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Review Article

Allergies to Infections: Understanding the Spectrum of Conjunctivitis

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Abstract

Conjunctivitis is described as any inflammatory condition of the membrane that covers the exposed sclera and borders the eyelids. This is the most common cause of "red eye." Conjunctiva inflammation is a symptom of many different disorders, collectively referred to as "conjunctivitis". Inflammations can be hyper acute, acute, or chronic, and they can have noninfectious or infectious origins. Conjunctiva injection, sometimes referred to as "red eye," is a typical presentation for a number of ocular diseases and may account for as much as 1% of primary care visits. When both of these symptoms are present, 59% of cases with "serious eye conditions," such as keratitis and anterior uveitis, may be identified. Moderate photophobia and anisocoria were significantly associated with "serious eye conditions. When detecting fungus in immunocompromised persons or those with chronic blepharitis, Sabouraud agar plates are advised. Anaerobic culture plates could also be helpful, especially for people who have had surgery or trauma in the past. Acute hemorrhagic conjunctivitis (AHC) is a highly infectious type of viral conjunctivitis. The symptoms include chemosis, subconjunctival hemorrhage, edema of the eyelids, dilated conjunctiva vessels, and a sensation of a foreign mass. Neisseria gonorrhea is often the cause of hyper acute conjunctivitis in sexually active adults and newborns. Ocular allergies can affect other parts of the eye, such as the cornea, eyelids, and conjunctiva. Leonardi et al. classified ocular allergy diseases into three primary groups according to the immune mechanism causing the ultimate clinical manifestation. Viral conjunctivitis patients experience burning, watery discharge, red eyes, irritation, light sensitivity and a sudden foreign body sensation. In addition to the previously stated symptoms, patients with bacterial conjunctivitis also experience mattering of the eyelids upon waking and mucopurulent discharge. General supportive therapy for conjunctivitis patients includes avoiding allergens (dust mites, pollens, and animals), using artificial tears, washing your hands properly, applying cold compresses, not scratching your eyes, and using a gentle cleaner to get rid of any debris or allergens.

Keywords: *Watery discharge, Bacterial conjunctivitis, Conjunctiva*

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Introduction:

Conjunctivitis is described as any inflammatory condition of the membrane that borders the eyelids and covers the exposed sclera. This is the most common cause of "red eye." Conjunctiva inflammation is a symptom of many different disorders, collectively referred to as "conjunctivitis". Inflammations can be hyper acute, acute, or chronic, and they can have noninfectious or infectious origins(Azari & Arabi, 2020). In the most current edition of the Third National Health and Nutrition Examination Survey, 40% of the participants in this American study said that they had episodes of ocular allergy (K. Singh et al., 2010). Allergy conjunctivitis encompasses a number of conditions, including atopic keratoconjunctivitis (AKC), vernal keratoconjunctivitis (VKC), perennial allergic conjunctivitis (PAC), and seasonal allergic conjunctivitis (SAC). AKC and VKC differ markedly from SAC and PAC in their clinical and pathophysiological features, even though they share certain common allergy markers (L. Bielory, 2000)(La Rosa et al., 2013). The signs and symptoms of ocular allergy are influenced by a variety of factors, including as immunological modulation, ocular microbial flora, genetics, and environmental factors (La Rosa et al., 2013). Among the goals of the treatment are the reduction of symptoms, signs, and aftereffects such chemosis, erythema, conjunctiva edema, and edema of the eyelids. The brows, eyelids, and lashes serve as barriers against allergies, and a healthy tear film further helps to keep allergens off the surface of the eyes. A weakening in any of these natural defenses might exacerbate allergy conjunctivitis. A wide range of illnesses, including both sexes, individuals of all ages, and people with all socioeconomic situations can be affected by conjunctivitis. Although precise data on the frequency or prevalence of all forms of conjunctivitis are lacking, it has been noted as one of the most common causes of patient self-referrals (Chiang et al., 1995). According to reports, around 60% of patients with acute conjunctivitis are prescribed antibiotic eye drops; the bulk of these prescriptions are written by doctors who are not ophthalmologists. For instance, 36% of patients who saw an ophthalmologist received antibiotic eye drops, compared to 68% of patients who saw a doctor in an emergency department. It's interesting to note that those with greater socioeconomic class had a higher likelihood of being prescribed medicine for conjunctivitis and filling it (Shekhawat et al., 2017). Conjunctivitis can be categorized in a number of ways, including according to its etiology, chronicity, severity, and degree of surrounding tissue involvement. Conjunctivitis can have either an infectious or non-infectious etiology. While allergy and toxin-induced conjunctivitis are among the most prevalent non-infectious etiologies, viral and bacterial conjunctivitis are the most common causes of infectious conjunctivitis. Conjunctivitis can be classified as acute, sub-acute, or chronic depending on how long it lasts. Acute conjunctivitis has a quick start and lasts four weeks or less (Alfonso et al., 2015). Furthermore, systemic illnesses such as nutritional deprivation (vitamin A deficiency), congenital metabolic syndromes, and immune-related diseases such as Reiter's, Stevens-Johnson syndrome (SJS), and keratoconjunctivitis sicca in rheumatoid arthritis, may be linked to conjunctivitis (Richner Hanhart syndrome and porphyria). It is crucial to distinguish conjunctivitis from other "red eye" conditions include acute angle closure glaucoma, uveitis, endophthalmitis, carotid cavernous fistula, cellulitis, and anterior segment tumors that can seriously impair vision or even cause death (de Laet et al., 2013)(Sati et al., 2013).

Figure 1: Redness is a result of ocular irritation and inflammation.

Identification or clinical assessment:

Conjunctiva injection, sometimes referred to as "red eye," is a typical presentation for a number of ocular conditions and may account for as much as 1% of all primary care visits (Narayana & McGee, 2015). Whether or not they are ophthalmologists, the clinicians should be aware that "red eye" can be the presenting symptom of serious eye conditions like uveitis, keratitis, or scleritis, or it can be a secondary symptom of more benign conditions that only affect the conjunctiva tissue, like conjunctivitis or subconjunctival hemorrhaged. In the past, it was believed that more serious eye issues were connected to irregularities in vision, excruciating pain, and photophobia (Narayana & McGee, 2015). 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."

How can we utilize the results of laboratories??

Clinicians may collect discharge samples from conjunctivitis patients' eyes and send them for microbiological investigation. In cases of suspected infectious newborn conjunctivitis, recurrent conjunctivitis, treatment-resistant conjunctivitis, conjunctivitis presenting with a significant purulent discharge, and cases suspicious for gonococcal or chlamydial infection, conjunctiva cultures are frequently the only procedures done (Azari & Barney, 2013). Gathering swabs from the discharge is preferred before starting antibiotic medication. The swabs are then plated in various growth medium in the laboratory to begin the culture process. When detecting fungus in immunocompromised persons or those with chronic blepharitis, Sabouraud agar plates are advised. Anaerobic culture plates could also be helpful, especially for people with a history of trauma or surgery (Drew et al., 2015). Antimicrobial therapy should be halted 48 hours before getting cultures if it has already begun. In a five-year analysis of 138 pediatric ocular surface infections, coagulase-negative staphylococci, Pseudomonas aeruginosa, and Staphylococcus aureus were the most prevalent microorganisms(Wong et al., 2011). Despite the fact that first studies from in-office fast antigen testing for adenoviruses indicate up to 94% specificity and 89% sensitivity(Drew et al., 2015).

Conjunctivitis caused by viruses:

In up to 90% of cases worldwide, adenoviruses are the most frequent cause of viral conjunctivitis. The human adenoviruses (HAdV) are composed of around 72 different genotypes that may be further classified into seven unique species (HAdV-A through HAdV-G). The species with the greatest number of members and the strongest association with viral conjunctivitis is the HAdV-D species. These genotypes have been made public by recent advancements in HAdV genome sequencing (G. Singh et al., 2015)(Kuo, 2019). Pharyngoconjunctival fever (PCF), which is brought on by HAdV types 3, 4, and 7, may be the most typical adenovirus infection in children(Li et al., 2018)(Sinclair et al., 2009). Fever, pharyngitis, periauricular lymphadenopathy, and severe follicular conjunctivitis are frequently present symptoms of this sickness. Other abnormalities of the ocular surface include edema, hyperemia, and petechial hemorrhages of the conjunctiva, which are caused by the interaction between pro-inflammatory cytokines and the conjunctiva vasculature (Harley et al., 2001).

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(Chigbu & Labib, 2018). According to some statistics, the likelihood of transmission of adenovirus conjunctivitis is up to 50%(Gallenga et al., 1999)(Udeh et al., 2008). According to one research, up to 46% of people with viral conjunctivitis had a positive viral culture produced from their hands. The virus may be disseminated by contaminated fingers, medical devices, contaminated water in swimming pools, or by sharing personal things(Jackson et al., 2002). 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(Bremond-Gignac et al., 2010). Although there is no one proven method of treatment for viral conjunctivitis, frequent use of artificial tears and ocular drops or cold compresses appear to be soothing. Many of the clinical signs and symptoms that with this circumstance(Varu et al., 2019)(Leibowitz, 1991).

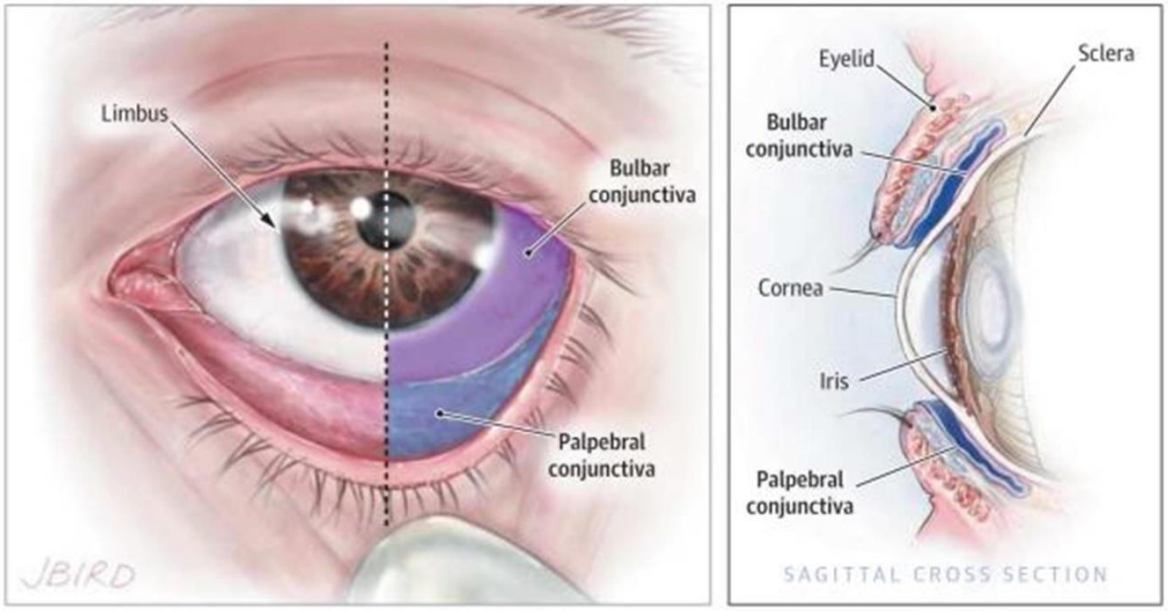

Figure 2: Normal structure of the conjunctiva

Conjunctiva herpes:

HSV infection is thought to be the root cause of 1.3–4.8% of all occurrences of acute conjunctivitis(Cronau et al., 2010)(Sheikh et al., 2012)(Papa et al., 2002). Herpes zoster virus 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 when the first and second branches of the trigeminal nerve are affected(Puri et al., 2011)(Sy et al., 2012).

An unexpected bleeding conjunctivitis:

Acute hemorrhagic conjunctivitis (AHC) is a highly infectious type of viral conjunctivitis. It manifests as subconjunctival hemorrhage, chemosis, edema of the eyelids, dilated conjunctiva vessels, and a sensation of a foreign mass (Lim & Yin Murphy, 1973)(Kono et al., 1975)(Zhang et al., 2017). Similar to other conjunctivitis types, AHC is thought to spread predominantly by hand-to-eye contact and infected fomites(Langford et al., 2015). By promoting frequent hand washing and limiting contact with those who are ill, medical intervention aims to primarily control the large outbreaks while also enacting preventative measures to safeguard the vulnerable groups, such as children, the elderly, pregnant women, and immunocompromised people(Zhang et al., 2017).

Infectious conjunctivitis:

Both the abnormal growth of the natural conjunctiva flora and direct contact with sick individuals can result in bacterial conjunctivitis (Shields & Sloane, 1991). Additionally, bacterial conjunctivitis is more likely to develop in people who have impaired tear production, disturbance of the natural epithelial barrier, aberrant adnexal structures, trauma, and immunosuppressed status(Varu et al., 2019)(S. A. Ali, Pathak, et al., 2023). The most frequent causes of acute bacterial conjunctivitis include Homophiles influenza, Staphylococcus species, Streptococcus species, Moraxella catarrhally, and gram-negative gut bacteria (Høvding, 2008). Nonetheless, highly pathogenic bacteria have the capacity to seriously damage the ocular surface and the eye (Shields & Sloane, 1991).

Chlamydia-related conjunctivitis:

Chlamydia trachomatis can cause ocular surface infections such as inclusion conjunctivitis, neonatal conjunctivitis, and trachoma. Serotypes D-K are responsible for adult inclusion conjunctivitis and neonatal conjunctivitis, whereas serotypes A, B, Ba, and C cause trachoma (Burton, 2007). According to reports, up to 54% of men and 74% of women have genital infections at the same time(Tabbara et al., 1999). 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(Darville, 2005)(Mallika et al., 2008).

Gonorrhea-induced conjunctivitis (GC):

Neisseria gonorrhea is commonly the cause of hyper acute conjunctivitis in people who are sexually active,

whether they are adults or infants (Shields & Sloane, 1991). Having N. gonorrhea in the eye increases the risk of developing corneal perforation(Høvding, 2008). When conjunctivitis appears in babies between the second and fifth day after birth, GC should be considered the most likely cause (Wang et al., 2019). Both newborn and non-neonatal individuals may exhibit conjunctiva injection, chemosis, and copious mucopurulent discharge during an eye exam. This kind of conjunctivitis may also be associated with periauricular lymphadenopathy and a sensitive globe (Wang et al., 2019).

Allergic conjunctivitis:

Ocular allergies can affect other parts of the eye, such as the cornea, eyelids, and conjunctiva. Leonardi et al. classified ocular allergy diseases into three primary groups according to the immune mechanism causing the ultimate clinical manifestation (Leonardi et al., 2007). IgE-mediated reactions include seasonal allergic conjunctivitis (SAC) and perennial allergic conjunctivitis (PAC), whereas combination IgE and non-IgE-mediated reactions include VKC and AKC. Non-IgE-mediated responses include giant papillary conjunctivitis (GPC) and contact keratoconjunctivitis (CDC) (Pucci et al., 2003).

Conjunctivitis Symptoms and Indications

Viral conjunctivitis patients experience burning, watery discharge, red eyes, irritation, light sensitivity, and a sudden foreign body sensation. All of the previously listed symptoms, together with mucopurulent discharge and mattering of the eyelids upon waking, are present in patients diagnosed with bacterial conjunctivitis (Taruc-Uy & Lynch, 2013).

Table: Conjunctivitis Symptoms and Indications

S. No.	Signs/Symptoms	Allergic	Bacterial	Viral	References
1.	Hyperemia	Mild to moderate	Moderate to severe	Mild to moderate	(Jackson, 1993) (Azari & Barney, 2013) (Cronau et al., 2010)
2.	Discharge	Mucoid, ropy	Mucopurulent "glued eyes"	Watery (may be thicker on awaking)	
3.	Pain	No	Mild to severe	Mild to none	
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 Unilateral commonly in herpes zoster	

Conjunctivitis Treatment Options

General supportive therapy for people with conjunctivitis include avoiding allergens (dust mites, pollens, and animals), using artificial tears, washing your hands properly, applying cold compresses, not scratching your eyes, and using a gentle cleaner to get rid of any debris or allergens (Reduction et al., 2021)(S. A. Ali, Ali, et al., 2023). The majority of viral conjunctivitis instances don't need special care; supportive care will suffice. Acyclovir, valacyclovir, and famciclovir are recommended as topical and oral antivirals to decrease the duration of herpes simplex conjunctivitis (S. Ali, Ali, et al., 2023).

Table: Options for Conjunctivitis Treatment

S. No.	Drug Type	Mechanism	Examples (Drug)	Adverse Effects	References
1.	Artificial tears	They serve as a barrier by diluting allergens and inflammatory mediators and	--	--	(B. Bielory & Bielory, 2010)

		flushing them away from the surface.			(Chen et al., 2014)
2.	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	(Azari & Barney, 2013) (Ono & Abelson, 2005)
3.	Topical vasoconstrictors	Provides short-term relief from vascular injection and erythema; can be used alone or in combination with antihistamines.	Naphazoline (Vasocon), phenylephrine, oxymetazoline, tetrahydrozoline (Visine)	May cause dependency with rebound conjunctival injection and inflammation as well as tachyphylaxis; ineffective against VKC, AKC	(Cronau et al., 2010) (Gooderham et al., 2018) (Castillo et al., 2015)
4.	Mast cell stabilizer	Do not cure current symptoms; they are used as a preventative measure; the mechanism is unknown, but it causes a reduction in mast cell degranulation to avoid the release of histamine and other chemotactic substances.	Cromolyn sodium, lodoxamine (Alomide), nedocromil (Alocril)	Does not treat acute symptoms	
5.	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	
6.	Topical NSAIDs	Inhibit the formation of prostaglandins and thromboxanes via acting on the	Ketorolac (Acular), flurbiprofen (Ocufen), diclofenac	May cause discomfort upon instillation	

		cyclooxygenase pathway.	(Voltaren Ophtha), bromfenac (Prolensa), nepafenac (Ilevro)		
7.	Topical corticosteroids	Prevents the synthesis of arachidonic acid, hence inhibiting the cyclooxygenase and lipoxygenase metabolic pathways; used to treat severe instances of chronic ocular allergies that do not respond to conventional treatment.	Loteprednol etabonate (Lotemax and Alrex), fluorometholone (Flarex), dexamethasone, prednisolone for severe cases	Delayed wound healing, secondary infection, elevated intraocular pressure, and cataract formation; lowest possible dose and concentration should be used for the shortest possible period	

Conjunctivitis prevention

Maintaining personal hygiene is the most crucial step in avoiding infectious conjunctivitis.

Although it is uncommon, upper respiratory tract infections and hands can spread bacterial conjunctivitis. Gonococcal infections can travel from the urine or vagina to the eye through the hands. This is a serious breach of common etiquette. To prevent ophthalmia neonatorum, prenatal care might involve the administration of antibiotics, antiseptics, or tetracycline eye ointment.

Adenovirus-caused viral conjunctivitis, in particular, may spread quickly throughout a community or an establishment like a school. Because of its high contagiousness, it needs to be controlled by maintaining strict hygiene regulations. Towels, face cloths, hands, and applanation tonometers are only a few places where it might spread.

It is not feasible to prevent allergic conjunctivitis unless the patient can change their work environment or surroundings, or locate and remove the allergen (such as pollen or animal hair) that is causing their allergy. Allergies caused by drugs can be managed by stopping the medication. Preservatives in eye drops, neomycin, and atropine are three of the most common sources of these adverse drug reactions.

Maintaining proper hand hygiene, avoiding touching your eyes with your hands, changing or cleaning your pillows often, using a fresh towel and washcloth every day, and not sharing eye makeup or personal eye care products can all help prevent conjunctivitis (GREEN, 1998)(Caldwell et al., 1992)(Lewis & Bhogal-Bhamra, 2021)(mark wood, 2020).

It is not feasible to prevent allergic conjunctivitis unless the patient can change their work environment or surroundings, or locate and remove the allergen (such as pollen or animal hair) that is causing their allergy. Allergies caused by drugs can be managed by stopping the medication. Preservatives in eye drops, neomycin, and atropine are three of the main culprits behind these adverse drug reactions (Jhanji et al., 2015).

To improve patient comfort and prevent scarring, if a membrane or faux membrane is present, it can be peeled at the slit lamp. Jeweler's forceps or a cotton swab soaked in topical anesthetic might be used to peel these membranes. Steroids used topically can help reduce symptoms. However, they may extend the duration of the virus's shedding. Patients should be informed that they should not return to work or school until their symptoms have decreased since they are very contagious. People who are using steroids may continue to discharge the virus even in the absence of any overt signs of sickness. Only those with significant conjunctiva injection or sub epithelial infiltrates who have visual impairments should utilize steroids(Usher et al., 2014)(Shiota et al., 2009)(Conde Bachiller et al., 2022).

Conclusion:

Conjunctivitis continues to be a common eye ailment that affects millions of people globally. To lessen the effects of conjunctivitis and enhance ocular health internationally, it is essential to comprehend the many types of the condition, its causes, an accurate diagnosis, and efficient treatment and preventive measures. In order to effectively manage conjunctivitis, the study highlights the significance of early diagnosis, adequate treatment, and preventative measures. Prospective investigations and sustained progress in this domain may yield better results for individuals and lessen the impact of conjunctivitis on worldwide ocular health.

References:

1. Alfonso, S. A., Fawley, J. D., & Lu, X. A. (2015). Conjunctivitis. In *Primary Care - Clinics in Office Practice*. https://doi.org/10.1016/j.pop.2015.05.001
2. Ali, S. A., Ali, S., Rastogi, S., Prasad, J., Kondrapu, P., Kumar, B., Sharma, A., & Pandey, K. (2023). *Endometriosis : A brief review of Pharmacological and Non-Pharmacological Treatment*. *12*(12), 1359–1379. https://doi.org/10.48047/ecb/2023.12.si12.123
3. Ali, S. A., Pathak, D., & Mandal, S. (2023). *INTERNATIONAL JOURNAL OF COVID-19 AND THEIR RELATIONSHIP WITH ENVIRONMENT*. *14*(1), 1–5.
4. Ali, S., Ali, S. A., Kondrapu, P., Tripathi, N., Kumar, P. B., Prasad, P. D., & Tonape, M. M. (2023). *A Brief Review Of Pathophysiology And Management Of Different Types Of Arthritis*. *12*(12), 199–230. https://doi.org/10.48047/ecb/2023.12.si12.016
5. Azari, A. A., & Arabi, A. (2020). Conjunctivitis: A Systematic Review. *Journal of Ophthalmic and Vision Research*. https://doi.org/10.18502/jovr.v15i3.7456
6. Azari, A. A., & Barney, N. P. (2013). Conjunctivitis: A systematic review of diagnosis and treatment. In *JAMA*. https://doi.org/10.1001/jama.2013.280318
7. Bielory, B., & Bielory, L. (2010). Atopic dermatitis and keratoconjunctivitis. In *Immunology and Allergy Clinics of North America*. https://doi.org/10.1016/j.iac.2010.06.004
8. Bielory, L. (2000). Allergic and immunologic disorders of the eye. Part II: Ocular allergy. *Journal of Allergy and Clinical Immunology*. https://doi.org/10.1067/mai.2000.111238
9. Bremond-Gignac, D., Mariani-Kurkdjian, P., Beresniak, A., El Fekih, L., Bhagat, Y., Pouliquen, P., Delval, L., Goldschmidt, P., Bingen, E., & Cochereau, I. (2010). Efficacy and safety of azithromycin 1.5% eye drops for purulent bacterial conjunctivitis in pediatric patients. *Pediatric Infectious Disease Journal*. https://doi.org/10.1097/INF.0b013e3181b99fa2
10. Burton, M. J. (2007). Trachoma: An overview. In *British Medical Bulletin*. https://doi.org/10.1093/bmb/ldm034
11. Caldwell, D. R., Verin, P., Hartwich-Young, R., Meyer, S. M., & Drake, M. M. (1992). Efficacy and safety of lodoxamide 0.1% vs cromolyn sodium 4% in patients with vernal keratoconjunctivitis. *American Journal of Ophthalmology*. https://doi.org/10.1016/S0002-9394(14)74786-5
12. Castillo, M., Scott, N. W., Mustafa, M. Z., Mustafa, M. S., & Azuara-Blanco, A. (2015). Topical antihistamines and mast cell stabilisers for treating seasonal and perennial allergic conjunctivitis. In *Cochrane Database of Systematic Reviews*. https://doi.org/10.1002/14651858.CD009566.pub2
13. Chen, J. J., Applebaum, D. S., Sun, G. S., & Pflugfelder, S. C. (2014). Atopic keratoconjunctivitis: A review. In *Journal of the American Academy of Dermatology*. https://doi.org/10.1016/j.jaad.2013.10.036
14. Chiang, Y. P., Wang, F., & Javitt, J. C. (1995). Office visits to ophthalmologists and other physicians for eye care among the U.S. population, 1990. *Public Health Reports*.
15. Chigbu, D. I., & Labib, B. A. (2018). Pathogenesis and management of adenoviral keratoconjunctivitis. In *Infection and Drug*

Resistance. https://doi.org/10.2147/IDR.S162669

16. Conde Bachiller, Y., Puente Gete, B., Gil Ibáñez, L., Esquivel Benito, G., Asencio Duran, M., & Dabad Moreno, J. V. (2022). COVID-19 pandemic: Impact on the rate of viral conjunctivitis. *Archivos de La Sociedad Espanola de Oftalmologia*. https://doi.org/10.1016/j.oftal.2021.03.002
17. Cronau, H., Kankanala, R. R., & Mauger, T. (2010). Diagnosis and management of red eye in primary care. In *American Family Physician*.
18. Darville, T. (2005). Chlamydia trachomatis infections in neonates and young children. *Seminars in Pediatric Infectious Diseases*. https://doi.org/10.1053/j.spid.2005.06.004
19. de Laet, C., Dionisi-Vici, C., Leonard, J. V., McKiernan, P., Mitchell, G., Monti, L., de Baulny, H. O., Pintos-Morell, G., & Spiekerkötter, U. (2013). Recommendations for the management of tyrosinaemia type 1. In *Orphanet journal of rare diseases*. https://doi.org/10.1186/1750-1172-8-8
20. Drew, R. J., Cole, T. S., & Newman, W. (2015). How to use··· eye swabs. *Archives of Disease in Childhood: Education and Practice Edition*. https://doi.org/10.1136/archdischild-2013-305271
21. Gallenga, P. E., Lobefalo, L., Colangelo, L., Della Loggia, G., Orzalesi, N., Velati, P., Bujtar, E., Ponte, F., Damiani, S., Bucci, M. G., Bonini, S., Curatola, M. R., Palma, L. A., Bonomi, L., Gerosa, L. T., Pagliarusco, A., Milan, E., & Jauch, A. (1999). Topical lomefloxacin 0.3% twice daily versus tobramycin 0.3% in acute bacterial conjunctivitis: A multicenter double-blind phase III study. *Ophthalmologica*. https://doi.org/10.1159/000027430
22. Gooderham, M., McDonald, J., & Papp, K. (2018). Diagnosis and management of conjunctivitis for the dermatologist. *Journal of Cutaneous Medicine and Surgery*. https://doi.org/10.1177/1203475417743233
23. GREEN, F. D. (1998). Eye Diseases in Hot Climates. *British Journal of Ophthalmology*. https://doi.org/10.1136/bjo.82.8.976b
24. Harley, D., Harrower, B., Lyon, M., & Dick, A. (2001). A primary school outbreak of pharyngoconjunctival fever caused by adenovirus type 3. *Communicable Diseases Intelligence*.
25. Høvding, G. (2008). Acute bacterial conjunctivitis. In *Acta Ophthalmologica*. https://doi.org/10.1111/j.1600-0420.2007.01006.x
26. Jackson, W. B. (1993). Differentiating conjunctivitis of diverse origins. *Survey of Ophthalmology*. https://doi.org/10.1016/0039-6257(93)90034-5
27. Jackson, W. B., Low, D. E., Dattani, D., Whitsitt, P. F., Leeder, R. G., & MacDougall, R. (2002). Treatment of acute bacterial conjunctivitis: 1% fusidic acid viscous drops vs. 0.3% tobramycin drops. *Canadian Journal of Ophthalmology*. https://doi.org/10.1016/S0008-4182(02)80114-4
28. Jhanji, V., Chan, T. C. Y., Li, E. Y. M., Agarwal, K., & Vajpayee, R. B. (2015). Adenoviral keratoconjunctivitis. In *Survey of Ophthalmology*. https://doi.org/10.1016/j.survophthal.2015.04.001
29. Kono, R., Sasagawa, A., Miyamura, K., & Tajiri, E. (1975). Serologic characterization and sero-epidemiologic studies on acute hemorrhagic conjunctivitis (AHC) virus. *American Journal of Epidemiology*. https://doi.org/10.1093/oxfordjournals.aje.a112112
30. Kuo, I. C. (2019). Adenoviral Keratoconjunctivitis: Diagnosis, Management, and Prevention. In *Current Ophthalmology Reports*. https://doi.org/10.1007/s40135-019-00207-y
31. La Rosa, M., Lionetti, E., Reibaldi, M., Russo, A., Longo, A., Leonardi, S., Tomarchio, S., Avitabile, T., & Reibaldi, A. (2013). Allergic conjunctivitis: A comprehensive review of the literature. In *Italian Journal of Pediatrics*. https://doi.org/10.1186/1824-7288-39-18
32. Langford, M. P., Anders, E. A., & Burch, M. A. (2015). Acute hemorrhagic conjunctivitis:

Anti-coxsackievirus a24 variant secretory immunoglobulin a in acute and convalescent tear. *Clinical Ophthalmology*. https://doi.org/10.2147/OPTH.S85358

33. Leibowitz, H. M. (1991). Antibacterial effectiveness of ciprofloxacin 0.3% opthalmic solution in the treatment of bacterial conjunctivitis. *American Journal of Ophthalmology*.
34. Leonardi, A., De Dominicis, C., & Motterle, L. (2007). Immunopathogenesis of ocular allergy: A schematic approach to different clinical entities. In *Current Opinion in Allergy and Clinical Immunology*. https://doi.org/10.1097/ACI.0b013e3282ef8674
35. Lewis, N., & Bhogal-Bhamra, G. (2021). Bacterial conjunctivitis: diagnosis and management. *Pharmaceutical Journal*. https://doi.org/10.1211/PJ.2021.1.87233
36. Li, J., Lu, X., Sun, Y., Lin, C., Li, F., Yang, Y., Liang, Z., Jia, L., Chen, L., Jiang, B., & Wang, Q. (2018). A swimming pool-associated outbreak of pharyngoconjunctival fever caused by human adenovirus type 4 in Beijing, China. *International Journal of Infectious Diseases*. https://doi.org/10.1016/j.ijid.2018.08.009
37. Lim, K. H., & Yin Murphy, M. (1973). Epidemic conjunctivitis in Singapore in 1970 and 1971. *Transactions of the Ophthalmological Society of New Zealand*.
38. Mallika, P. S., Asok, T., Faisal, H. A., Aziz, S., Tan, A. K., & Intan, G. (2008). Neonatal conjunctivitis - A review. In *Malaysian Family Physician*.
39. mark wood. (2020). *Mark Wood FRCS PCEA Kikuyu Eye Unit PO Box 45, Kikuyu Kenya*. 19–20.
40. Narayana, S., & McGee, S. (2015). Bedside Diagnosis of the "Red Eye": A Systematic Review. *American Journal of Medicine*. https://doi.org/10.1016/j.amjmed.2015.06.026
41. Ono, S. J., & Abelson, M. B. (2005). Allergic conjunctivitis: Update on pathophysiology and prospects for future treatment. *Journal of Allergy and Clinical Immunology*. https://doi.org/10.1016/j.jaci.2004.10.042
42. Papa, V., Aragona, P., Scuderi, A. C., Blanco, A. R., Zola, P., Di Bella, A., Santocono, M., & Milazzo, G. (2002). Treatment of acute bacterial conjunctivitis with topical netilmicin. *Cornea*. https://doi.org/10.1097/00003226-200201000-00010
43. Pucci, N., Novembre, E., Lombardi, E., Cianferoni, A., Bernardini, R., Massai, C., Caputo, R., Campa, L., & Vierucci, A. (2003). Atopy and serum eosinophil cationic protein in 110 white children with vernal keratoconjunctivitis: Differences between tarsal and limbal forms. *Clinical and Experimental Allergy*. https://doi.org/10.1046/j.1365-2222.2003.01538.x
44. Puri, L. R., Shrestha, G. B., Shah, D. N., Chaudhary, M., & Thakur, A. (2011). Ocular manifestations in herpes zoster ophthalmicus. *Nepalese Journal of Ophthalmology : A Biannual Peer-Reviewed Academic Journal of the Nepal Ophthalmic Society : NEPJOPH*. https://doi.org/10.3126/nepjoph.v3i2.5271
45. Reduction, D., Of, A., Reducing, D., In, T., & Animals, O. F. D. (2021). *Plant Archives*. *21*(table 1), 2184–2185. https://doi.org/10.51470/PLANTARCHIVES.2021.v21.no2.085
46. Sati, A., Sangwan, V. S., & Basu, S. (2013). Porphyria: Varied ocular manifestations and management. *BMJ Case Reports*. https://doi.org/10.1136/bcr-2013-009496
47. Sheikh, A., Hurwitz, B., van Schayck, C. P., McLean, S., & Nurmatov, U. (2012). Antibiotics versus placebo for acute bacterial conjunctivitis. *Cochrane Database of Systematic Reviews*. https://doi.org/10.1002/14651858.cd001211.pub3
48. Shekhawat, N. S., Shtein, R. M., Blachley, T. S., & Stein, J. D. (2017). Antibiotic Prescription Fills for Acute Conjunctivitis among Enrollees in a Large United States Managed Care Network. *Ophthalmology*. https://doi.org/10.1016/j.ophtha.2017.04.034
49. Shields, T., & Sloane, P. D. (1991). A comparison of eye problems in primary care

and ophthalmology practices. *Family Medicine*.

50. Shiota, H., Ohno, S., Aoki, K., Azumi, A., Ishiko, H., Inoue, Y., Usui, N., Uchio, E., Kaneko, H., Kumakura, S., Tagawa, Y., Tanifuji, Y., Nakagawa, H., Hinokuma, R., Yamazaki, S., & Yokoi, N. (2009). Guideline for the nosocomial infections of adenovirus conjunctivitis. In *Nippon Ganka Gakkai zasshi*.
51. Sinclair, R. G., Jones, E. L., & Gerba, C. P. (2009). Viruses in recreational water-borne disease outbreaks: A review. In *Journal of Applied Microbiology*. https://doi.org/10.1111/j.1365-2672.2009.04367.x
52. Singh, G., Zhou, X., Lee, J. Y., Yousuf, M. A., Ramke, M., Ismail, A. M., Lee, J. S., Robinson, C. M., Seto, D., Dyer, D. W., Jones, M. S., Rajaiya, J., & Chodosh, J. (2015). Recombination of the epsilon determinant and corneal tropism: Human adenovirus species D types 15, 29, 56, and 69. *Virology*. https://doi.org/10.1016/j.virol.2015.08.018
53. Singh, K., Axelrod, S., & Bielory, L. (2010). The epidemiology of ocular and nasal allergy in the United States, 1988-1994. *Journal of Allergy and Clinical Immunology*. https://doi.org/10.1016/j.jaci.2010.06.050
54. Sy, A., McLeod, S. D., Cohen, E. J., Margolis, T. P., Mannis, M. J., Lietman, T. M., & Acharya, N. R. (2012). Practice patterns and opinions in the management of recurrent or chronic herpes zoster ophthalmicus. *Cornea*. https://doi.org/10.1097/ICO.0b013e31823cbe6a
55. Tabbara, K. F., El-Sheikh, H. F., Islam, S. M. M., & Hammouda, E. (1999). Treatment of acute bacterial conjunctivitis with topical lomefloxacin 0.3% compared to topical ofloxacin 0.3%. *European Journal of Ophthalmology*. https://doi.org/10.1177/112067219900900403
56. Taruc-Uy, R. L., & Lynch, S. A. (2013). Diagnosis and Treatment of Osteoarthritis. *Primary Care - Clinics in Office Practice*, *40*(4), 821–836. https://doi.org/10.1016/j.pop.2013.08.003
57. Udeh, B. L., Schneider, J. E., & Ohsfeldt, R. L. (2008). Cost effectiveness of a point-of-care test for adenoviral conjunctivitis. *American Journal of the Medical Sciences*. https://doi.org/10.1097/MAJ.0b013e3181637417
58. Usher, P., Keefe, J., Crock, C., & Chan, E. (2014). Appropriate prescribing for viral conjunctivitis. In *Australian Family Physician*.
59. Varu, D. M., Rhee, M. K., Akpek, E. K., Amescua, G., Farid, M., Garcia-Ferrer, F. J., Lin, A., Musch, D. C., Mah, F. S., & Dunn, S. P. (2019). Conjunctivitis Preferred Practice Pattern®. *Ophthalmology*. https://doi.org/10.1016/j.ophtha.2018.10.020
60. Wang, M. F., Wang, L., & Li, L. F. (2019). Gonococcal conjunctivitis after incomplete treatment of gonococcal urethritis. *Infection and Drug Resistance*. https://doi.org/10.2147/IDR.S199163
61. Wong, V. W. Y., Lai, T. Y. Y., Chi, S. C. C., & Lam, D. S. C. (2011). Pediatric ocular surface infections: A 5-year review of demographics, clinical features, risk factors, microbiological results, and treatment. In *Cornea*. https://doi.org/10.1097/ICO.0b013e31820770f4
62. Zhang, L., Zhao, N., Huang, X., Jin, X., Geng, X., Chan, T. C., & Liu, S. (2017). Molecular epidemiology of acute hemorrhagic conjunctivitis caused by coxsackie A type 24 variant in China, 2004-2014. *Scientific Reports*. https://doi.org/10.1038/srep45202