed: 8644817]
- [44] Warren D, Nelson KE, Farrar JA, et al. A large outbreak of epidemic keratoconjunctivitis: problems in controlling nosocomial spread. *J Infect Dis.* 1989; 160(6):938–943. [PubMed: 2555421]
- [45] Skevaki CL, Galani IE, Pararas MV, et al. Treatment of viral conjunctivitis with antiviral drugs. *Drugs.* 2011; 71(3):331–347. [PubMed: 21319870]

- [46] Monnerat N, Bossart W, Thiel MA, [Povidone-iodine for treatment of adenoviral conjunctivitis: an in vitro study]. *Klinische Monatsblätter für Augenheilkunde*. 2006 May [PubMed PMID: 16705502]
- [47] Cronau H, Kankanala RR, Mauger T. Diagnosis and management of red eye in primary care. *Am Fam Physician*. 2010; 81(2):137–144. [PubMed: 20082509]
- [48] Leibowitz HM. The red eye. *N Engl J Med*. 2000; 343(5):345–351. [PubMed: 10922425]
- [49] Wilhelmus KR. Diagnosis and management of herpes simplex stromal keratitis. *Cornea*. 1987; 6(4):286–291. [PubMed: 3319411]
- [50] Puri LR, Shrestha GB, Shah DN, Chaudhary M, Thakur A. Ocular manifestations in herpes zoster ophthalmicus. *Nepal J Ophthalmol*. 2011; 3(2):165–171. [PubMed: 21876592]
- [51] Sy A, McLeod SD, Cohen EJ, et al. Practice patterns and opinions in the management of recurrent or chronic herpes zoster ophthalmicus. *Cornea*. 2012; 31(7):786–790. [PubMed: 22269677]
- [52] Owen CG, Shah A, Henshaw K, et al. Topical treatments for seasonal allergic conjunctivitis: systematic review and meta-analysis of efficacy and effectiveness. *Br J Gen Pract*. 2004; 54(503): 451–456. [PubMed: 15186569]
- [53] Mannis, MJ. Plotnik, RD. Bacterial conjunctivitis. In: Tasman, W.; Jaeger, EA. editors. *Duanes Ophthalmology on CD-ROM*. Lippincott Williams & Wilkins; 2006.
- [54] 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(3):289–296. [PubMed: 2844979]
- [55] Epling J, Smucny J. Bacterial conjunctivitis. *Clin Evid*. 2005; 2(14):756–761. [PubMed: 16620434]
- [56] Workowski KA, Berman S, Centers for Disease Control and Prevention (CDC). Sexually transmitted diseases treatment guidelines, 2010. *MMWR Recomm Rep*. 2010; 59(RR-12):1–110. [PubMed: 21160459]
- [57] Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *American Academy of Pediatrics. Management and prevention of infectious diseases: Exclusion and return to care*. external icon In: *Red Book: 2018 Report of the Committee on Infectious Diseases*. 31st ed. Elk Grove Village, IL: American Academy of Pediatrics. 2018; 125–36.
- [58] Sheikh A, Hurwitz B, van Schayck CP, McLean S, Nurmatov U. Antibiotics versus placebo for acute bacterial conjunctivitis. *Cochrane Database Syst Rev*. 2012; 9:CD001211.
- [59] Sheikh A, Hurwitz B. Topical antibiotics for acute bacterial conjunctivitis: Cochrane systematic review and meta-analysis update. *Br J Gen Pract*. 2005; 55(521):962–964. [PubMed: 16378567]
- [60] Szaflik J, Szaflik JP, Kaminska A, Levofloxacin Bacterial Conjunctivitis Dosage Study Group. Clinical and microbiological efficacy of levofloxacin administered three times a day for the treatment of bacterial conjunctivitis. *Eur J Ophthalmol*. 2009; 19(1):1–9. [PubMed: 19123142]
- [61] Ohnsman CM. Exclusion of students with conjunctivitis from school: policies of state departments of health. *J Pediatr Ophthalmol Strabismus*. 2007; 44(2):101–105. [PubMed: 17410961]
- [62] Shanmuganathan VA, Armstrong M, Buller A, Tullo AB. External ocular infections due to methicillin-resistant *Staphylococcus aureus* (MRSA). *Eye (Lond)*. 2005; 19(3):284–291. [PubMed: 15375372]
- [63] Freidlin J, Acharya N, Lietman TM, et al. Spectrum of eye disease caused by methicillin-resistant *Staphylococcus aureus*. *Am J Ophthalmol*. 2007; 144(2):313–315. [PubMed: 17659970]
- [64] Shields T, Sloane PD. A comparison of eye problems in primary care and ophthalmology practices. *Fam Med*. 1991; 23(7):544–546. [PubMed: 1936738]
- [65] Katusic D, Petricek I, Mandic Z, et al. Azithromycin vs. doxycycline in the treatment of inclusion conjunctivitis. *Am J Ophthalmol*. 2003; 135(4):447–451. [PubMed: 12654359]
- [66] Postema EJ, Remeijer L, van der Meijden WI. Epidemiology of genital chlamydial infections in patients with chlamydial conjunctivitis. *Genitourin Med*. 1996; 72(3):203–205. [PubMed: 8707324]
- [67] Kumaresan JA, Mecaskey JW. The global elimination of blinding trachoma: progress and promise. *Am J Trop Med Hyg*. 2003; 69(5) (suppl):24–28. [PubMed: 14692677]
- [68] Avery, RK. Baker, AS. *Albert and Jakobiec's Principle and Practice of Ophthalmology*. 3rd ed. Saunders Elsevier; Philadelphia, PA: 2008. Chlamydial disease; p. 4791–4801.
- [69] Bielory BP, O'Brien TP, Bielory L. Management of seasonal allergic conjunctivitis: guide to therapy. *Acta Ophthalmol*. 2012; 90(5):399–407. [PubMed: 22067457]
- [70] Rosario N, Bielory L. Epidemiology of allergic conjunctivitis. *Curr Opin Allergy Clin Immunol*. 2011; 11(5):471–476. [PubMed: 21785348]

- [71] American Academy of Ophthalmology Cornea/External Disease Preferred Practice Pattern Panel. Conjunctivitis Preferred Practice Pattern®. San Francisco, CA: American Academy of Ophthalmology; 2018. Available from <https://www.aao.org/preferredpractice-pattern/conjunctivitis-ppp-2018>. Accessed November 26, 2018.
- [72] Bielory L. Allergic conjunctivitis: the evolution of therapeutic options. *Allergy Asthma Proc.* 2012; 33(2):129–139. [PubMed: 22525389]
- [73] Leonardi A, De Dominicis C, Motterle L. Immunopathogenesis of ocular allergy: a schematic approach to different clinical entities. *Curr Opin Allergy Clin Immunol* 2007; 7:429–435.
- [74] Wong AH, Barg SS, Leung AK. Seasonal and perennial allergic conjunctivitis. *Recent Pat Inflamm Allergy Drug Discov* 2014;8:139–153.
- [75] Owen CG, Shah A, Henshaw K, et al. Topical treatments for seasonal allergic conjunctivitis: systematic review and meta-analysis of efficacy and effectiveness. *Br J Gen Pract.* 2004; 54(503): 451–456. [PubMed: 15186569]
- [76] Yaylali V, Demirlenk I, Tatlipinar S, et al. Comparative study of 0.1% olopatadine hydrochloride and 0.5% ketorolac tromethamine in the treatment of seasonal allergic conjunctivitis. *Acta Ophthalmol Scand.* 2003; 81(4):378–382. [PubMed: 12859265]
- [77] Donshik PC, Pearlman D, Pinna J, et al. Efficacy and safety of ketorolac tromethamine 0.5% and levocabastine 0.05%: a multicenter comparison in patients with seasonal allergic conjunctivitis. *Adv Ther.* 2000; 17(2):94–102. [PubMed: 11010060]
- [78] Baudouin C. Allergic reaction to topical eyedrops. *Curr Opin Allergy Clin Immunol.* 2005; 5(5): 459–463. [PubMed: 16131924]
- [79] Newburger JW, Takahashi M, Gerber MA, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a statement for health professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. *Pediatrics.* 2004; 114(6):1708–1733. [PubMed: 15574639]
- [80] Gregory DG. The ophthalmologic management of acute Stevens-Johnson syndrome. *Ocul Surf.* 2008; 6(2):87–95. [PubMed: 18418506]
- [81] Miller NR. Diagnosis and management of dural carotid-cavernous sinus fistulas. *Neurosurg Focus.* 2007; 23(5):13