

Conjunctivitis and its classification:

Conjunctiva:

Conjunctiva is a thin, translucent membrane lining the anterior part of the sclera and inside of the eyelids. It has two parts, bulbar and palpebral. The bulbar portion begins at the edge of the cornea and covers the visible part of the sclera; the palpebral part lines the inside of the eyelids. Inflammation or infection of the conjunctiva is known as conjunctivitis¹.

Conjunctivitis:

Conjunctivitis refers to any inflammatory condition of the membrane that lines the eyelids and covers the exposed surface of the sclera. It is the most common cause of “red eye.” The aetiology can usually be determined by a careful history and an ocular examination, but microbiological investigation may be necessary to establish the diagnosis or to guide therapy².

The prevalence of conjunctivitis varies according to the underlying cause, which may be influenced by the patient’s age, as well as the season of the year. Viral conjunctivitis is the most common cause of infectious conjunctivitis³. Bacterial conjunctivitis is the second most common cause and is responsible for the majority of cases in children. Allergic conjunctivitis is the most frequent cause, is observed more frequently in spring and summer. Conjunctivitis can be divided into infectious and non-infectious causes. Viruses and bacteria are the most common infectious causes⁴.

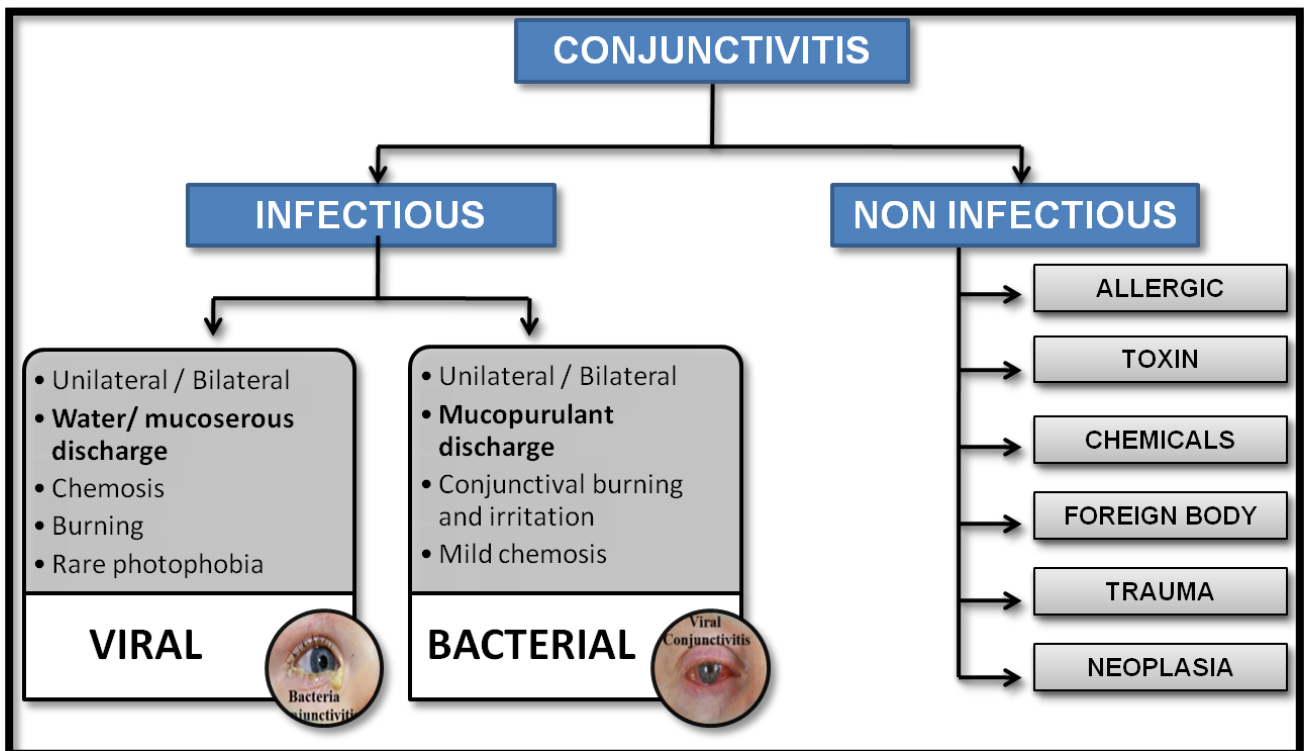
Non-infectious conjunctivitis includes allergic, toxic and cicatricial conjunctivitis, as well as inflammation secondary to immune-mediated diseases and neoplastic processes. The disease can also be classified into acute, hyperacute, and chronic according to the mode of onset and the severity of the clinical response⁵. Furthermore, it can be either primary or secondary to systemic diseases such as gonorrhoea, chlamydia, graft-vs-host disease, and Reiter syndrome, in which case systemic treatment is warranted⁴. *Neisseria* infection should be suspected when severe, bilateral, purulent conjunctivitis is present in a sexually active adult or in a neonate three to five days postpartum⁵. Conjunctivitis caused by *Chlamydia trachomatis* or *Neisseria gonorrhoeae* requires aggressive antibiotic therapy, but conjunctivitis due to other bacteria is usually self-limited⁶. For diagnosis and detection of conjunctivitis caused by *Chlamydia trachomatis*, algorithm used for suspected viral conjunctivitis will be followed.

Chronic conjunctivitis is usually associated with blepharitis, recurrent styes or meibomianitis. Treatment requires good eyelid hygiene and the application of topical antibiotics as determined by culture. Allergic conjunctivitis is distinguished by severe itching and allergen exposure. This condition is generally treated with topical antihistamines, mast-cell stabilizers or anti-inflammatory agents⁷.

Patients with viral conjunctivitis typically present with an acute red eye, watery discharge, conjunctival swelling, a tender preauricular node and in some cases, photophobia and a foreign-body sensation⁸. Occasionally, patients also have subconjunctival hemorrhage. Both eyes may be affected simultaneously, or the second eye may become involved a few days after the first eye. Some patients have an associated upper respiratory tract infection^{9,10}.

It is important to differentiate conjunctivitis from other sight-threatening eye diseases that have similar clinical presentation and to make appropriate decisions about further testing, treatment, or referral. An algorithmic approach may be helpful in diagnosis and treatment.

Figure 1: Suggested algorithm for classification of acute conjunctivitis:



VIRAL CONJUNCTIVITIS:

The viruses that most commonly cause conjunctivitis typically produce an acute unilateral follicular conjunctivitis with discharge, followed by involvement of the second eye within 2 to 10 days. There may be associated foreign body sensation, ipsilaterally tender, small preauricular lymphadenopathy, low grade fever, lid edema, conjunctival hyperaemia, petechial or subconjunctival haemorrhage, pseudo membrane or true membrane formation and corneal epithelial changes.

Figure 2: Classification of viral conjunctivitis based on the aetiology:

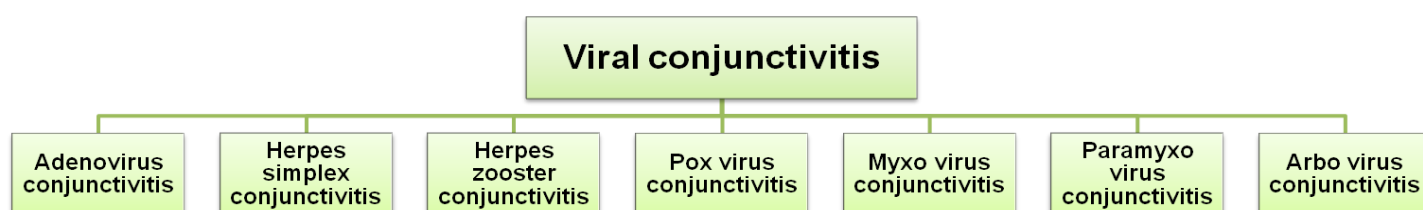
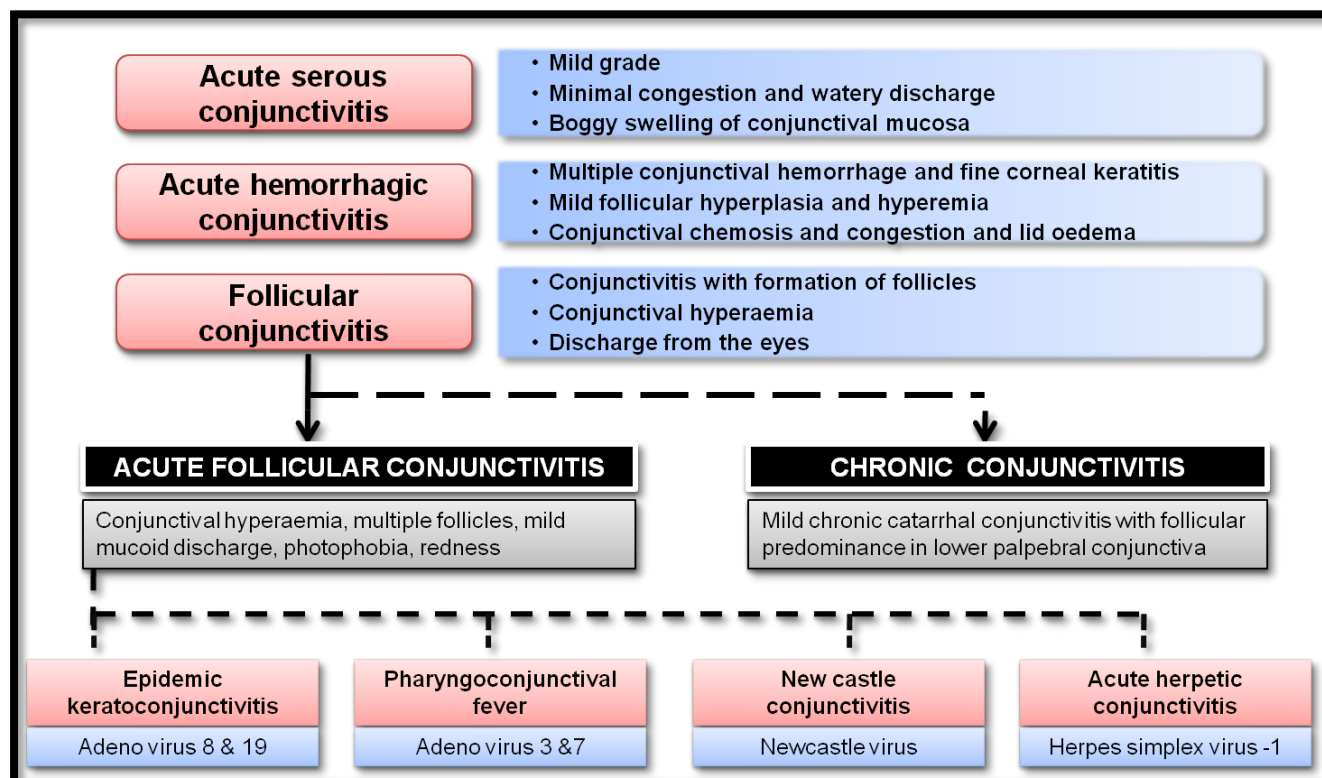


Figure 3: Suggestive algorithm for classification of viral conjunctivitis based on clinical presentation:



Epidemic keratoconjunctivitis (EKC):

EKC is characterised with severe and presents with watery discharge, hyperaemia, chemosis and ipsilateral lymphadenopathy. Occasionally papillary hypertrophy, sub conjunctival and eyelid haemorrhages, pseudo or true membranes and muco purulent discharge occur¹¹.

Pharyngo conjunctival fever (PCF)

It is characterized by abrupt onset of fever, pharyngitis, bilateral conjunctivitis and by periauricular lymph node enlargement. Usually seen in school going children and young adults occurs in outbreaks. Sporadic cases are seen in all age groups. PCF has an incubation period of 6-9 days. Adeno virus Serotypes 3, 4 and 7 are commonly associated and less common types are 1, 11, 14, 16-19 and 37⁹.

These viruses also cause non-specific conjunctivitis and chronic papillary conjunctivitis. The viruses spread rapidly in the community as a result of respiratory tract to eye, eye to eye and via infected tissues and clothes and other fomites and contaminated swimming pools.

Follicular conjunctivitis:

Eyelid vesicles, preauricular lymphadenopathy and sometimes ulcerative blepharitis, usually unilateral may be diagnosed as due to Herpes Simplex Virus. Enterovirus 70 and Coxsackie A24 can cause bilateral follicular conjunctivitis of sudden onset with conjunctival haemorrhages, transient keratitis^{12, 13}.

Herpes Conjunctivitis:

Herpes simplex virus comprises 1.3% to 4.8% of all cases of acute conjunctivitis. Conjunctivitis caused by the virus is usually unilateral. The discharge is thin and watery, and accompanying vesicular eyelid lesions may be present. Topical and oral antivirals are recommended to shorten the course of the disease. Topical corticosteroids should be avoided because they potentiate the virus and may cause harm. Herpes zoster virus, responsible for shingles, can involve ocular tissue, especially if the first and second branches of the trigeminal nerve are involved¹⁴. Eyelids (45.8%) are the most common site of ocular involvement, followed by the conjunctiva (41.1%). Corneal complication and uveitis may be present in 38.2% and 19.1% of cases, respectively. Patients with suspected eyelid or eye involvement or those presenting with Hutchinson sign (vesicles at the tip of the nose, which has high correlations with corneal involvement) should be referred for a thorough ophthalmic

evaluation. Treatment usually consists of a combination of oral antivirals and topical steroids¹⁵.

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The basic approaches to the virological investigations, collection and processing of specimens for detection and isolation of the infectious agent followed described in this suggested algorithm were based on our (SankaraNethralaya) experience from 1991 till date in the field of ocular virology⁽¹⁷⁻²⁵⁾.

Laboratory investigations:

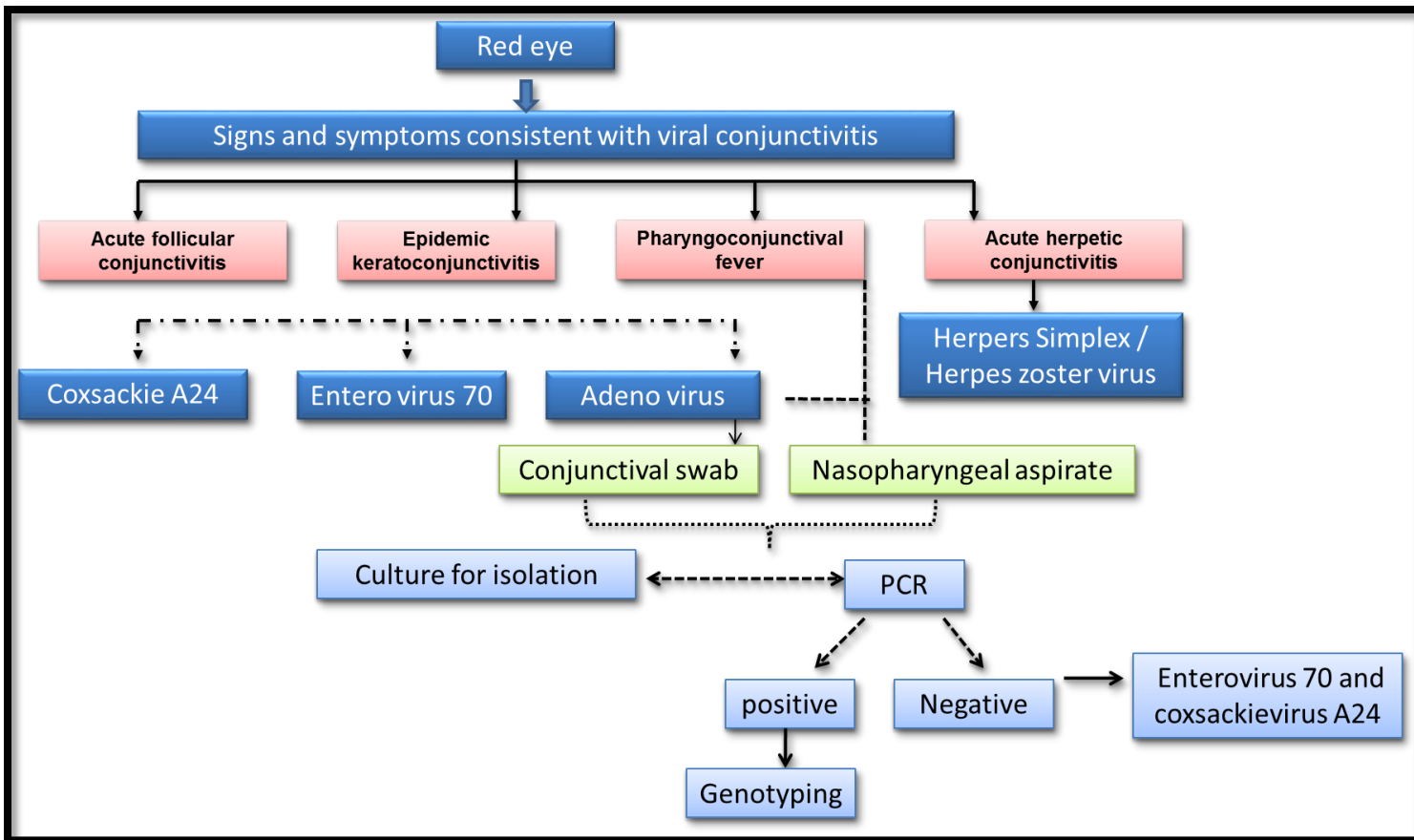
- Conjunctival material may be collected by the trained technologist.
- No topical anaesthetic is needed.
- Sterile cotton swab to be used.
- Patient is requested to look up, the lower eye lid is pulled down using thumb with sterile gauze and swab is rubbed over the lower conjunctival sac from medial to lateral side
- The procedure is often slightly painful.
- The collected material need to be put in to a vial containing viral transportation medium (1% Minimal essential medium) and sent fresh to the laboratory.
- The swabs need to inoculate into the tissue culture.
- Immunofluorescent tests directed against viral antigens can be performed.
- Polymerase chain reaction based diagnosis help in rapid diagnosis of the infectious agent.
- Combination of both conventional cell culture technique and PCR helps in rapid and sensitive diagnosis.

Prophylaxis:

- Viral conjunctivitis often occurs in community epidemics, with the virus transmitted in schools, workplaces and physicians offices. The usual modes of transmission are contaminated fingers, medical instruments and swimming pool water. Proper hand and instrument washing following patient contact can help to reduce the spread of this highly contagious infection.
- Since the ocular infection is contagious for at least seven days, patients should be instructed to avoid direct contact with other persons for at least one week after the

onset of symptoms. Treatment is supportive. Cold compresses and topical vasoconstrictors may provide symptomatic relief. Topical antibiotics are rarely necessary, because secondary bacterial infection is uncommon.

Figure 4: Differential diagnosis of viral conjunctivitis:



References:

1. Leibowitz HM. The red eye. *N Engl J Med.* 2000; 343(5):345–351.
2. American Academy of Ophthalmology. Cornea/External Disease Panel. Preferred Practice Pattern Guidelines: Conjunctivitis-Limited Revision. American Academy of Ophthalmology; San Francisco, CA: 2011.
3. Stenson S, Newman R, Fedukowicz H. Laboratory studies in acute conjunctivitis. *Arch Ophthalmol.* 1982; 100(8):1275–1277.
4. American Academy of Ophthalmology. Cornea/External Disease Panel. Preferred Practice Pattern Guidelines: Conjunctivitis-Limited Revision. American Academy of Ophthalmology; San Francisco, CA: 2011
5. Mannis, MJ.; Plotnik, RD. Bacterial conjunctivitis. In: Tasman, W.; Jaeger, EA., editors. *Duanes Ophthalmology on CD-ROM.* Lippincott Williams & Wilkins; 2006.
6. 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.
7. Skevaki CL, Galani IE, Pararas MV, et al. Treatment of viral conjunctivitis with antiviral drugs. *Drugs.* 2011; 71(3):331–347.
8. 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.
9. Yannof, J.; Duker, JS., editors. *Ophthalmology.* 2nd ed. Mosby; Spain: 2004. Disorders of the conjunctiva and limbus; p. 397-412.
10. Morrow GL, Abbott RL. Conjunctivitis. *Am Fam Physician.* 1998; 57(4):735–746.
11. 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.
12. 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.
13. 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.
14. Wilhelmus KR. Diagnosis and management of herpes simplex stromal keratitis. *Cornea.* 1987; 6(4):286–291.

15. Puri LR, Shrestha GB, Shah DN, Chaudhary M, Thakur A. Ocular manifestations in herpes zoster ophthalmol
16. 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. *micus. Nepal J Ophthalmol.* 2011; 3(2):165–171.
17. Dalapathy S, Lily TK, Roy S, Madhavan HN. Development and use of nested polymerase chain reaction (PCR) for the detection of adenovirus from conjunctivitis specimens. *J Clin Virol.* 1998; 11: 77-84.
18. Murray PR, Baron EJ, Jorgensen J MP, Landry ML. *Manual of Clinical Microbiology.* 9th Edn. ASM press. 2007:1589.
19. Madhavan HN. Laboratory investigations on viral and Chlamydia trachomatis infections of the eye: SankaraNethralaya experiences. *Indian J Ophthalmol.* 1999; 47: 241-246.
20. Madhavan HN, Malathy J, Priya K. An outbreak of acute conjunctivitis caused by Coxsackie virus A 24. *Indian J Ophthalmol.* 2000; 48: 159.
21. Janani MK, Malathi J, Madhavan HN. Isolation of a variant human adenovirus identified based on phylogenetic analysis during an outbreak of acute keratoconjunctivitis in Chennai. *Indian J Med Res.* 2012; 136: 260-264.
22. Madhavan HN, Rao SK, Natarajan K, Seethalakshmi G, Jayanthi I, Roy S. Evaluation of laboratory tests for diagnosis of chlamydial infections in conjunctival specimens. *Indian J Med Res* 1994; 100:5-9.
23. Madhavan HN. Evaluation of rapid culture method for detection of adenovirus from conjunctival specimens. *Invest Ophthalmol Vis Sci (Abstract)* 1992; 33:S853.
24. Madhavan HN, Ong KH, Sekar B, Radhika G. Rapid diagnosis of herpes simplex virus infection. *Indian J Virol* 1991; 7:22-25.
25. Ismail, A. M., T. Cui, K. Dommaraju, G. Singh, S. Dehghan, J. Seto, S. Shrivastava, Hajib Narahari Madhavan et al. 2018. “Genomic analysis of a large set of currently—and historically—important human adenovirus pathogens.” *Emerging Microbes & Infections* 7 (1): 10.