

## Conjunctivitis in unusual populations: A review of rare cases and challenges in diagnosis and management

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World Journal of Advanced Research and Reviews, 2023, 19(03), 1326–1336

Publication history: Received on 16 August 2023; revised on 26 September 2023; accepted on 28 September 2023

Article DOI: <https://doi.org/10.30574/wjarr.2023.19.3.1999>

### Abstract

Conjunctivitis is defined as any inflammatory condition of the membrane that borders the eyelids and covers the exposed sclera. It is the most frequent reason for "red eye." The word "conjunctivitis" refers to a wide range of illnesses that manifest as conjunctival inflammation. Hyper acute, acute, or chronic inflammations are all possible, and their causes might be infectious or noninfectious. Conjunctival injection, sometimes known as "red eye," is a common presentation for various ocular illnesses and can represent up to 1% of all visits to the primary care physician. The presence of these two symptoms may identify 59% of instances with "serious eye conditions," including anterior uveitis and keratitis. Anisocoria and moderate photophobia were substantially related with "serious eye conditions. Before beginning antibiotic therapy, it is preferable to collect swabs from the discharge. The swabs are then cultured in the lab by placing them in different growth media. It is recommended to use Sabouraud agar plates to detect fungus in immunocompromised individuals and those with persistent blepharitis. Additionally, anaerobic culture plates may be beneficial, particularly for individuals who have a history of prior surgery or trauma. A very contagious kind of viral conjunctivitis is acute hemorrhagic conjunctivitis (AHC). It presents with a feeling of a foreign body, excessive weeping, and edema of the eyelids, dilated conjunctival vessels, chemosis, and subconjunctival hemorrhage. When a person is sexually active as an adult or a newborn, Neisseria gonorrhoeae is frequently the cause of hyperacute conjunctivitis. Conjunctiva, eyelids, and cornea can all be impacted by ocular allergies along with other ocular surface areas. Ocular allergy disorders have been divided into three main categories by Leonardi et al based on the immunological mechanism responsible for the final clinical appearance. Patients suffering with viral conjunctivitis have quick onset foreign body feeling, red eyes, irritation, light sensitivity, burning, and watery discharge. Patients with bacterial conjunctivitis have all of the aforementioned symptoms as well as mucopurulent discharge and matting of the eyelids upon awakening. For individuals with conjunctivitis, general supportive therapies include allergen avoidance (pollens, animals, and dust mites), the use of artificial tears, proper hand hygiene, cold compresses, avoidance of eye rubbing, and mild cleanser to remove any allergens or debris.

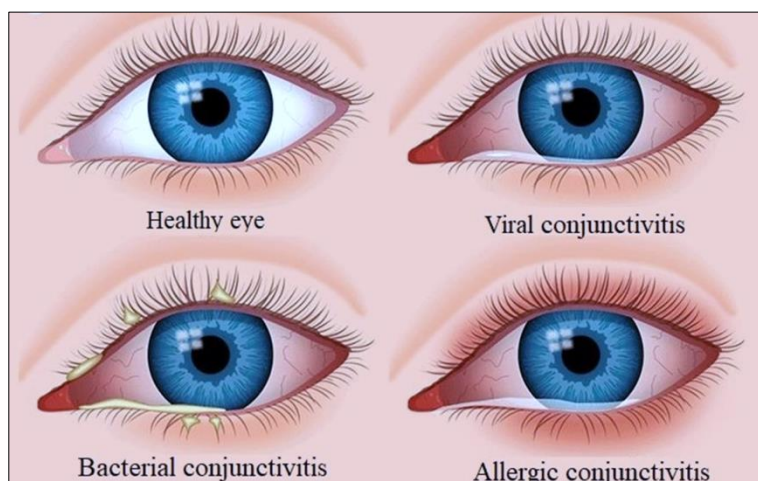
**Keywords:** Acute Hemorrhagic Conjunctivitis; Conjunctiva; Viral Conjunctivitis; Conjunctival Inflammation

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## 1. Introduction

Conjunctivitis is defined as any inflammatory condition of the membrane that borders the eyelids and covers the exposed sclera. It is the most frequent reason for "red eye." The word "conjunctivitis" refers to a wide range of illnesses that manifest as conjunctival inflammation. Hyper acute, acute, or chronic inflammations are all possible, and their causes might be infectious or noninfectious [1]. 40% of this American test group had episodes of ocular allergies, according to the most current Third National Health and Nutrition Examination Survey [2]. AKC and VKC are very different from SAC and PAC in terms of their clinical and pathophysiological characteristics, despite having some similar allergy markers [3][4]. Numerous variables, including genetics, environmental factors, ocular microbial flora, and immunological modulation, contribute to the symptoms and indications of ocular allergy. The decrease of signs, symptoms, and sequelae, such as erythema, chemosis, conjunctival edema, and edema of the eyelids, are among the treatment's objectives. Allergens are blocked by the brows, eyelids, and eyelashes, and a healthy tear film also aids in removing allergens from the ocular surface. Allergy conjunctivitis may get worse if any of these natural defenses are compromised [4].

Conjunctivitis is a broad classification of disorders that afflict people of all ages, from various socioeconomic backgrounds, and of both sexes. Conjunctivitis has been listed as one of the most typical reasons for patient self-referral, despite the fact that there are no accurate statistics that show the frequency or prevalence of all types of conjunctivitis [5]. According to reports, antibiotic eye drops are prescribed for approximately 60% of patients with acute conjunctivitis, and the vast majority of these doctors are not ophthalmologists. For instance, 36% of patients who saw an ophthalmologist received antibiotic eye drops, compared to 68% of those who saw a doctor in an emergency room. It's interesting to note that individuals with better socioeconomic class were more likely to get and fill a prescription for conjunctivitis [6]. There are many ways to categorize conjunctivitis, including etiology, chronicity, severity, and amount of surrounding tissue involvement. An infectious or non-infectious agent may be the cause of conjunctivitis. While allergies and toxin-induced conjunctivitis are among the most frequent non-infectious etiologies, viral conjunctivitis and bacterial conjunctivitis are the two most frequent infectious conjunctivitis causes. Acute conjunctivitis is defined as having a sudden onset and lasting four weeks or less, sub-acute conjunctivitis, or chronic conjunctivitis lasting longer than four weeks [7]. Conjunctivitis can also be caused by other systemic conditions, such as immune-related diseases like Reiter's, Stevens-Johnson syndrome (SJS), and keratoconjunctivitis sicca in rheumatoid arthritis, nutritional deficiencies like a lack of vitamin A, and congenital metabolic syndromes like Richner-Hanhart syndrome and porphyria. Other "red eye" conditions include acute angle closure glaucoma, uveitis, endophthalmitis, carotid cavernous fistula, cellulitis, and anterior segment tumors must be recognized from conjunctivitis in order to prevent significant vision loss or death [8][9].



**Figure 1** Types of Conjunctivitis (Pink Eye)

## 2. Viral conjunctivitis

Adenovirus infection of the ocular surface frequently causes viral conjunctivitis, which is the most common underlying cause of infectious conjunctivitis [10][11]. Research has been done on the varicella zoster virus (VZV), enterovirus, and other viruses that may less frequently be the cause of viral conjunctivitis [12].

### **2.1. Virus-induced conjunctivitis**

Adenoviruses are to blame for up to 90% of viral conjunctivitis cases worldwide. Human adenoviruses (HAdV) may be divided into seven distinct species (HAdV-A through HAdV-G), with HAdV-D species having the most members and the strongest connection with viral conjunctivitis. Recent advances in HAdV genome sequencing have revealed these genotypes. [13][14]. Pharyngoconjunctival fever (PCF), which is brought on by HAdV types 3, 4, and 7, is most certainly the most frequent adenovirus infection in children [15][16]. This condition typically includes fever, pharyngitis, per auricular lymphadenopathy, and acute follicular conjunctivitis. As a result of the interplay between pro-inflammatory cytokines and the conjunctival vasculature, other abnormalities of the ocular surface include edema, hyperemia, and conjunctival petechial hemorrhages [17].

Another tissue that might suffer negative effects in EKC is the cornea. The virus's ability to replicate in the corneal epithelium can result in localized regions of epithelial opacities and superficial punctate keratopathy [18]. According to some statistics, the likelihood of transmission of adenovirus conjunctivitis is up to 50% [19][20]. One study found that up to 46% of patients with viral conjunctivitis had their hands used to obtain a positive viral culture. The virus can spread through shared personal items, polluted water in swimming pools, contaminated medical instruments, and contaminated fingers [21]. Due of viral conjunctivitis's high contagiousness, frequent hand washing, thorough medical equipment disinfecting, and the segregation of patients with conjunctivitis from the getting some slumber in the medical professional's office recommended [22]. Although there is no one proven treatment for viral conjunctivitis, regular use of artificial tears, ocular drops, or cold compresses appears to be soothing. Numerous clinical signs and symptoms are present in this circumstance [23][24].

### **2.2. Herpes conjunctivitis**

HSV infection is thought to be the root cause of 1.3–4.8% of all occurrences of acute conjunctivitis [25][26][27]. Herpes zoster can cause ocular involvement in 41.1% of cases, eyelid lesions in 45.8% of cases, uveitis in 38.2% of cases, and conjunctivitis in 19.1% of cases. This is especially true if the first and second branches of the trigeminal nerve are affected [28][29].

### **2.3. A severe case of hemorrhagic conjunctivitis**

A very contagious kind of viral conjunctivitis is acute hemorrhagic conjunctivitis (AHC). It presents with a feeling of a foreign body, excessive weeping, and edema of the eyelids, dilated conjunctival vessels, chemosis, and sub-conjunctival hemorrhage [30][31][32]. AHC is believed to spread mostly by hand-to-eye contact and infected fomites, similar to other kinds of conjunctivitis [33]. Large-scale outbreaks are primarily contained through medical intervention, but precautions are also taken to safeguard the most vulnerable populations, including children, the elderly, pregnant women, and people with compromised immune systems. These precautions include frequent hand washing and limiting contact with the ill [32].

### **2.4. Bacterial conjunctivitis**

Direct contact with infected people can cause bacterial conjunctivitis, as can aberrant expansion of the natural conjunctival flora [34]. Additionally, those who have decreased tear production, disruption of the normal epithelial barrier, aberrant adnexal structures, trauma, and immunosuppressed condition are more susceptible to develop bacterial conjunctivitis [23][35]. Homophiles influenza, Staphylococcus species, Streptococcus species, Moraxella catarrhalis, and gram-negative gut bacteria are the most common causes of acute bacterial conjunctivitis [36]. However, highly pathogenic bacteria have the capacity to seriously injure the ocular surface and the eye [34].

### **2.5. Conjunctivitis from chlamydia**

Chlamydia trachomatis may cause a variety of ocular surface diseases, including trachoma, neonatal conjunctivitis, and inclusion conjunctivitis. Trachoma is caused by serotypes A, B, Ba, and C, whereas adult inclusion conjunctivitis and newborn conjunctivitis are caused by serotypes D-K [37]. According to estimates, genital infections can occur simultaneously in up to 54% of males and 74% of women [38]. Neonatal conjunctivitis caused by Chlamydia trachomatis is more frequent than gonococcal conjunctivitis (GC) is regarded as the most prevalent viral cause of global prevalence of newborn conjunctivitis [39][40].

### **2.6. Conjunctivitis caused by gonorrhea (GC)**

Neisseria gonorrhoea is commonly the cause of hyper acute conjunctivitis in people who are sexually active, whether they are adults or newborns [34]. Having N. gonorrhoea in the eye increases the risk of developing corneal perforation [36]. When newborns exhibit conjunctivitis between days 2 and 5 following delivery, GC should be taken into account

as the likely culprit [41]. An eye exam may indicate conjunctival injection, chemosis, and substantial mucopurulent discharge in newborn and non-neonatal populations. A sensitive globe and periauricular lymphadenopathy may also accompany this kind of conjunctivitis [41].

### 2.7. Inflammatory conjunctivitis

Conjunctiva, eyelids, and cornea can all be impacted by ocular allergies along with other ocular surface areas. Ocular allergy illnesses were divided into three main categories by Leonardi et al. based on the immunological mechanism underlying the final clinical presentation [42]. Seasonal allergic conjunctivitis (SAC) and perennial allergic conjunctivitis (PAC) are IgE-mediated responses, whereas VKC and AKC are mixed IgE and non-IgE mediated responses. Giant papillary conjunctivitis (GPC) and contact dermatitis conjunctivitis (CDC) are examples of non-IgE-mediated reactions [43].

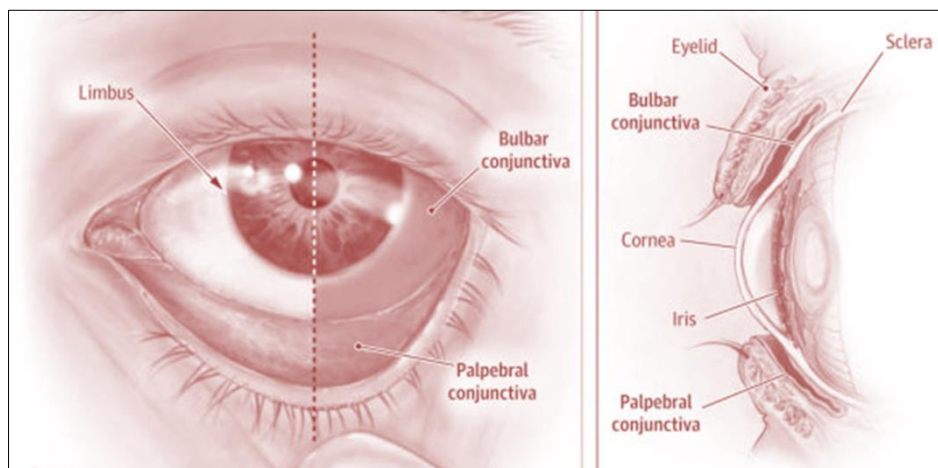


Figure 2 Regular conjunctival anatomy

### 3. Signs and symptoms of conjunctivitis

Patients with viral conjunctivitis experience an abrupt start of watery discharge, red eyes, discomfort, light sensitivity, and a foreign body feeling. Patients with bacterial conjunctivitis exhibit all of the aforementioned symptoms, as well as mucopurulent discharge and matting of the eyelids upon awakening [44].

Table 1 Signs and Symptoms of Conjunctivitis

S. No.	Signs/Symptoms	Allergic	Bacterial	Viral	References
1.	Hyperemia	Mild to moderate	Moderate to severe	Mild to moderate	[45]
2.	Discharge	Mucoid, ropy	Mucopurulent "glued eyes"	Watery (may be thicker on awaking)	[46]
3.	Pain	No	Mild to severe	Mild to none	[25]
4.	Itch	Yes	Mild	Some	
5.	Vision change	None	Blurry to diminished	Possible impairment	
6.	Ocular involvement	Bilateral	Initially unilateral	Bilateral; second eye involved less severe	

### 4. Diagnosis or clinical examination

Conjunctival injection, sometimes referred to as "red eye," is a frequent symptom of a number of ocular diseases and accounts for up to 1% of all visits to the primary care physician [47]. Conjunctivitis or subconjunctival hemorrhage are examples of more benign conditions that only affect the conjunctival tissue that "red eye" can be a secondary symptom

of, while uveitis, keratitis, or scleritis are examples of more serious conditions that "red eye" can be the presenting sign for. In the past, it was believed that more serious ocular issues were associated with aberrant vision, excruciating discomfort, and photophobia [47]. These two signs might indicate the existence of "serious eye conditions," such as anterior uveitis and keratitis, in 59% of cases. Moderate photophobia and anisocoria were strongly associated with "serious eye conditions."

**Table 2** A prescription to help identify the primary causes of conjunctivitis

Clinical history and examination results	The most likely causes	References
<b>Alarming signs and symptoms</b>		[48]
Vision loss, excruciating discomfort, painful pupillary response, anisocoria, and orbital signs	Glaucoma, parasellar pathology, uveitis, scleritis, keratitis, glaucoma, or orbital pathology	[49]
<b>Chronicity</b>		
Sudden onset, less than four weeks in duration	Acute systemic reactions (SJS/TEN), allergic conjunctivitis, and infectious conjunctivitis	[50]
Chronic course, sneaky onset	Systemic disease-related conjunctivitis, toxic conjunctivitis, and allergic conjunctivitis	[51]
Recurring subject	Conjunctivitis brought on by an allergy or a systemic illness	[52]
<b>Connected symptoms</b>		[20]
Arthritis, or pharyngeal lesions, genito-perineal involvement, and skin lesions	Conjunctivitis linked to viral and systemic disorders	
<b>Drug history</b>		
Long-term use of eye drops	Conjunctivitis that is toxic or allergic	
Beginning a systemic medicine recently	Acute systemic reactions (SJS/TEN)	

SJS: Stevens - Johnson syndrome, TEN: Toxic Epidermal Necrolysis

#### 4.1. How are laboratory results useful to us?

Patients with conjunctivitis may have discharge samples taken from their eyes and sent for microbiological testing. When gonococcal or chlamydial infection is suspected, when conjunctivitis is persistent, when it is resistant to therapy, when there is a substantial purulent discharge, or when conjunctivitis in a newborn is considered to be contagious, conjunctival cultures are typically only carried out in these circumstances [46]. It is preferable to collect swabs from the discharge before taking antibiotics. The swabs are then grown in the lab using different growth media. Sabouraud agar plates are suggested for the identification of fungi in immunocompromised individuals and people with chronic blepharitis. Additionally, anaerobic culture plates may be beneficial, particularly for those with a history of prior surgery or trauma [53]. If antimicrobial therapy has already started, it should be stopped 48 hours before acquiring cultures. In a five-year analysis of 138 pediatric ocular surface infections, coagulase-negative staphylococci, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* were the most prevalent pathogens [54]. Despite the fact that preliminary studies on in-office rapid antigen testing for adenoviruses demonstrates up to 94% specificity and 89% sensitivity [53].

#### 5. Treatment options for conjunctivitis

General supportive therapy for people with conjunctivitis include avoiding allergens (pollens, animals, and dust mites), using artificial tears, maintaining good hand hygiene, using cold compresses to the affected eye, and using a gentle cleaner to get rid of any allergens or debris [55][56]. The majority of viral conjunctivitis patients just require supportive care, which is sufficient. Topical and oral antivirals (acyclovir, valacyclovir, and famciclovir) are recommended to shorten the course of herpes simplex conjunctivitis [57].

**Table 3** Treatment Options for Conjunctivitis

S. No.	Drug Type	Mechanism	Examples (Drug)	Adverse Effects	References
	Artificial tears	They serve as a barrier by diluting allergens and inflammatory mediators and flushing them away from the surface.	--	--	[58] [59]
	Topical antihistamines	Histamine is competitively and reversibly blocked at H1 and H2 ocular receptors, relieving acute feelings of itching and redness.	Antazoline, emedastine (Emadine), levocabastine (Livostin)	Increased lacrimation, eye irritation	[46] [60]
	Topical vasoconstrictors	Offers momentary relief from erythema and vascular injection; can be taken alone or in conjunction with antihistamines	Naphazoline (Vasocon), phenylephrine, oxymetazoline, tetrahydrozoline (Visine)	Ineffective against VKC and AKC; may lead to dependence with rebound conjunctival injection, irritation, and tachyphylaxis	[25] [61] [62]
	Mast cell stabilizer	Do not cure current symptoms; they are used as a preventative measure; the mechanism is unknown, However, in order to prevent the release of histamine and other chemotactic chemicals, it reduces mast cell degranulation	Cromolyn sodium, lodoxamine (Alomide), nedocromil (Alocril)	Does not treat acute symptoms	
	Combination antihistamine/mast cell stabilizer	Dual-action medicines that provide rapid histamine receptor antagonism as well as long-term disease prevention-altering the mast cell's stability	Azelastine (Optivar, Optilast), epinastine (Elestat, Relestat), ketotifen (Zaditor), olopatadine (Pataday, Patanol)	Stinging, burning, bitter taste, headache, and sedation are mild and transient	
	Topical NSAIDs	Inhibit the formation of prostaglandins and thromboxanes via acting on the cyclooxygenase pathway.	Ketorolac (Acular), flurbiprofen (Ocufen), diclofenac (Voltaren Ophtha), bromfenac (Prolensa), nepafenac (Ilevro)	May cause discomfort upon instillation	
	Topical corticosteroids	Prevents the synthesis of arachidonic acid, hence inhibiting the cyclooxygenase and lipoxygenase metabolic pathways; used to treat severe instances of chronic ocular	Loteprednol etabonate (Lotemax and Alrex), fluorometholone (Flarex), dexamethasone,	Increased intraocular pressure, secondary infection, and delayed wound healing and	

		allergies that are resistant to traditional therapy	prednisolone for severe cases	for cataract formation; lowest possible dose and concentration should be used for the shortest possible period	
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### 5.1. Traditional medicine to treat conjunctivitis

For thousands of years, medicinal plants have been utilized as a traditional form of therapy for a wide range of human illnesses in many different regions of the world. In rural areas of developing countries, herbal materials continue to be the primary source of treatments. Herbal eye drops are a polyherbal mixture used for degenerative ocular problems, anti-inflammatory, and antihistaminic effects [63][64]. It is difficult to treat eye issues in the medical system without causing any negative side effects from chemical medications. But these days, with the aid of natural medications, it is only marginally successful. Due to their effectiveness, lack of side effects, and inexpensive cost, attempts have been undertaken to find novel medicinal plants from various sources. In the world, 200 plants have been found to help cure eye conditions, and Traditional Indian Medicine has categorized different plant species for their ophthalmic qualities [65][66][67][68].

Many plants are employed in ocular problems in the Ayurvedic School of medicine, including those found in the Charak Samhita, Sushrut Samhita, Ras Tarang, Bhavprakasha, Nayan Drastam, and Astanghriday. These texts were written in ancient India. Numerous eye conditions and diseases, including conjunctivitis, glaucoma, and cataracts, have been extensively described in Ayurveda (an Indian school of medicine). Their causes and therapies have also been discussed. The medicinal plants used in the treatment of eye problems are described in certain sources. Reviews of plants used in the treatment of eye problems may include the common name, scientific name, family, component utilized, and reference of the plant [69][70][71].

## 6. Prevention of conjunctivitis

The most crucial element in avoiding infectious conjunctivitis is personal hygiene. Even though bacterial conjunctivitis is not prevalent, it can be transmitted through upper respiratory tract diseases or by touching. Hands can spread gonococcal infection from the genital tract or urine to the eye. There has been a major violation of proper hygiene here. Pregnant women may use antibiotics, antiseptics, tetracycline eye ointment, or povidone iodine drops to avoid ophthalmia neonatorum. Adenovirus-related viral conjunctivitis, in example, can quickly spread over a neighborhood or a building like a school. It can spread via hands, face cloths, towels, and applanation tonometer's, to name a few. Because it is so contagious, it must be controlled by imposing strict hygiene standards. It is impossible to prevent allergic conjunctivitis unless the patient is able to change his or her environment or place of employment, or identify and get rid of the allergen that is causing the allergy, such pollen or animal fur. Allergies caused by drugs can be cured by stopping the medication. Three of the most common culprits for these adverse drug reactions include atropine, neomycin, and eye drop preservatives. Conjunctivitis can be prevented by practicing good hand hygiene, avoiding touching your eyes with your hands, using fresh towels and washcloths every day, refraining from sharing towels and washcloths, routinely cleaning or replacing pillows, and refraining from sharing eye makeup or other personal eye care products. [72][73][74][75].

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A membrane or pseudo membrane that is present can be peeled at the slit lamp to enhance patient comfort and avoid scarring. These membranes can be peeled with jeweler's forceps or a cotton swab covered in topical anesthetic. Using steroids topically may aid with symptom relief. However, they could extend the amount of time the virus sheds. Patients should be advised that because their symptoms are so infectious, they should hold off on going back to work or school until they have subsided. People who are using steroids may continue to discharge the virus even when they have no outward signs of disease. Only those with severe conjunctival injection or subepithelial infiltrates that have affected vision should use steroids [78][79][80].



## 7. Conclusion

The conjunctiva, the membrane that covers the eyelids and sclera, becomes inflamed when conjunctivitis, a common eye ailment, develops. It can have various causes, including viral and bacterial infections, allergies, and other underlying health conditions. This article provides an overview of different types of conjunctivitis, their signs and symptoms, diagnostic approaches, treatment options, and prevention measures. Viral conjunctivitis, often caused by adenovirus infection, is highly contagious and presents with symptoms such as redness, irritation, and watery discharge. Allergic conjunctivitis, on the other hand, is triggered by allergens and is associated with itching, redness, and excessive tearing. Diagnosing conjunctivitis involves a clinical examination, medical history, and sometimes laboratory tests, such as conjunctival cultures in cases of suspected infection. Treatment options include artificial tears, topical antihistamines, vasoconstrictors, mast cell stabilizers, and in severe cases, topical corticosteroids. Traditional herbal remedies are also used in some cultures for treating conjunctivitis. Prevention of infective conjunctivitis emphasizes personal hygiene, including regular handwashing and avoiding contact with contaminated objects. Allergic conjunctivitis prevention often involves identifying and avoiding allergens. Additionally, pregnant women can take preventive measures to avoid neonatal conjunctivitis caused by infections.

conjunctivitis is a common and diverse eye condition with various causes and treatment options. Early diagnosis and appropriate management can help alleviate symptoms and prevent complications. Additionally, maintaining good hygiene practices and identifying and avoiding triggers can contribute to preventing conjunctivitis in some cases

## Compliance with ethical standards

### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

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