

Differentiating the Various Causes of Pediatric Conjunctivitis

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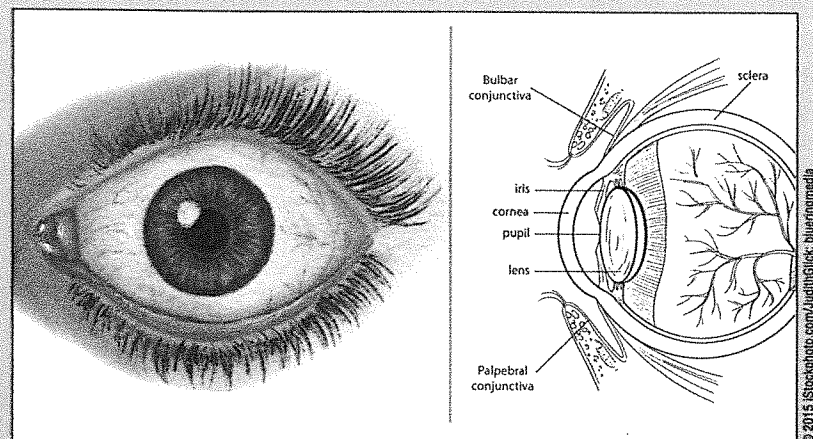
The conjunctiva is a thin, transparent mucous membrane consisting of 3 sections. The bulbar conjunctiva covers the sclera, while the palpebral conjunctiva forms a layer on the inner surface of the eyelids. The forniceal conjunctiva forms a loose fold between the upper eyelid and the sclera, permitting free movement of the eyeball (Figure 1). The conjunctiva serves to lubricate the eyeball, secreting tear fluid. Goblet cells in the bulbar conjunctiva secrete mucin.

Inflammation of the conjunctiva, or conjunctivitis, is frequently known as “pink eye”, particularly in its milder manifestations. Infectious conjunctivitis can be extremely contagious. In an outbreak of the disease at Dartmouth College in the winter of 2002, 13.8% of students contracted bacterial conjunctivitis, including 22% of the first-year student class.¹ The causative organism in the outbreak was *Streptococcus pneumoniae*. The risk factors identified were: close contact with an infected student, wearing contact lenses, membership on a sports team, and

attending parties. The outbreak was controlled following an awareness campaign that promoted hand-washing, early treatment, and avoidance of sharing towels, utensils, and drinking glasses.

Conjunctivitis is a very common disease, with an incidence of approximately 6 million cases each year in the United States. Depending on the cause and the health of the patient, it is most often a relatively mild condition

Figure 1. The Anatomy of the Conjunctiva



The conjunctiva serves to lubricate the eyeball, secreting tear fluid. Goblet cells in the bulbar conjunctiva secrete mucin.

Source: Azari AA, et al. *JAMA*. 2013;310(16):1721-1730.

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Overview

Acute bacterial conjunctivitis affects approximately 1 of every 8 children each year, and 5 million cases occur in the United States annually. Although acute bacterial conjunctivitis is frequently self-limiting, the use of antibiotic eye drops have

been associated with modestly improved rates of clinical and microbiological remission in comparison with the use of placebo. While prescribing an antibiotic, pediatricians should have in mind the most likely pathogen and the cost and adverse effects of each drug. Also, they should be aware of the rise of bacterial resistance and current resistance patterns. New antimicrobial agents that treat ocular infections effectively and have a low potential for the development of resistance could be a part of strategies to prevent the global increase in ocular pathogen resistance. It is critical for pediatricians to be aware of the new guidelines and best practices for diagnosis and management of conjunctivitis-otitis syndrome. Leading experts will discuss the different causes and appropriate treatment of conjunctivitis in pediatric populations, as well as diagnosis and treatments for conjunctivitis with concurrent otitis media that are effective and least likely to result in antimicrobial resistance in this population.

Target Audience

The intended audience for the activities is pediatricians, pediatric nurse practitioners, and other health care professionals involved in the treatment of patients with conjunctivitis.

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of short duration. There are 3 major subtypes, classified according to their etiology: allergic, bacterial, and viral. The clinical presentation is quite similar across these subtypes. All 3 commonly present with conjunctival redness and watery discharge. Mucoïd discharge may also occur. Pruritus and irritation are more frequently seen in patients with allergic conjunctivitis, but may also be present in viral and bacterial infections. Both viral and bacterial infections may produce a purulent discharge. Follicle formation occurs mainly in viral and bacterial subtypes, but is occasionally also seen with allergy. Overall, only one symptom (redness) is seen in more than half of bacterial infections, and this is seen with equal frequency in viral disease (Table 1). Diagnosis is thus challenging, and it is unsurprising that clinicians are able to correctly diagnose the disease subtype only about 50% of the time.

Conjunctivitis in adult patients typically has an allergic or viral etiology. In contrast, conjunctivitis in children is predominantly bacterial in origin.^{2,3} Pediatric conjunctivitis is a common reason for pediatric primary care visits. Depending on etiology, it can be very contagious, so the affected child is usually kept away from day care or school, which frequently results in lost time from work for parents.

Originally, it was believed that about half of pediatric conjunctivitis was bacterial in origin. As physicians

recommend antibiotics in 80% to 95% of cases, it was thought that antibiotics were over-prescribed. However, subsequent studies have shown that the incidence of bacterial etiology approximates the prescribing rate quite closely.^{4,5} Weiss and colleagues found bacterial infection in 76 of 95 (80%) randomly selected outpatients aged 4 months to 12 years. Of the remainder, 13% had viral infections, while only 2% of the group had conjunctivitis that was allergic in origin.⁴ The most commonly cultured pathogenic organisms were *H. influenzae*, *S. pneumoniae*, and *M. catarrhalis*, which together accounted for approximately 88% of the

Conjunctivitis in children is predominantly bacterial in origin and is a common reason for primary care visits.

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bacterial isolates from conjunctival scrapings taken from 74 patients. These findings were confirmed in a more recent prospective study conducted in a children's hospital emergency department. In this investigation, 78% of children with conjunctivitis had positive bacterial cultures.⁵ *H. influenzae* was the most common causative organism, accounting for 82% of infections. *S. pneumoniae* and *S. aureus* made up the remainder of cases in this study. The investigators found that the combination of a history of gluey or sticky eyelids or eyelashes and the physical finding of mucoïd or purulent discharge was highly diagnostic, with a posttest probability of 96%, compared to subjective scoring by physicians for a positive culture, which was 50.6%. A clinical picture of red eye together with mucopurulent discharge and normal

Table 1. Signs and Symptoms of Conjunctivitis According to Etiology (% of Cases)

Symptom	Etiology		
	Allergic	Viral	Bacterial
Redness	38	81*	83
Purulent discharge	N/A	25	28
Mucoïd discharge	18	19	17
Irritation/foreign body sensation	52	19	17
Watery discharge/tearing	48	50	39
Itching	86	38	33
Follicles present	8	47	42

*Symptoms seen in half or more cases of a particular etiology marked in bold.

Source: Fitch CP, et al. *Ophthalmology*. 1989;96(8):1215-1220; Solomon AS. *Arch. Ophthalmol*.1985;103(7):891; Kosirukvongs P, et al. *Asian Pac J Allergy Immunol*. 2001;19(4):237-244.

vision is strongly indicative of bacterial infection. Otitis media may also be present in about one-third of cases.

Allergic conjunctivitis, the inflammatory response of the conjunctiva to allergens such as pollen, animal dander, and other environmental antigens, is the most frequent type of conjunctivitis in the general population,⁴ although it is far less common in children.² In the United States, 90% of cases consist of seasonal allergic conjunctivitis. Allergic conjunctivitis is encountered in up to 40% of the population, although only about 10% of these individuals seek medical help. As a result, the condition tends to be underdiagnosed.² The primary symptom is itching and treatment consists of topical antihistamines and mast-cell stabilizers, in addition to the use of saline solution to dilute and remove the allergens. The causative antigens should be avoided, if possible. Allergy can be largely ruled out if itching, burning, or stinging are absent. Conversely, if itching is present, there should be a high suspicion for an allergic cause.²

Viral conjunctivitis is the most common overall cause of infectious conjunctivitis in the total population.² Viruses cause up to 80% of all cases of acute conjunctivitis. As with allergic conjunctivitis, the viral form of the condition is much less common in children. There is no effective treatment for viral infections, except for herpes simplex; antihistamines and artificial tears may be used to provide symptomatic relief.

Viral infection is more difficult to eliminate from the diagnosis, as the typical clinical signs and symptoms are indistinguishable from those of bacterial infection (Table 1). One of the most common causes of acute conjunctivitis is epidemic keratoconjunctivitis (EKC), a highly contagious adenovirus infection.⁶ This severe form of the disease is characterized by the sudden onset of acute follicular conjunctivitis, and usually occurs in both eyes. Although EKC is a self-limiting disease that tends to resolve spontaneously within 1 to 3 weeks without significant complications, corneal opacity may persist for several months in up to 50% of cases, during which time visual acuity may be significantly reduced and glare symptoms may be present. In some cases, changes in the cornea can cause permanent loss of vision. Adenoviral conjunctivitis can be diagnosed with the help of a commercially available in-office test kit.

Herpes simplex is another viral cause of conjunctivitis. A characteristic branching pattern on the cornea is visible with fluorescein staining, although it is not apparent

during a normal office examination. The use of topical corticosteroids, which is not recommended for any ophthalmic purpose in pediatric practice, should be assiduously avoided in the presence of herpes infection, as they may cause serious exacerbation of *H. simplex* infections. If herpetic infection is suspected, the patient should be referred to ophthalmology for further evaluation and treatment.

The etiology of conjunctivitis changes with age.⁷ In neonates, common causes include chemical irritation due to silver nitrate prophylaxis, *C. trachomatis* and *N. gonorrhoea*, which may occur in the first 4 days of life. Because neonatal conjunctivitis caused by these sexually transmitted diseases can have severe consequences, bacterial culture should be performed for all affected newborns.⁸ Rapid diagnosis and treatment of conjunctivitis in neonates is of great importance, and treatment with topical erythromycin ointment and IV or IM third-generation cephalosporin should be initiated immediately. Treatment can be modified as indicated when laboratory results are available. *C. trachomatis* is the most common infectious agent causing neonatal conjunctivitis. The baby can become infected as it passes through the birth canal. Infants with *Chlamydia*-infected mothers have a

25% to 50% risk of infection.⁸ *Chlamydia* infection carries significant risk for life-threatening pneumonia in neonates and systemic therapy is therefore necessary. The usual treatment is oral erythromycin (50 mg/kg/d QID) for 14

days. A second course is sometimes needed to eradicate the infection.

Neisseria conjunctivitis is also cause for concern, as it is one of the few organisms that can penetrate a normal intact cornea, leading to perforation. Gonococcal conjunctivitis can progress very rapidly, thus the need for immediate therapy prior to obtaining culture results. Fortunately, *Neisseria* conjunctivitis is relatively rare in the United States, thanks to routine prophylaxis for neonates.

In infants and toddlers, *H. influenzae* and *S. pneumoniae* are more common. When otitis media is present, *H. influenzae* predominates. As children reach school age and progress to adolescence, the proportion of viral and allergic etiologies increases.

In the great majority of cases, bacterial, viral and allergic conjunctivitis, and pink eye, as well as dry eye can be diagnosed and treated effectively in the office. However, if the patient is experiencing significant pain or strong light sensitivity, or if they have blurred vision,

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further evaluation is required, and the child should be referred to an ophthalmologist.

A frequently asked question is whether an eye culture is necessary in conjunctivitis. In most cases, it is not necessary. Signs indicative of the need for a culture include vision loss, eye pain, or lack of response to topical therapy, resulting in the patient returning with persistent symptoms. Other reasons to consider a culture include recurrent episodes of conjunctivitis, a history of herpes, or a neonate. Persistent or severe symptoms of red eye may be a sign of other, perhaps more serious conditions,² including dry eye, blepharitis, uveitis associated with juvenile rheumatoid arthritis, congenital glaucoma, cellulitis, subconjunctival hemorrhage, toxic conjunctivitis, Stevens Johnson syndrome, or corneal ulcer. Therefore, symptoms that suggest the need for a culture by their persistence or severity also point to the need to refer the patient for further evaluation. An algorithm published recently in the *Journal of the American Medical Association (JAMA)* is helpful in identifying acute conjunctivitis using a focused ocular history along with a penlight eye examination (Figure 2).

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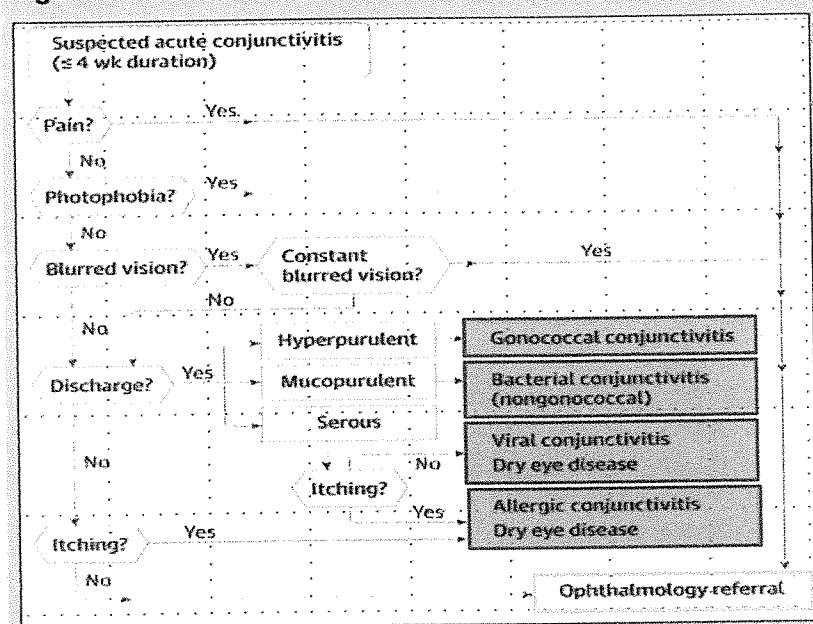
Even if it is not possible to consistently identify the etiology of the conjunctivitis using this tool, it is helpful in differentiating conjunctivitis from other conditions that cause similar ocular symptoms.

Treatment

Empirical topical antibiotic therapy has long been favored when bacterial conjunctivitis is suspected. This antibiotic therapy is believed to increase the rate of recovery, reduce relapse, and help reduce the risk of sight-threatening complications. However, the emergence of concerns about bone marrow aplasia associated with chloramphenicol, together with the problems of increasing bacterial resistance to broad-spectrum antibiotics, have raised questions about the routine use of antibiotics in infections, such as sinusitis, otitis media, and sore throat (pharyngitis/tonsillitis), which frequently resolve spontaneously.⁹

In order to examine the question of whether antibiotic therapy is justified in bacterial conjunctivitis, a Cochrane literature review was conducted.⁹ The review confirmed that acute bacterial conjunctivitis is frequently a self-limiting condition; meta-analysis indicated that clinical remission occurred within 2 to 5 days in 64% (95% confidence interval (CI) 57% to 71%) of patients treated with placebo. Nevertheless, it was also found that treatment with antibiotics produced significantly better rates of clinical remission (days 2 to 5: relative risk (RR) 1.31 95% CI 1.11 to 1.55, number needed-to-treat (NNT) = 5). In addition, late clinical remission (days 6 to 10) appeared to improve with antibiotic use (RR 1.27 95% CI 1.00 to 1.61, NNT=5). Microbiological remission also improved with antibiotics. No serious adverse events were reported in the trials, suggesting a favorable risk-benefit ratio for antibiotic use. The authors noted that clinical data is very limited, and there is a lack of information on patient-oriented outcomes and cost-effectiveness.

Figure 2. Acute Conjunctivitis Diagnostic Algorithm



AMA algorithm is helpful in identifying acute conjunctivitis using a focused ocular history along with a penlight eye examination.

Source: Azari AA, et al. *JAMA*. 2013;310(16):1721-1730.

Table 2. Common Antibiotics Used in Treating Pediatric Conjunctivitis

Antibiotic	Class	Age Approved
Erythromycin	Macrolide	Infants/newborns
Tobramycin	Aminoglycoside	≥2 months
Moxifloxacin	4th generation fluoroquinolone	≥4 months
Polymyxin B and trimethoprim	Polymixin + dihydrofolate red. Inhib.	≥2 months
Ciprofloxacin	2nd generation fluoroquinolone	≥1 year
Oflaxacin	2nd generation fluoroquinolone	≥1 year
Levofloxacin	3rd generation fluoroquinolone	≥1 year
Gatifloxacin	4th generation fluoroquinolone	≥1 year
Besifloxacin	4th generation fluoroquinolone	≥1 year
Azithromycin	Macrolide	≥1 year

Source: http://www.aaopt.org/sites/default/files/userfiles/2014_Handouts/GO-15.pdf

A number of antibiotics are indicated for use in pediatric conjunctivitis, from erythromycin, which may be used in neonates, to 2nd, 3rd, and 4th generation fluoroquinolones. Moxifloxacin is approved for use at 4 months, while several others are approved for 1-year-olds and above (Table 2).

Selection of an agent for use in bacterial conjunctivitis should take several factors into consideration, including a rapid rate of activity against the pathogen, coverage of the main causative organisms (*H. influenzae*, *S. pneumoniae*, *M. catarrhalis*, and *S. aureus*) with a low rate of resistance in these bacteria, low ocular toxicity, and good tolerance and convenience. The newer-generation fluoroquinolones, with their rapid action against target organisms, fit this profile well.¹⁰

For the pediatrician, treatment with antibiotics has several potential advantages. Shortening the course of the disease and uncomfortable symptoms by several days is a clear benefit to younger patients. The office visit allows the pediatrician to ensure the symptoms do not signify a more serious problem, requiring further care. Treatment may help to limit the spread of the disease, reduce the small risk of sight-threatening complications, and hasten the

patient's return to school or day care, freeing the parent to return to work.

Contact Lenses

When considering early antibacterial therapy versus watchful waiting, one important factor to consider is the use of contact lenses. While allergy to the lenses themselves can be a cause of conjunctivitis, more importantly, their incorrect use can promote microbial growth. Poor hygiene associated with the use of prescription and cosmetic contact lenses is a significant risk factor for ocular

infection. Contact lenses appear to favor the development of gram negative infections, such as *Pseudomonas aeruginosa*,³ and bacterial keratitis occurs in up to 30 per 100,000 contact lens wearers. The Centers for Disease Control

and Prevention (CDC) *Morbidity and Mortality Weekly Report (MMWR)* for November 14, 2014 describes contact lens use as the major risk factor for microbial keratitis.¹¹ The report notes that 230,000 doctor's office and outpatient clinic visits and 19,000 emergency department visits for corneal disorders involving contact lenses occurred in 2010, of which 20.5% were made by patients aged less than 25 years. Therefore, it is probable that

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most pediatricians will encounter patients with contact lens-related infections from time to time. The use of contact lenses is important to include in the patient history.

Evidence for empirical antibiotic treatment of bacterial conjunctivitis in contact lens wearers is scarce, as clinical trials either exclude them or do not specify contact lens use in the trial design.³ However, as there is a high risk for keratitis, these patients should be treated immediately with topical antibiotics and referred to an ophthalmologist.² Laboratory tests to identify bacteria and sensitivity to antibiotics should be performed in these patients, to guide further treatment. Microbial conjunctivitis associated with contact lens use can progress very rapidly, and may lead to complications such as hypopyon formation and corneal ulceration within 24 hours. Such serious infections can produce scarring and permanent loss of vision.

Patients who wear contact lenses should be counseled to practice good lens hygiene, including:

- Do not sleep with the lenses in unless specifically prescribed by a physician.
- Do not use water to store or wet the lenses.
- Do not swim or shower with the lenses in.
- If red eye develops, remove the lenses immediately and see an eye care practitioner as soon as possible, to ensure no serious infection is present.

Infections due to poor hygiene associated with the use of contact lenses may have etiologies not otherwise commonly seen in conjunctivitis. Since 2006, there have been 3 very serious outbreaks of corneal infection due to contact lens use caused by the protozoan *Acanthamoeba*, which is most common among contact lens wearers,³ and the fungus *Fusarium*.¹²⁻¹⁴

Summary

In summary, bacterial conjunctivitis is common in the pediatric age group. It is frequently self-limiting, but the pediatrician nevertheless has the opportunity to reduce the severity and duration of the disease with the use of topical antibiotics. For neonates, and if the patient reports pain, light sensitivity, or decreased vision, referral should be made to an ophthalmologist. Contact lens wearers are a group particularly susceptible to

serious, rapidly progressing infections, and should be quickly treated and referred. Finally, steroid use should be avoided by pediatricians in eye disease.

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