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Review article on: Conjunctivitis

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➤ Abstract:

Around the world, conjunctivitis is a prevalent illness seen in ophthalmology clinics. Alarming indicators of more serious intraocular disorders, including as excruciating discomfort, blurred vision, and painful pupillary reactions, must be taken into account when treating suspected cases of conjunctivitis. In addition, patients with unusual results and a chronic course should have a comprehensive physical exam and medical and ophthalmology history taken. Conjunctival involvement in a systemic disease may be detected based on concurrent physical exam findings and pertinent history. The most frequent underlying cause of conjunctivitis is still viral conjunctivitis. Although less common, bacterial conjunctivitis is the second most common kind of infectious conjunctivitis.

Nearly half of the population experiences allergic conjunctivitis, which is characterized by itchiness, mucoid discharge, chemosis, and edema of the eyelids. In a patient with conjunctival irritation and discharge, prolonged use of eye drops with preservatives suggests that toxic conjunctivitis is the underlying cause of the condition. A early diagnosis, accurate classification of the various etiologies, and suitable treatment are all necessary for effective conjunctivitis care.

➤ **Keywords:**

Allergic, Bacterial, Conjunctivitis, COVID-19, Coronavirus, Viral, Toxic.

➤ **Introduction:**

Inflammation and swelling of the conjunctival tissue, engorgement of the blood vessels, ocular discharge, and discomfort are all symptoms of conjunctivitis. Conjunctivitis affects a large number of people globally and is one of the most common causes of office visits to general medical and ophthalmology clinics. It has been stated that non-ophthalmologists such as internists, family medicine doctors, pediatricians, and nurse practitioners diagnose more than 80% of all acute instances of conjunctivitis. This places a significant financial strain on the healthcare system and accounts for a significant amount of office visits across several medical specialties. Treatment for bacterial conjunctivitis is thought to cost \$857 million yearly in the United States alone. (1)

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. (2) It's interesting to note that patients with higher socioeconomic class were more likely to get and fill a prescription for conjunctivitis.

Conjunctivitis can be categorized in a number of ways, including according to the cause, how severe it is, how long it lasts, and how much surrounding tissue is affected. Conjunctivitis can have an infectious or non-infectious origin. The most frequent causes of infectious conjunctivitis are viral conjunctivitis and bacterial conjunctivitis, while allergy and toxin-induced conjunctivitis are among the most prevalent non-infectious etiologies. Conjunctivitis can be classified as acute, subacute, or chronic depending on how long it has been present. Acute conjunctivitis has a rapid start and a duration of four weeks or less. (3)

Additionally, conjunctivitis may be classified as severe when the symptoms are severe and there is a lot of mucopurulent discharge coming from the eyes. In viral keratoconjunctivitis and blepharconjunctivitis, respectively, the surrounding tissue, such as the margins of the eyelids and the cornea, may also be affected by conjunctivitis.

➤ **Types Of Conjunctivitis:**

Type	Conjunctival	Itching	Discharge	Lymphadenopathy	Associated Fever and Sore Throat
Viral Adenoviral HSV VZV	Follicular	Minimal	Watery	Common (~50%)	Common
Bacterial Nongonococcal Gonococcal	Papillary	Minimal	Purulent Mucopurulent Hyperpurulent	Uncommon	Occasionally
Chlamydial	Follicular	Minimal	Mucopurulent	Common	No
Allergic	Papillary with chemosis	Severe	Watery Mucoid	None	No

Note: Data from these studies.^{1,2,18}

Abbreviations: HSV, herpes simplex virus; VZV, varicella (herpes) zoster virus.

(4) **Table 1****1. Viral Conjunctivitis**

The majority (65–90%) of instances of viral conjunctivitis are caused by adenoviruses, although 1.3–4.8% of cases of acute conjunctivitis are brought on by the herpes simplex virus (HSV). Varicella (herpes zoster) virus (VZV) and Molluscum contagiosum are two more viruses linked to conjunctivitis. (5) (6) Adenoviruses are non-enveloped viruses with a low susceptibility to cleaning. Due in part to the virus's ability to live for weeks at room temperature in a desiccated form, adenoviral conjunctivitis is extremely infectious. The virus may spread directly through shared objects or indirectly through physical contact, with a 10–50% chance of transmission. The signs and symptoms of adenoviral conjunctivitis resolve after 5 to 14 days, and the condition is self-limiting. Frequently, the illness begins as unilateral and progresses to affecting both eyes. (7) (8)

Numerous ocular infections, such as pharyngoconjunctival fever and epidemic keratoconjunctivitis (EKC; patient images are displayed in Figure 1), are linked to specific adenovirus serotypes. Pharyngoconjunctivitis frequently shows symptoms on both sides, including fever and enlarged periauricular lymph nodes. EKC, which is characterized by fluid discharge, edema, and redness, as well as involvement of lymph nodes on both sides of the neck, is more severe due to the negative impact it can have on visual acuity. Due to the high contagiousness of EKC, asymptomatic people who have acquired the illness run the risk of unintentionally spreading the virus. (9)

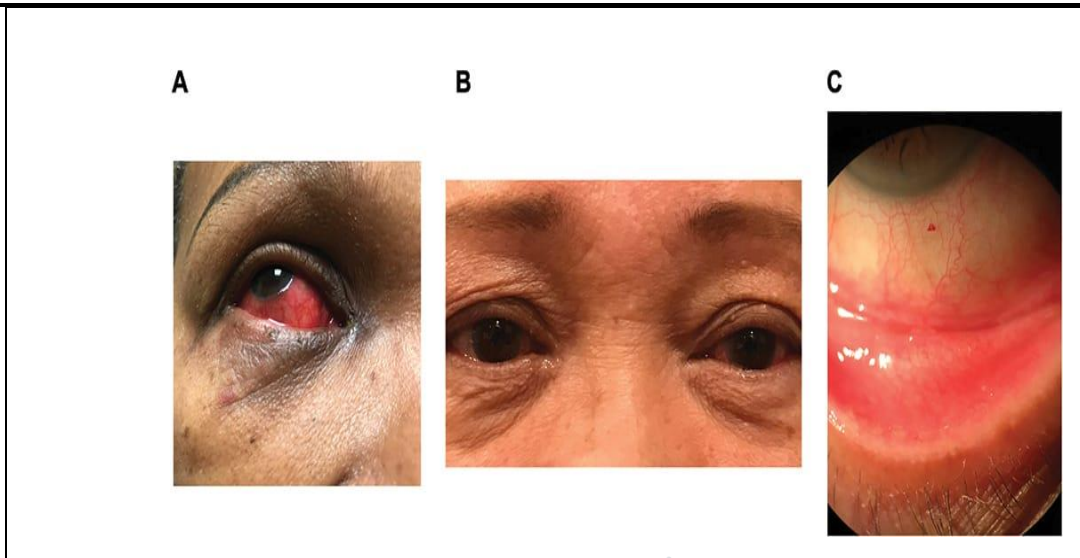


Figure 1.keratoconjunctivitis

The risk of developing VZV conjunctivitis increases if you have active chicken pox or have previously had shingles or chicken pox. The appearance of this disease is frequently unilateral. Eyelid, conjunctival, corneal, or uveal inflammation are recognizable symptoms of VZV conjunctivitis. Increased intraocular pressure, which in some circumstances may reach dangerous levels, is a symptom of uveitis. In most cases, VZV conjunctivitis resolves in a few days. As topical antivirals alone are ineffective in treating VZV conjunctivitis, a combination of oral antivirals and topical corticosteroids might be used with caution to manage VZV conjunctivitis. (10) (11)

2.Bacterial conjunctivitis.

Bacterial conjunctivitis is more frequent in children, despite being less common in adults than viral conjunctivitis. Direct contact with infected people can cause bacterial conjunctivitis, as can an abnormal expansion of the natural conjunctival flora. Common transmission pathways include contaminated fomites, oculogenital spread, and infected fingers. (12) Additional factors that enhance the risk of developing bacterial conjunctivitis include impaired tear production, disturbance of the natural epithelial barrier, aberrant adnexal structures, trauma, and immunosuppressed status.

Staphylococcus species, Haemophilus influenza, Streptococcus species, Moraxella catarrhalis, and gram-negative gut bacteria are the most frequent causes of acute bacterial conjunctivitis. Minor epidemics may develop in younger children as a result of H. influenzae or S. pneumoniae. In addition to mild conjunctival hyperemia and increased ocular discharge, acute bacterial conjunctivitis presents with these symptoms (Figure 2.)



Figure 2.bacterial conjunctivitis.

Sticky eyelids and itching may be present in about 90% of those who have bacterial conjunctivitis, according to several studies; these findings are followed by less common signs and symptoms include purulent discharge and ocular burning. An upper respiratory tract infection and acute otitis media may coexist with H. influenza conjunctivitis. (13)There doesn't appear to be a substantial difference between different antibiotics in terms of providing a clinical cure for bacterial conjunctivitis, and all broad-spectrum antibiotic eye drops appear to be helpful in treating the condition. (14)

Local antibiotic availability, patient allergies, resistance tendencies, and cost are influencing factors. A comprehensive systematic analysis found that when patients had positive bacterial cultures, topical antibiotics were more successful in achieving clinical and microbiological cure.However, when alternate antibiotic administration frequencies were used, there was no discernible change in the clinical cure rate. Topical steroids should not be used since they prolong the sickness' duration and exacerbate the infection. (15) (16)

Some systemic and dermatological conditions associated with conjunctivitis.

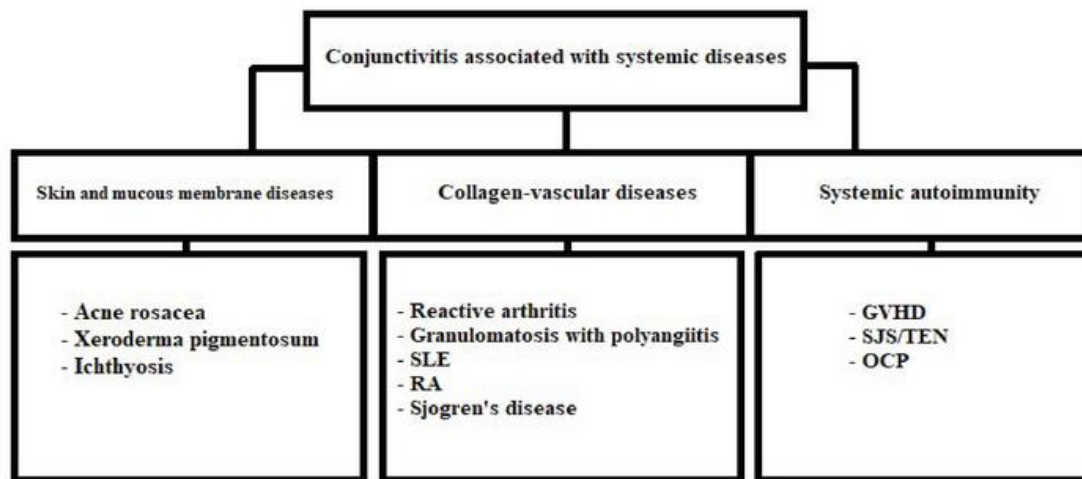


Table 2.conjunctivitis associated with systemic disease (17)

3.Chlamydial conjunctivitis.

Numerous ocular surface infections, such as trachoma, newborn conjunctivitis, and inclusion conjunctivitis, can be brought on by Chlamydia trachomatis. While trachoma is brought on by serotypes A, B, Ba, and C, newborn conjunctivitis and adult inclusion conjunctivitis are caused by serotypes D-K. According to reports, inclusion conjunctivitis accounts for 1.8–5.6% of all cases of acute conjunctivitis. (18) Most instances are unilateral and also involve a vaginal infection. Patients frequently exhibit moderate mucopurulent discharge and follicular conjunctivitis that lasts for weeks to months at the time of presentation. According to reports, up to 54% of men and 74% of women may have several genital infections. Oculogenital spread is a common way for the disease to spread. Topical antibiotics should not be added to systemic antibiotic treatments such as oral azithromycin and doxycycline since they do not work as well. It is necessary to treat sexual partners and search for signs of gonorrhea coinfection. (19) (20) (21)

Trachoma, the most common infectious cause of blindness in the world, affects 40 million people worldwide and is more common in places with inadequate hygiene. Although mucopurulent discharge is the initial presenting symptom, scarring of the cornea, conjunctiva, and eyelids may cause vision loss in the later stages. In addition to oral tetracycline or erythromycin for three weeks, a single dosage of oral azithromycin (20 mg/kg) is particularly efficient. Additionally, patients may receive a six-week course of treatment with topical antibiotic ointments including tetracycline and erythromycin. (22) Chlamydia can result from passing through an infected birth canal to cause conjunctivitis in babies. The acute phase is marked by purulent discharge, erythema, and edema of the eyes and conjunctiva and commonly starts between days 5 and 14 after vaginal delivery. newborn conjunctivitis secondary to C. trachomatis is thought to be the most common infectious cause of newborn conjunctivitis globally, outpacing gonococcal conjunctivitis (GC) in terms of prevalence. (23) Although the chlamydial conjunctivitis has a moderate course, cases that go untreated have been observed to leave damage on the cornea and/or conjunctiva. It is significant to highlight that newborns exposed to chlamydia have a 20% chance of developing pneumonia; of these, 50% show signs of a history of conjunctivitis. (23) (24)

According to a recent meta-analysis, systemic erythromycin therapy, administered orally four times daily at a dose of 50 mg/kg for two weeks, is preferable to topical antibiotic therapy alone. Erythromycin outperformed azithromycin in a recent trial examining the treatment of neonatal chlamydial conjunctivitis; nevertheless, the risk of pyloric stenosis associated with erythromycin use may limit its therapeutic use in neonates in the future. Azithromycin administration less frequently could also increase compliance. (26) (27)

4.Gonococcal conjunctivitis (GC).

Although GC is frequently thought of as a disorder that only affects newborns, it also affects people of various ages. In newborns and sexually active adults, Neisseria gonorrhoeae is a frequent cause of hyperacute conjunctivitis. (25) A high frequency of corneal perforation is linked to N. gonorrhoea ocular infection. When newborns exhibit conjunctivitis between days 2 and 5 following delivery, GC should be taken into consideration as the likely culprit. An eye exam may indicate conjunctival injection, chemosis, and abundant mucopurulent discharge in both neonatal and non-neonatal populations. This kind of conjunctivitis may also be accompanied by a sensitive globe and periauricular lymphadenopathy. (29) Neonatal patients are advised to get a single dose of ceftriaxone (25 to 50 mg/kg) or cefotaxime (100 mg/kg IV or IM), as well as hourly irrigation of the ocular area with saline. A combination of 1 gm of IM ceftriaxone administered as a single dose and 1 gm of oral azithromycin (which is used to treat the frequently occurring chlamydial coinfection) can be used to treat non-neonates. Adults do not require irrigation of the ocular surface with saline solution. (30)



Figure 3. Gonococcal conjunctivitis (31)

5. Allergic conjunctivitis.

Conjunctiva, eyelids, and cornea can all be impacted by ocular allergies along with other ocular surface areas. 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: IgE-mediated reactions, such as seasonal allergic conjunctivitis (SAC) and perennial allergic conjunctivitis (PAC); combined IgE and non-IgE-mediated reactions, such as VKC and AKC; and non-IgE-mediated reactions, such as giant papillary conjunctivitis (GPC). (32)

6. Vernal keratoconjunctivitis (VKC).

VKC is regarded as a disease that affects young men who reside in warmer areas. Adults can be impacted by VKC despite the fact that children are typically the patients for diagnosis. This syndrome is frequently explained by a combination of IgE and non-IgE reactions in response to general stimuli including wind, dust, and sunlight. As a result, tests for blood IgE antibodies and skin reactions to well-known allergens are typically negative. It is supported by both clinical and histological evidence that T-helper 2 and IgE play complementary roles in the development of VKC. It is supported by both clinical and histological evidence that T-helper 2 and IgE play complementary roles in the development of VKC. IL-17 has recently been associated with VKC, and serum levels of this cytokine can indicate the severity of the condition. A substantial correlation between VKC and other autoimmune disorders, such as atopy, is suggested by the high percentage of antinuclear antibodies (ANA) positivity and family history of autoimmune disorders in individuals with VKC. (33) (34)

Patients with VKC have documented both common seasonal patterns and perpetual variants. It is impossible to diagnose VKC without papillary hyperplasia, which also makes it possible to distinguish it from other related conditions as SAC and PAC. (35) The primary clinical signs and symptoms of VKC are photophobia, conjunctival injection, excessive tearing, and acute itching. The three clinical varieties of VKC are mixed, palpebral, and limbal. The limbus thickens and becomes gelatinous in the limbus with limbal type; while the disease is active, Horner-Trantas spots are typically visible at the superior limbal borders. Giant papillae, and the resulting cobblestone appearance, are the distinguishing feature of the palpebral VKC. The mixed kind simultaneously possesses palpebral and limbal VKC characteristics. (36)

The tarsal conjunctival papillae's mechanical damage and the inflammatory reactions brought on by the production of cytokines are two factors that contribute to the corneal pathology found in VKC. Eosinophils and mast cells that have invaded the conjunctival tissue are thought to release the inflammatory mediators. Up to 6% of individuals may experience the development of corneal plaques and ulcers, which aggravates the clinical

symptoms and impairs vision. These ulcers are typically present in the top portions of the cornea as oval lesions with raised edges around a persistent epithelial defect covered by eosinophilic and epithelial debris. (37)

7. Atopic keratoconjunctivitis (AKC).

Chronic allergic illness of the cornea, conjunctiva, and eyelids are features of AKC. Approximately 95% of people with AKC also have atopic dermatitis (AD), which is regarded as having an ocular component. Less than half of AD patients, however, experience ocular tissue involvement. (38) (39) The conjunctival epithelial cells and the inflammatory cells that have invaded the conjunctival tissues in AKC both release a large number of cytokines. This results in ongoing remodeling of the connective tissue on the ocular surface, which promotes mucus metaplasia, scarring, and corneal neovascularization. Although sporadic cases can be seen in early childhood and the fifth decade of life, AKC is commonly diagnosed in the second and third decades of life. Clinicians may be able to identify this disorder from VKC based on the patient's age at onset, the severity of the disease, and clinical manifestations.

Epiphora, itching, redness, and impaired vision are clinical signs of AKC. Although there have been reports of unilateral illness, presentations are frequently bilateral. The skin of the eyelids could be edematous and have a sandpaper-like texture. Conjunctival scarring is prevalent, and conjunctival injection and chemosis can range in severity. Giant papillae and trantas dots could be present or absent. Contrary to VKC, AKC is linked to corneal vascularization and opacities as well as conjunctival fibrosis. Patients with AKC frequently get an early cataract surgery because this disorder is linked to the development of "atopic cataracts" at a relatively young age. In addition to nuclear, cortical, and even posterior subcapsular cataracts, shield-like cataracts can also develop. For common allergens, around 50% of AKC patients test negative. (40)

8. Giant papillary conjunctivitis (GPC).

GPC is characterized by papillary enlargement of the superior tarsal conjunctiva, which is similar to vernal conjunctivitis. Although GPC is typically thought of as a side effect of using contact lenses, it has also been linked to corneal foreign bodies, filtering blebs, ocular prosthesis, exposed sutures, limbal dermoids, and tissue adhesives. The typical symptoms of GPC include increased mucus production and lowered contact lens tolerance. Mast cells and eosinophils may be present in the conjunctiva, although IgE or histamine levels in the tears of GPC patients do not rise. (41)

GPC has been described with either hydroxyethyl methacrylate (HEMA), silicone polymers, or the new gas permeable polymers, and it can happen with both hydrogel and hard contact lenses. However, rigid contact lenses experience it less frequently. The persistent inflammatory damage to the ocular surface seen in this syndrome can be a result of mechanical injuries brought on by contact lens wear and inflammatory responses brought on by lens surface proteins. (42)

9. Contact allergy.

The type-IV delayed hypersensitivity reaction, or CDC, is characterized by the interaction of antigens with T cells and the subsequent release of cytokines. To create the final allergens that can elicit an immune response, low molecular weight allergens interact with host proteins. Poison ivy, poison oak, neomycin, nickel, latex, and atropine and its derivatives are a few of the identified allergens for the CDC. The process by which memory T cells are created from resident T cells of the ocular tissue is referred to as primary sensitization, and the interaction between these memory cells and allergens is covered in the subsequent elicitation phase. The etiology of CDC also involves regulatory T cells and Th cells that produce IL-17. (43)

Contact allergy affects the conjunctiva, cornea, and eyelids similarly to AKC. In later stages of the disease, the condition may also be accompanied with cicatrization, follicular response, swelling of the lids, and itching. The involvement of the cornea can take the form of grayish stromal infiltrates, pseudodendritic keratitis, or punctate keratitis.

➤ Treatment.

The mainstay of treatment for many types of allergies, including allergic conjunctivitis, is avoiding the allergens. Artificial tears serve as a barrier, dilute different allergens, and flush inflammatory mediators from the eye's surface. Anti-histamines, mast cell stabilizers, and lubricating eye solutions are among the treatments for allergic conjunctivitis. Numerous studies have shown that topical antihistamines and mast cell stabilizers are more effective than placebo at reducing allergic conjunctivitis symptoms, and antihistamines are also better at reducing symptoms in the short term than mast cell stabilizers. Olopatadine, ketotifen, azelastine, and epinastine are a few eye drop formulations having dual action (antihistamine and mast cell-stabilizing actions) that have recently been released on the market. (44)

Patients with allergic conjunctivitis frequently take oral antihistamines to treat their ocular symptoms. Because they have fewer negative systemic side effects, second generation antihistamines are preferable. Unfortunately, oral antihistamines cause eye dryness, which exacerbates allergic conjunctivitis symptoms. Steroids should only be used sparingly and in specific circumstances. If the condition is severe, topical and oral treatment may also be necessary in addition to supratarsal injections; regrettably, any route of corticosteroid administration is linked to the development of cataracts and increased intraocular pressure. Ketorolac and diclofenac are two examples of non-steroidal anti-inflammatory medications that can be added to the treatment plan to get extra advantages. Additionally, alternative steroid-sparing medications like tacrolimus and cyclosporine-A can effectively treat severe and persistent forms of ocular allergies. (45)

Recent years have seen a rise in the popularity of allergen-specific immunotherapy, which works by creating clinical tolerance to a particular allergen. If you have allergic rhinoconjunctivitis and particular IgE antibodies, this seems to be a successful therapy choice. Sublingual immunotherapy (SLIT) has caught allergists' interest as an alternative to immunotherapy, which is typically administered through subcutaneous injections. The ocular and nasal symptoms of allergic conjunctivitis have been demonstrated to be significantly improved by SLIT, with a higher benefit for the nasal symptoms. (46)

➤ Conjunctivitis associated with systemic diseases.

Conjunctivitis may be the first sign of many systemic diseases; as a result, in some circumstances, a complete medical history and systemic evaluation may aid in the early detection of numerous potentially life-threatening and disabling problems.

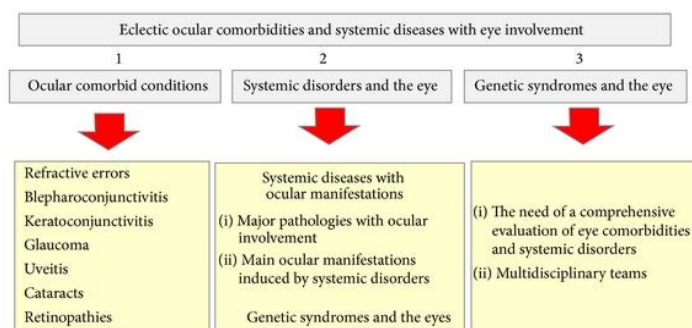


Figure 4. Conjunctivitis Associated with systemic disease (47)

➤ Summary.

Conjunctivitis is thought to be the cause of 1% of all patient visits to their primary care physician, and it is estimated that infectious conjunctivitis costs the US healthcare system more than \$800 million yearly. Eliminating serious ocular diseases that present with "red eye" and mimic conjunctivitis is the first step in treating a patient with suspected conjunctivitis. This requires taking a thorough medical history, completing a thorough physical and ophthalmologic examination. Imaging and ancillary laboratory tests are crucial aspects of assessing these patients.

In order to narrow the differential diagnosis and identify the underlying cause of the conjunctivitis, it is crucial to obtain a thorough history. Studies have shown that relying solely on the presenting signs and symptoms can be misleading and frequently results in an incorrect diagnosis. The most frequent causes of infectious conjunctivitis are viral conjunctivitis and bacterial conjunctivitis. Since adenoviruses account for the majority of viral conjunctivitis cases, using a quick antigen test to identify adenoviral conjunctivitis may be an effective way to prevent overusing antibiotics. (48)

In 50% of conjunctivitis cases, bacterial pathogens are isolated, and 60% of culture-positive cases are known to be self-limited. Patients who do not react to treatment, as well as those suspected of having a chlamydial infection and hyperacute conjunctivitis, should have cultures taken from their conjunctival swabs. Contact lens wearers and suspected cases of chlamydial and gonococcal conjunctivitis are typically advised to receive treatment with topical antibiotics. Seasonal allergies cause the majority of occurrences of allergic conjunctivitis. Mast cell stabilizers and antihistamines are frequently used to treat allergic conjunctivitis. (49) (50)

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