AHMAD B. TARABISHY, MD

Cole Eye Institute, Cleveland Clinic

BENNIE H. JENG, MD

Cole Eye Institute, Cleveland Clinic; Assistant Professor of Ophthalmology, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University

Bacterial conjunctivitis: A review for internists

ABSTRACT

Bacterial conjunctivitis is common and occurs in patients of all ages. Typical signs are a red eye and purulent drainage that persists throughout the day. Gonococcal and chlamydial conjunctivitis must be treated with systemic antibiotics. Bacterial conjunctivitis due to most other organisms can be treated empirically with topical antibiotics. Red flags suggesting a complicated case requiring referral to an ophthalmologist include reduced vision, severe eye pain, a hazy-appearing cornea, contact lens use, and poor response to empirical treatment.

KEY POINTS

Viral conjunctivitis typically presents as an itchy red eye with mild watery discharge. Many patients have signs and symptoms of a viral upper respiratory tract infection (eg, cough, runny nose, congestion) and have been in contact with a sick person.

Having both eyes glued shut in the morning had an odds ratio of 15:1 in predicting a positive bacterial culture, whereas either itching or previous conjunctivitis made a bacterial cause less likely.

In adults, *Neisseria gonorrhoeae* causes hyperacute conjunctivitis and is associated with concurrent, often asymptomatic genital infection. Gonococcal conjunctivitis should be treated with a single dose of ceftriaxone (Rocephin) 1 g intramuscularly plus saline eye-washing.

Corticosteroid drops should not be prescribed for a red eye before consultation with an ophthalmologist because these drops may worsen some conditions. B ACTERIAL CONJUNCTIVITIS is common in children and adults presenting with a red eye. Although most cases are self-limited, appropriate antimicrobial treatment accelerates resolution and reduces complications. It is critical to differentiate bacterial conjunctivitis from other types of conjunctivitis and more serious vision-threatening conditions so that patients can be appropriately treated and, if necessary, referred to an ophthalmologist.

This paper is an overview of how to diagnose and manage bacterial conjunctivitis for the office-based internist.

CAUSES VARY BY AGE

Conjunctivitis is a generic term for inflammation of the conjunctiva due to various infectious agents (bacteria, viruses, or fungi) and noninfectious causes (eg, allergic, chemical, and mechanical). The organisms that cause bacterial conjunctivitis tend to differ by patient age (TABLE 1).

In neonates, conjunctivitis is predominantly bacterial, and the most common organism is *Chlamydia trachomatis*. Chlamydial conjuctivitis typically presents with purulent unilateral or bilateral discharge about a week after birth in children born to mothers who have cervical chlamydial infection. Many infants with chlamydial conjunctivitis develop chlamydial pneumonitis: approximately 50% of infants with chlamydial pneumonitis have concurrent conjunctivitis or a recent history of conjunctivitis.¹

Source of funding: Dr. Jeng is supported in part by a Research to Prevent Blindness Challenge Grant to the Department of Ophthalmology of the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, and National Institutes of Health 1KL2 RR024990 Multidisciplinary Clinical Research Career Development Programs Grant.

TABLE 1

Common causes of bacterial conjunctivitis in the United States

Neonates

Chlamydia trachomatis Staphylococcus aureus Haemophilus influenzae Streptococcus pneumoniae

Children

H influenzae S pneumoniae S aureus

Adults

S aureus
Coagulase-negative Staphylococcus organisms
H influenzae
S pneumoniae

Neisseria gonorrhoeae is a rare cause of neonatal conjunctivitis. The onset is somewhat earlier than in chlamydial conjunctivitis, ie, in the first week of life, and this organism classically causes severe "hyperacute" conjunctivitis with profuse discharge and may result in corneal involvement and perforation. Routine antibiotic prophylaxis at birth has markedly reduced its incidence and complications.

Other bacteria that can cause neonatal conjunctivitis include *Staphylococcus aureus*, *Haemophilus influenzae*, and *Streptococcus pneumoniae*.²

In children, bacterial conjunctivitis is most often caused by *H influenzae* or *S pneumoniae*, which accounted for 29% and 20% of cases, respectively, in a prospective study in Israel.³ Whether patients had been vaccinated against *H influenzae* in this study is unclear.

H influenzae conjunctivitis spreads easily in schools and households. It is associated with concurrent upper respiratory tract infections and otitis media (conjunctivitis-otitis syndrome): 45% to 73% of patients with purulent conjunctivitis also have ipsilateral otitis media.⁴

S pneumoniae, the second most common cause of bacterial conjunctivitis in children, is a common cause in epidemic outbreaks among young adults. Newly described unencapsulated pneumococcal strains caused outbreaks that

affected 92 recruits at a military training facility and 100 students at Dartmouth University.⁵ S *pneumoniae* is also associated with conjunctivitis-otitis syndrome, accounting for approximately 23% of culture-proven cases.⁴

Moraxella species, S aureus, and coagulasenegative staphylococci are less common causes of bacterial conjunctivitis in children.^{6–8}

In adults, the most common causes of bacterial conjunctivitis are *S aureus* and *H influenzae*. Conjunctivitis caused by *S aureus* is often recurrent and associated with chronic blepharoconjunctivitis (inflammation of the eyelid and conjunctiva). The conjunctivae are colonized by *S aureus* in 3.8% to 6.3% of healthy adults.^{9–11} In addition, about 20% of people normally harbor *S aureus* continually in the nasal passages, and another 60% harbor it intermittently; in both cases, the bacteria may be a reservoir for recurrent ocular infection.¹²

Other organisms that commonly cause conjunctivitis in adults are *S pneumoniae*, coagulase-negative staphylococci, and *Moraxella* and *Acinetobacter* species.¹³

■ HOSPITAL-ACQUIRED CONJUNCTIVITIS

Little has been published about hospitalacquired conjunctivitis. In a neonatal intensive care unit, the most common organisms isolated in patients with conjunctivitis were coagulase-negative staphylococci, S aureus, and Klebsiella species.14 We found that about 30% of children who developed bacterial conjunctivitis after 2 days of hospitalization at Cleveland Clinic harbored gram-negative organisms. In addition, in patients who were found to have conjunctivitis caused by Staphylococcus species, the rate of methicillin resistance was higher in those hospitalized for more than 2 days than those with Staphylococcus species who were hospitalized for less than 2 days. This suggests that the bacterial pathogens encountered in hospitalized children with conjunctivitis differ from those found in the outpatient setting.¹⁵

■ EYE DISORDERS PREDISPOSE TO INFECTION

The conjunctiva is a transparent membrane that covers the sclera and lines the inside of

H influenzae conjunctivitis spreads easily in schools and households the eyelid. It is a protective barrier against invading pathogens and lubricates the ocular surface by secreting components of the tear film (although the lacrimal glands contribute more to the tear film).

Several unique anatomic and functional features of the ocular surface help prevent bacterial infection in the healthy eye. The tear film contains secreted immunoglobulins, lysozyme, complement, and multiple antibacterial enzymes, and it is continuously being flushed and renewed, creating a physically and immunologically adverse environment for bacterial growth.

Disorders involving the eyelids or tear film such as chronic dry eye and lagophthalmos (in which the eye cannot close completely) may predispose the eye to frequent infections. Also, an adjacent focus of infection, such as inflammation of the lacrimal gland (dacryocystitis), can cause recurrent or chronic conjunctivitis.¹⁶

CLINICAL FEATURES OF BACTERIAL CONJUNCTIVITIS

Inflammation of the conjunctiva causes injection (dilation of conjunctival vessels) and in some cases chemosis (conjunctival edema). Discharge may be seen in bacterial, viral, or allergic conjunctivitis. In bacterial conjunctivitis, discharge varies from mild to severe but usually appears purulent (FIGURE 1) and persists throughout the day. Meibomian gland secretions in the medial canthus that accumulate during sleep and are not present during the day should not be confused with true discharge.

Bacterial conjunctivitis is commonly classified according to its clinical presentation: hyperacute, acute, or chronic.

Hyperacute bacterial conjunctivitis presents with the rapid onset of conjunctival injection, eyelid edema, severe, continuous, and copious purulent discharge, chemosis, and discomfort or pain.

N gonorrhoeae is a frequent cause of hyperacute conjunctivitis in sexually active patients; the patient usually also has N gonorrhoeae genital infection, which is often asymptomatic. N gonorrhoeae conjunctivitis also occurs in neonates, as noted above.



FIGURE 1. Bacterial conjunctivitis. Note the purulent discharge, the red eye, and chemosis.

The cornea is frequently involved, and untreated cases can progress within days to corneal perforation. Unlike most other types of conjunctivitis, gonococcal conjunctivitis should be treated as a systemic disease, with both systemic and topical antibacterial therapy.²

Acute bacterial conjunctivitis typically presents abruptly with red eye and purulent drainage without significant eye pain, discomfort, or photophobia. Visual acuity does not typically decrease unless large amounts of discharge intermittently obscure vision.

Chronic bacterial conjunctivitis, ie, red eye with purulent discharge persisting for longer than a few weeks, is generally caused by *Chlamydia trachomatis* or is associated with a nidus for infection such as in dacryocystitis.

■ BACTERIAL CONJUNCTIVITIS VS OTHER CAUSES OF A RED EYE

Clinical signs and symptoms of infection with certain organisms have been extensively described, but a meta-analysis¹⁷ found no evidence that these textbook features help to distinguish between bacterial and viral causes of conjunctivitis. Instead, whether a bacterial cause was likely was best determined from just three features: having both eyes glued shut in the morning had an odds ratio of 15:1 in predicting a positive bacterial culture, and either itching or previous conjunctivitis made a bacterial cause less likely.¹⁸

In general, however, viral conjunctivitis typically presents as an itchy red eye with mild watery discharge. Many patients have signs In bacterial conjunctivitis, mild to severe purulent discharge persists throughout the day

TABLE 2

Differential diagnosis of a red eye

Acute glaucoma* Allergic conjunctivitis Anterior uveitis* Blepharitis

Chemical conjunctivitis

Dry eye

Episcleritis

Foreign body*

Infectious conjunctivitis

Keratitis*

Scleritis*

Subconjunctival hemorrhage

*Associated with severe pain, decreased vision, or a hazy cornea and requires urgent referral to an ophthalmologist

and symptoms of a viral upper respiratory tract infection (eg, cough, runny nose, congestion) and have been in contact with a sick person. Ipsilateral preauricular lymphadenopathy is common in viral conjunctivitis and strongly suggests this diagnosis.¹⁹

Viral conjunctivitis is often epidemic and is easily contagious. Several epidemics have been traced to eyecare facilities. Adenovirus conjunctivitis is extremely contagious and can be transmitted both between people and via inanimate objects; it has been reported to be spread by workers in health care facilities.²⁰

Allergic conjunctivitis is also common. Patients typically report itching and redness of both eyes in response to an allergen exposure. Other allergic symptoms may be present, such as allergic rhinosinusitis, asthma, or atopic dermatitis in response to seasonal or perennial environmental allergens.

Other causes of a red eye. Many patients with a red eye have conjunctivitis, but other conditions can also present in a similar manner. Whether a patient has a serious vision-threatening condition (eg, acute-angle closure glaucoma, microbial keratitis, or anterior uveitis) can usually be determined with a focused ophthalmologic history and physical examination. Any alarming clinical features such as severe pain, decreased vision, or a hazy cornea in a patient with a red eye should alert

the clinician to a more serious condition and prompt a referral to an ophthalmologist for an urgent evaluation (TABLE 2). A complete review for internists on how to manage a red eye was recently published in this journal.²¹

■ TREATMENT

Systemic treatment needed for gonococcal or chlamydial infections

The US Centers for Disease Control and Prevention recommend treating gonococcal conjunctivitis with ceftriaxone (Rocephin) 1 g in a single intramuscular dose plus topical saline lavage of the eye.^{22,23} Sexual partners of the patient should be referred for evaluation and treatment, as should mothers of affected neonates and the mother's sexual partners.

Chlamydial conjunctivitis is also treated with systemic antibiotics. In neonates, the treatment is the same as for pneumonia caused by *C trachomatis*: erythromycin taken orally for 14 days. In adults, it can be treated with a single oral dose of azithromycin (Zithromax) 1 g.

Some authors recommend that *H influenzae* conjunctivitis also be treated with systemic antibiotics, as it is frequently associated with concurrent otitis media.²⁴

Topical antibiotics hasten cure

Other types of bacterial conjunctivitis usually resolve spontaneously: early placebo-controlled studies found that more than 70% of cases of bacterial conjunctivitis resolve within 8 days.²⁵ However, treatment with antibacterial agents leads to a faster clinical and microbiological cure²⁶ and reduces the chance of rare complications²⁷ and of transmitting the infection.

A number of topical antibiotics are effective for treating bacterial conjunctivitis (TABLE 3),^{28,29} but there is no firm rule about which one to use because no significant differences have been found in clinical outcomes with different agents.²⁸ Factors such as cost, local resistance data, and risk of adverse effects should be considered; however, we know of no studies of the cost-effectiveness of treating bacterial conjunctivitis.

Is culture necessary?

A predictable set of organisms accounts for most cases of bacterial conjunctivitis in out-

There is no firm rule on which topical antibiotic to use

patients, so many physicians start therapy empirically without culturing the conjunctiva. But in the hospital the organisms and their antibiotic resistance patterns are more varied, so culturing the conjunctiva before starting broad-spectrum therapy may be warranted.¹⁵ For an outpatient with possible hyperacute conjunctivitis, it is reasonable to perform a Gram stain in the office if the facilities exist, but it is not essential because urgent referral to an ophthalmologist is warranted regardless of the results to rule out corneal involvement.

Unfortunately, antibiotic resistance is increasing even among outpatients. Susceptibility of the most common ocular pathogens to ophthalmic antimicrobial agents has dropped dramatically: S pneumoniae and S aureus have developed high rates of resistance.³⁰ Recent data also suggest that treatment with topical ophthalmic antibiotics can induce resistance among colonizing bacteria in nonocular locations.31 Widespread systemic treatment with azithromycin or tetracycline for control of endemic trachoma in two villages in Nepal resulted in increased rates of antibiotic resistance among nasopharyngeal isolates of S pneumoniae. S aureus is developing resistance to methicillin and to fluoroquinolones, such as levofloxacin (Levaquin).32,33 But fluoroquinolones are still effective against most bacteria that cause conjunctivitis or keratitis, and because they penetrate the cornea well, they should be used if clinical features suggest corneal involvement. Remember also that most patients recover without treatment even if the organism has appreciable antibiotic resistance.²⁸

Corticosteroids should be avoided

Although corticosteroid drops (either alone or combined with antibiotic drops) may quickly relieve symptoms, some conditions that present as a red eye with watery discharge, such as herpetic keratitis, worsen with corticosteroid use. We recommend that internists avoid prescribing corticosteroid drops.

Remove contact lenses, replace eye drops

Contact lenses should be taken out until an infection is completely resolved. Disposable

TABLE 3

Topical antibiotics used to treat bacterial conjunctivitis

Bacitracin (Ak-Tracin, Bacticin)

Chloramphenicol (AK-Chlor, Chloroptic, Chloromycetin)

Ciprofloxacin (Ciloxan)

Gatifloxacin (Zymar)

Gentamicin (Gentak, Gentasol)

Levofloxacin (Quixin)

Moxifloxacin (Vigamox)

Neomycin (Neosporin)

Ofloxacin (Ocuflox)

Polymyxin B and trimethoprim (Polytrim)

Sulfacetamide (Cetamide, Ocusulf-10, Sodium Sulamyd, Sulf-10)

Tobramycin (AK-Tob, Tobrex)

lenses should be thrown away. Nondisposable lenses should be cleaned thoroughly as recommended by the manufacturer, and a new lens case should be used.

Patients who use prescription eye drops for glaucoma should continue to use them, but the bottles should be replaced in case they have been contaminated by inadvertent contact with the eve.

Over-the-counter lubricating eye drops may be continued if desired, but a fresh bottle or vial should be used.

■ WHEN TO REFER

Red flags indicating that a patient may have a serious vision-threatening condition that requires urgent referral to an ophthalmologist include severe eye pain or headache, photophobia, decreased vision, or contact lens use. Patients with hyperacute cases should also be referred at once to rule out corneal involvement, although the internist should start treatment for gonorrhea. In addition, patients with apparent bacterial conjunctivitis that does not improve after 24 hours of antibiotic treatment should also be referred to an ophthalmologist.

Antibiotic resistance is increasing, even in outpatients

TARABISHY AND JENG

REFERENCES

- 1. Tipple MA, Beem MO, Saxon EM. Clinical characteristics of the afebrile pneumonia associated with Chlamydia trachomatis infection in infants less than 6 months of age. Pediatrics 1979; 63:192-197.
- 2. De Toledo AR, Chandler JW. Conjunctivitis of the newborn. Infect Dis Clin North Am 1992; 6:807-813.
- 3. Buznach N, Dagan R, Greenberg D. Clinical and bacterial characteristics of acute bacterial conjunctivitis in children in the antibiotic resistance era. Pediatr Infect Dis J 2005: 24:823-828.
- 4. Bodor FF. Conjunctivitis-otitis syndrome. Pediatrics 1982; 69:695-698.
- Crum NF, Barrozo CP, Chapman FA, Ryan MA, Russell KL. An outbreak of conjunctivitis due to a novel unencapsulated Streptococcus pneumoniae among military trainees. Clin Infect Dis 2004;
- 6. Gigliotti F, Williams WT, Hayden FG, et al. Etiology of acute conjunctivitis in children. J Pediatr 1981: 98:531-536.
- 7. Weiss A, Brinser JH, Nazar-Stewart V. Acute conjunctivitis in childhood. J Pediatr 1993; 122:10-14.
- Block SL, Hedrick J, Tyler R, et al. Increasing bacterial resistance in pediatric acute conjunctivitis (1997-1998). Antimicrob Agents Chemother 2000; 44:1650-1654.
- 9. Singer TR, Isenberg SJ, Apt L. Conjunctival anaerobic and aerobic bacterial flora in paediatric versus adult subjects. Br J Ophthalmol 1998; 72:448-451.
- 10. Kato T, Hayasaka S. Methicillin-resistant Staphylococcus aureus and methicillin-resistant coagulase-negative staphylococci from conjunctivas of preoperative patients. Jpn J Ophthalmol 1998; 42:461-465.
- 11. Nakata K, Inoue Y, Harada J, et al. A high incidence of Staphylococcus aureus colonization in the external eyes of patients with atopic dermatitis. Ophthalmology 2000; 107:2167-2171.
- 12. Kluytmans J, van Belkum A, Verbrugh H. Nasal carriage of Staphylococcus aureus: epidemiology, underlying mechanisms, and associated risks. Clin Microbiol Rev 1997; 10:505-520.
- 13. Kowalski RP, Karenchak LM, Romanowski EG. Infectious disease: changing antibiotic susceptibility. Ophthalmol Clin North Am 2003; 16:1-9.
- 14. Haas J, Larson E, Ross B, See B, Saiman L. Epidemiology and diagnosis of hospital acquired conjunctivitis among neonatal intensive care unit patients. Pediatr Infect Dis J 2005; 24:586-589.
- 15. Tarabishy AB, Hall GS, Procop GW, Jeng BH. Bacterial culture isolates from hospitalized pediatric patients with conjunctivitis. Am J Ophthalmol 2006: 142:678-680.
- 16. Limberg MB. A review of bacterial keratitis and bacterial conjunctivitis. Am J Ophthalmol 1991; 112:25-95.
- 17. 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; 327:789.
- 18. Rietveld RP, ter Riet G, Bindels PJ, Sloos JH, van Weert HC. Predicting bacterial cause in infectious conjunctivitis: cohort study on informa-

- tiveness of combinations of signs and symptoms. BMJ 2004; 329:206-210.
- Syed NA, Hyndiuk RA. Infectious conjunctivitis. Infect Dis Clin North Am 1992; 6:789-805.
- 20. Azar MJ, Dhaliwal DK, Bower KS, Kowalski RP, Gordon YJ. Possible consequences of shaking hands with your patients with epidemic keratoconjunctivitis. Am J Ophthalmol 1996; 121:711-712.
- 21. Galor A, Jeng BH. The red eye: a primer for the internist. Cleve Clin J Med 2008: 75:137-144.
- Centers for Disease Control and Prevention, Workowski KA, Berman SM. Sexually transmitted diseases treatment guidelines, 2006. MMWR Recomm Rep 2006; 55(RR11):1-94. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5511a1.htm. Erratum in: MMWR Recomm Rep 2006; 55:997. Accessed 4/30/08.
- Haimovici R, Roussel TJ. Treatment of gonococcal conjunctivitis with single-dose intramuscular ceftriaxone. Am J Ophthalmol 1989: 107:511-514.
- Bodor FF. Systemic antibiotics for treatment of the conjunctivitis-otitis media syndrome. Pediatr Infect Dis J 1989; 8:287-290.
- 25. Gigliotti F, Hendley JO, Morgan J, Michaels R, Dickens M, Lohr J. Efficacy of topical antibiotic therapy in acute conjunctivitis in children. J Pediatr 1984; 104:623-626.
- Sheikh A, Hurwitz B. Topical antibiotics for acute bacterial conjunctivitis: Cochrane systematic review and meta-analysis update. Br J Gen Pract 2005; 55:962-964.
- 27. Aung T, Chan TK. Nosocomial Klebsiella pneumoniae conjunctivitis resulting in infectious keratitis and bilateral corneal perforation. Cornea 1998: 17:558-561.
- 28. Baum J, Barza M. The evolution of antibiotic therapy for bacterial conjunctivitis and keratitis: 1970-2000. Cornea 2000; 19:659-672.
- 29. Schlech BA, Alfonso E. Overview of the potency of moxifloxacin ophthalmic solution 0.5% (VIGAMOX). Surv Ophthalmol 2005; 50:S7-S15.
- 30. Chalita MR, Höfling-Lima AL, Paranhos A Jr, Schor P, Belfort R Jr. Shifting trends in in vitro antibiotic susceptibilities for common ocular isolates during a period of 15 years. Am J Ophthalmol 2004;
- 31. Gaynor BD, Chidambaram JD, Cevallos V, et al. Topical ocular antibiotics induce bacterial resistance at extraocular sites. Br J Ophthalmol 2005: 89:1097-1099
- 32. Marangon FB, Miller D, Muallem MS, Romano AC, Alfonso EC. Ciprofloxacin and levofloxacin resistance among methicillin-sensitive Staphylococcus aureus isolates from keratitis and conjunctivitis. Am J Ophthalmol 2004: 137:453-458.
- 33. Goldstein MH, Kowalski RP, Gordon YJ. Emerging fluoroquinolone resistance in bacterial keratitis: a 5-year review. Ophthalmology 1999; 106:1313-1318.

ADDRESS: Bennie H. Jeng, MD, Cole Eye Institute, i32, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195; e-mail jengb@ccf.org.

As editors, we'd like you to look into every Dear Doctor: issue, every page of the Cleveland Clinic Journal of Medicine. We'd like to know... We put it in writing...please put it in writing for us. 1 How many issues do you look into? We want to hear from you. Here's our goal: CLEVELAND CLINIC JOURNAL OF MEDICINE MAII ☐ Most □Half □Few The Cleveland Clinic Foundation 2 How do you read the average issue? 9500 Euclid Avenue, NA32 Cleveland, Ohio 44195 Here's our goal: **PHONE** 216.444.2661 **☑** Cover-to-cover **FAX** 216.444.9385 ☐ Most articles **E-MAIL** ccim@ccf.org ☐ Selected articles