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On the cover:
Top photo: Bilateral purulent discharge characteristic of bacterial conjunctivitis.
Bottom photo: Watery discharge typical of viral conjunctivitis.

Conjunctivitis in Children: Challenges and Choices

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Coutesy of Rudolph S. Wagner, MD

The child with "pink eye" or "red eye" presents a variety of challenges and choices to the pediatric practitioner, in both the diagnosis and treatment of this common and vexing condition. Pink eye may arise from any number of infectious or inflammatory causes, including bacterial, viral, or allergic conjunctivitis and other, possibly more serious, conditions. When a thorough history and a careful examination confirm a diagnosis of bacterial conjunctivitis, the clinician can make a treatment decision based on what is known about the efficacy and safety of the available options. While doing so, it is important to keep in mind the potential for antibiotic resistance and to consider when a referral for subspecialist care is warranted.

BY WAY OF BACKGROUND

In children, bacterial conjunctivitis is more common than viral or allergic types,

occurs in all geographic areas and in all races, and is seen with equal frequency among boys and girls. A landmark study among 99 children with conjunctivitis (mean age, 4.4 years) and 102 controls (mean age, 4.9 years) conducted in 1981 showed that three organisms are primarily responsible for pediatric bacterial conjunctivitis: *Haemophilus influenzae* (42% of affected children), *Streptococcus pneumoniae* (12%), and adenoviruses (20%).[1] In this study, only three patients were infected simultaneously with two of the pathogens. Children with adenoviral disease tended to be older than those with bacterial infection, but the age ranges overlapped considerably, with one quarter of those with adenovirus infection younger than 3.5 years of age and 11% of youngsters in the bacterial group older than 8.5 years of age.[1]

The two primary agents of bacterial conjunctivitis have remained essentially unchanged over the years. A 1993 study in nearly 100 patients with acute conjunctivitis showed that bacterial infections predominated—in 76 patients vs. 12 with viral infection—and that the most common bacterial culprits were *H influenzae*, *S pneumoniae*, and *Moraxella catarrhalis*, in that order.[2] The children ranged in age from 4 months to 12 years. Similarly, a 2007 study in 111 children from 1 month to 18 years of age confirmed earlier findings. Overall, 78% of patients with conjunctivitis had positive bacterial cultures; *H influenzae* accounted for 82% and *S pneumoniae* for 16%.[3]

In a series reported in 2010, *H influenzae* accounted for 68% of bacterial conjunctivitis in 238 culture-positive patients 6 months to 17 years of age. *S pneumoniae* accounted for 20% of cases.[4] Most conjunctivitis caused by *H influenzae* is untypeable, which may help explain why use of the pneumococcal and *H influenzae* type b (Hib) vaccines has not changed the etiology of acute conjunctivitis.[3] In the 2007 and 2010 studies, *Staphylococcus aureus* was the third most common bacterial cause of conjunctivitis, accounting for 2% and 8% of cases, respectively.[3,4]

RECENT OUTBREAKS

Highly contagious adenovirus is a common cause of conjunctivitis outbreaks, having been reported on military bases, eye clinics, and child care centers.[5] Yet several recent outbreaks serve notice that bacteria also can be the culprit and that assumptions can't be made about which age groups will be hit hardest by which pathogen. In 2002, Dartmouth College in New Hampshire experienced an outbreak of bacterial conjunctivitis, though a viral cause initially was suspected.[6] Almost 14% of the student body (698 of 5060 students) was diagnosed with conjunctivitis between January 1 and April 12; 5% of that group had repeated infections.[6] Bacteria isolated from conjunctival swabs were identified as an atypical, unencapsulated strain of *S pneumoniae* (110 swabs) or *H influenzae* (19 swabs). One specimen grew both pathogens.[6] Few large outbreaks of pneumococcal conjunctivitis had been reported previously.

In the Dartmouth outbreak, factors associated with developing conjunctivitis included having a roommate or other close contact with an infection, playing on a var-

Table 1. Differential diagnosis of pink eye in children

Bacterial infection	
Typical bacterial conjunctivitis	Hyperacute bacterial conjunctivitis (rare—typically associated with *Neisseria gonorrhoeae* in neonates)
Hordeolum (stye)	Trachoma
Viral infection	
"Typical" viral conjunctivitis	Pharyngoconjunctival fever
Herpes simplex	Acute hemorrhagic conjunctivitis
Allergic conditions	
"Typical" seasonal or perennial allergic conditions	Giant papillary conjunctivitis
Vernal conjunctivitis (limbal and palpebral forms)	
Ocular inflammation	
Blepharitis (eyelids)	Dacrocystitis (lacrimal sac)
Endophthalmitis (ocular cavities and adjacent structures)	Meibomianitis (sebaceous meibomian glands in lids)
Episcleritis (tissues overlying sclera)	Keratitis (corneal)
Iritis (iris)	Uveitis, anterior or granulomatous (uvea)
Congenital conditions	
Nasolacrimal duct obstruction	Mucoceles
Infantile glaucoma	
Injuries	
Hyphema	Perforation
Corneal abrasion	Corneal or conjunctival foreign body
Systemic illness	
Ataxia-telangiectasia	Cat-scratch disease
Kawasaki syndrome	Lyme disease
Juvenile rheumatoid arthritis	Molluscum contagiosum
Varicella	
Other causes	
Ocular rosacea	Trichiasis (rubbing of inturned eyelashes against the eyeball)
Sources: Wagner RS[9]; Wagner RS[14]; Wagner RS, et al.[22]	

sity sports team, going to a gym, attending a fraternity/sorority party, living in a fraternity house, wearing contact lenses, sleeping with contact lenses, smoking, and sharing drinking glasses. In the middle of the Dartmouth outbreak, Princeton University in New Jersey also experienced an increase in bacterial conjunctivitis (274 students), and strains of *S pneumoniae* that could be serotyped were found to be identical to the strain identified at Dartmouth.[6] In these college settings, a viral cause of conjunctivitis would have been considered much more likely than a bacterial one.

The same strain of *S pneumoniae* also caused an outbreak of conjunctivitis in the fall of 2002 at an elementary school in Maine, the first time this particular strain had been reported as the cause of a conjunctivitis outbreak among schoolchildren.[7] First graders were most severely affected (38% attack rate), followed by morning kindergarten children (29%), second grade youngsters (26%), and afternoon kindergarten students (4%). Classroom teachers, other staff members, and students' family members also became infected.

In 2003, Puerto Rico was struck by a major outbreak of acute hemorrhagic conjunctivitis caused by coxsackievirus A24.[8] From August through October, an estimated 490,000 people developed the infection. School-aged children (5-18 years of age) and those living in urban rather than rural areas were at highest risk.[8]

MAKING THE DIAGNOSIS

"Pink eye" is purely a descriptive term to characterize inflammation of the conjunctiva. The clinician must consider not only bacterial, viral, or allergic causes of a pink or red eye, but also such possibilities as trauma, congenital anomalies, and underlying systemic illness (***Table 1***). In sorting out the choices, a thorough medical history and a careful eye examination are essential.[9] Occasionally, additional diagnostic tests are appropriate (see box, "*Going beyond the history and exam*"). In some cases, suspected bacterial conjunctivitis may turn out to be a herpes simplex infection, with potentially serious outcome. Prescribing an antibiotic for a viral infection, for example, not only can result in a hypersensitivity reaction to the antibiotic but, in certain situations, can worsen the patient's condition, as when prolonged use of a topical aminoglycoside proves toxic to the corneal epithelium[10] (see box, "*Why are antibiotics prescribed inappropriately for viral conjunctivitis?*").

Taking the history. Ask about any recent trauma to the eye or exposure to chemicals or other noxious substances. Most dangerous are cleaning agents, particularly those containing lye or other alkaline products. Any such exposure should lead to immediate flushing of the eye, using large volumes of water, followed by immediate referral to an ophthalmologist. "Super glue," though often associated with eye injuries, usually does not cause permanent damage once the eyelids are separated but does warrant an ophthalmologic consultation.[9]

The ocular examination. If possible, record the visual acuity in each eye. Use a penlight to examine the eyelids and lashes for evidence of inflammation or blepharitis. Look for irregularities in the shape

of the pupil, and determine the presence of direct and consensual pupillary reaction. Irregular pupil size or shape suggests severe ocular trauma, as does the absence of a deep-formed anterior chamber, the presence of blood in the anterior chamber (hyphema), or visible prolapse of the iris or other uveal tissue (***Table 2***).[9] Light sensitivity suggests iritis from trauma, endogenous uveitis (as in juvenile rheumatoid arthritis), corneal abrasion, or congenital glaucoma. Other features of congenital glaucoma may include excessive tear production or a large cornea and globe in one or both eyes, or corneal haze or opacity. The finding of congenital glaucoma represents an ocular emergency, usually requiring surgery to lower the intraocular pressure. Also check the cornea for clarity and the possibility of foreign bodies.[9]

Inspect the bulbar and palpebral conjunctivae for the presence of foreign bodies. Look for discharge or follicular reaction, findings that would be consistent with conjunctivitis. Be sure to evaluate the red reflex with the ophthalmoscope before examining the retina.[9]

If the child is unwilling or unable to open the eye so you can examine it properly, try instilling a topical anesthetic agent, such as 0.5% proparacaine HCl or 0.5% tetracaine. If the instillation relieves the pain and the child opens the eye, suspect a corneal abrasion or foreign body.

GOING BEYOND THE HISTORY AND EXAM

In certain situations, diagnostic tests or procedures are helpful for determining the cause of red eye.[1] Culturing, while generally not necessary, is essential in a neonate to rule out *Neisseria gonorrhoeae* and *Chlamydia trachomatis*, infections that can result in severe ocular damage.[1,2] Occasionally, it may also be advisable to culture in a young child, if symptoms persist despite antibiotic treatment of reasonable duration or if the history is obscure or unknown. The clinician must weigh the advantages and disadvantages of delaying treatment while awaiting culture results vs. treating empirically, guided by clinical observations.[2]

Cultures also may be useful for recurrent or severe purulent conjunctivitis or when the infection has not responded to treatment.[1] Viral cultures are not routinely used to establish a diagnosis either, but a rapid in-office immunodiagnostic test is available for detecting adenovirus.[1]

Though unusual in the pediatric office setting, cytology, in the form of Gram and Giemsa stains of eye debris, also can be helpful when the infection has resisted treatment or has been overtreated.[2]

If the child has a unilateral red eye and the history suggests a foreign body or an abrasion, the clinician might be able to confirm the diagnosis right in the office. First apply a fluorescein strip to the eye after wetting it with an anesthetic, then visualize the cornea under cobalt-blue filtered light, using a Woods lamp or even a filter over a penlight.

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Table 2. When red eye suggests trauma

Condition	Signs/symptoms	Comments
Severe ocular trauma	Irregularity of pupil size or shape; absence of deep-formed anterior chamber; hyphema; visible prolapse of iris or other uveal tissue	Merits ophthalmologic referral
Corneal foreign body	Speck on corneal surface	Sometimes can be flushed out with stream of water or ophthalmic irrigating solution but usually requires removal by ophthalmologist. Conjunctival foreign body may be removed by gently rubbing the eyelid or instilling a topical anesthetic and sweeping the fornix conjunctiva with a cotton-tip applicator
Corneal abrasion	Pain in eye; foreign body sensation	Confirm diagnosis by instilling anesthetic drops, applying fluorescein dye to the eye, and inspecting cornea with a cobalt-filtered penlight. Apply a tight pressure patch to keep the eyelid closed. Consider using an antibiotic ointment—one that is for ophthalmic use only.
Subconjunctival hemorrhage	Hemorrhage from conjunctival and episcleral vessels with or without conjunctival laceration	Usually resolves spontaneously, requiring no treatment. Topical antibiotic drops prevent secondary infection, especially when laceration is present
Iritis	Photophobia; deep conjunctival or episcleral blood vessel injection around the limbus; decreased vision in affected eye; involved eye may have smaller pupil	Merits referral to an ophthalmologist
Hyphema	Blood in anterior chamber; sign of severe trauma; heme may layer out inferiorly as a red line behind the cornea	Typically resolves within 1 week. Tends to rebleed if child resumes normal activities before blood clot resolves, with serious consequences. Requires regular ophthalmologic examination to measure intraocular pressure and monitor changes in degree of hyphema
Perforating ocular injury	Evidence of corneal trauma or opacity; irregular pupil; flat or shallow anterior chamber	Calls for immediate referral to an ophthalmologist

Source: Wagner RS.[9]

Table 3. Diagnostic clues associated with red eye

Signs/symptoms in addition to red eye	Possible diagnosis
Crusting Burning sensation Watery tearing	Blepharitis
Excessive tear production (epiphora) Light sensitivity Large cornea and globe (uni- or bilateral) Corneal haze or opacity secondary to corneal edema	Congenital glaucoma
Epiphora Accumulation of mucoid material on lashes and lower lid margin	Nasolacrimal duct obstruction
Large tortuous vessels on bulbar conjunctiva, most prominent in exposed canthal regions Typically appears between 1 and 6 years of age	Ataxia-telangiectasia
Bilateral bulbar conjunctiva injection combined with mucous membrane and cutaneous findings associated with Kawasaki syndrome	Kawasaki syndrome
Anterior uveitis or iritis Perilimbal conjunctival injection Photophobia	Juvenile rheumatoid arthritis
Focal conjunctival vesicle in association with other facial lesions of varicella	Varicella

Source: Wagner RS.[9]

Although some cases of conjunctivitis start in one eye and then spread to the other, a unilateral red eye should cause the clinician to stop, pause, and consider other diagnoses. The possibilities are many, from trauma or a foreign body to herpetic infection, uveitis, and intra-ocular inflammation. Pain is not typically present in children with conjunctivitis; eye pain may be the result of a corneal abrasion, herpetic keratitis, or a contact lens-related ulcer, among other possible causes.

Chronicity is another diagnostic clue. Because bacterial conjunctivitis typically resolves on its own within 10 days, a red eye that has persisted for a longer period points to another diagnosis. In fact, some clinicians believe that a child who does not exhibit a response to a highly effective topical ocular antibiotic within 24 hours probably has something other than bacterial conjunctivitis.[11] ***Table 3*** summarizes medical conditions associated with various diagnostic findings.

WHAT KIND OF CONJUNCTIVITIS?

When the history and examination suggest a bacterial, viral, or allergic conjunctivitis,

Table 4. Is it bacterial, viral, or allergic conjunctivitis—or something else?

Probably bacterial conjunctivitis	Probably allergic conjunctivitis
Gluey or sticky eyelids upon awakening, combined with mucoid or purulent discharge Crusting/gluing of eyelashes and eyelids Purulent, thick, yellow-green discharge Swelling, "gritty" feeling Bilateral presentation Develops in winter Papillary conjunctival response to slit-lamp exam Presents concurrently with otitis media Presents concurrently with rhinitis, sinusitis Child tends to be younger—mean age 3.1-3.6 years	Itching Presents bilaterally Presents in spring or fall Acute onset of conjunctival injection and edema Lid edema Large papules on palpebral conjunctivae of the upper lid Watering Stringy, ropy discharge, if any
Probably viral conjunctivitis	**Probably something else***
Presents unilaterally, then spreads to the other eye Opacities in the cornea Tearing, fever Serous, clear, watery discharge Presents with concurrent systemic viral infection, especially pharyngitis or sore throat Follicular conjunctival response to slit-lamp exam Develops in spring or fall Child tends to be older—mean age 8.5 years	Unilateral red eye Condition is chronic Red eye duration 2 weeks or longer Light sensitivity Pain Decreased visual acuity

*When red eye is associated with loss of vision, severe pain, changes in eye movement, irregularity in pupil shape or reactivity, changes in the red reflex, or a new droopy eyelid, the "something else" is probably more serious than conjunctivitis and merits an ophthalmologic referral.[1]

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the next task is to sort out those possibilities (***Table 4***).

Bacterial conjunctivitis. The combination of a history of gluey or sticky eyelids in the morning and a mucoid or purulent discharge is highly predictive—96% probability—of bacterial conjunctivitis.[3] Crusting or gluing of eyelashes and eyelids may also be associated with a positive bacterial culture, as may the absence of a burning sensation in the eyes and lack of a watery discharge. Bacterial conjunctivitis tends to present bilaterally, though sometimes it can begin in one eye before spreading to the other. When left untreated, the infection lasts for 8-10 days.[12] The mean age of the child with bacterial conjunctivitis is 3.1-3.6 years.[1]

Viral conjunctivitis. The second most common type of conjunctivitis in children, viral infection can be difficult to

distinguish from its bacterial counterpart.[3] Unlike bacterial conjunctivitis, a viral infection tends to present unilaterally, then spread to the other eye. Viral conjunctivitis also differs from bacterial in its association with opacities in the cornea that may affect vision.

Children with viral conjunctivitis generally have a concurrent systemic viral infection, most likely of the upper respiratory tract; the combination of conjunctivitis and sore throat suggests a viral origin. Symptoms of adenovirus conjunctivitis may persist for 2 weeks or even longer, and the infection often is accompanied by a watery discharge from the eyes. Preauricular lymph nodes are considerably more common in viral conjunctivitis but are not diagnostic. The mean age of the child with viral conjunctivitis is 8.5 years.[1]

Allergic conjunctivitis. Itching is the chief clue to allergic conjunctivitis, which is typically bilateral. Allergic conjunctivitis most often is seasonal, triggered by airborne pollen. Itching is intense in the spring and fall. Acute onset of conjunctival redness and edema or lid edema also are characteristic of this condition, as are large papules on the palpebral conjunctivae of the upper lid.[9] The eyes may water; any discharge will be stringy or ropy in character, not green or purulent, as with bacterial conjunctivitis.

Perennial allergic conjunctivitis most often is associated with exposure to house dust mites, cat dander, air pollutants, and other allergens that are found in the environment throughout the year. The symptoms tend to be chronic rather than seasonal in nature.[13]

WHY ARE ANTIBIOTICS PRESCRIBED INAPPROPRIATELY FOR VIRAL CONJUNCTIVITIS?

- Clinician is unable to determine the etiology
- "It might help the patient."
- "The patient (Mom) expects antibiotics."
- Easier, faster to write an Rx than to explain why antibiotics are inappropriate
- Return-to-school rules call for treatment

DIAGNOSES THAT MUST NOT BE OVERLOOKED

One of the viral causes of conjunctivitis, herpes simplex infection, has potentially disastrous consequences, including corneal opacification and loss of vision.[14] It is also important to recognize conjunctivitis-otitis media syndrome.

Herpes simplex conjunctivitis. Distinguishing herpes simplex infection from other causes of viral conjunctivitis can be difficult. Typically, the conjunctivitis is unilateral, and the child may have vesicles on skin surrounding the eye or eyelids.[14] Infection generally is accompanied by severe ocular pain or discomfort. The child may have recently had a viral illness or close contact with someone who did. The conjunctivitis may be preceded by fever, exposure to strong sunlight, or mild trauma.[14]

Fluorescein staining of the cornea that

shows a dendritic or branching pattern generally points to the diagnosis of herpes simplex conjunctivitis (see case histories on pages 13 and 14). But even a penlight examination may reveal an irregularity on the corneal surface and gray or white discoloration in the corneal lesion. Suspicion of this condition calls for prompt referral to an ophthalmologist.[14]

Conjunctivitis-otitis media syndrome. Be sure to check for otitis media in any child with conjunctivitis.[9,15] Irritability and a purulent discharge from the eyes are hallmarks of conjunctivitis-otitis syndrome, though the first symptoms usually are low-to-moderate grade fever, mucopurulent rhinorrhea, and a cough. Two or 3 days later, conjunctivitis and otitis appear; the child wakes up with eyelashes crusted together and pain in the ear.[9] In the majority of cases the syndrome is caused by *H influenzae*; if left untreated, the conjunctivitis can progress to septicemia or meningitis.[14] About one-quarter to one-third of children with conjunctivitis also have otitis media,[1,15] and some have no ear pain.

CHOOSING A TOPICAL ANTIBIOTIC

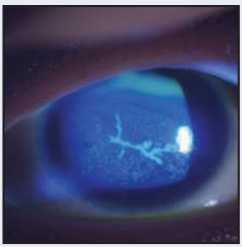
Although bacterial conjunctivitis usually is benign and resolves on its own within 8-10 days, the highly infectious condition brings discomfort, poses a risk of ready transmission to others, and results in school and day-care absences (see box, "*When to return to school?*")[11,16] Staying out of school also results in parental absence from work, with accompanying economic repercussions.[16] The 2003 epidemic in Puerto Rico, for example, accounted for a total of 850 person-years of missed work (not including missed work for child care) and 315,000 visits to physicians' offices, resulting in $30 million in lost worker productivity and health expenses during a 3-month period.[8] Antibiotic treatment is recommended for this self-limited disease because it helps shorten the duration of illness, controls its level of contagiousness, and curbs the emergence of resistant strains by effectively eradicating the responsible pathogens.[11]

A number of topical antibiotic agents are available for treating bacterial conjunctivitis.[17] It is important to remember that all agents approved by the FDA for treatment of bacterial conjunctivitis are regarded as effective in doing so. Treatment decisions for each individual patient should be guided by certain basic considerations, including the drug's level of bioavailability and whether and how rapidly it eradicates the organism. Some topical agents are bactericidal (killing the organism) whereas others are bacteriostatic (temporarily inhibiting microorganism growth;[17] see box, "*Key considerations for treatment*").

Systemic treatment of bacterial conjunctivitis occasionally is warranted when symptoms are especially severe and is essential when the infection is associated with otitis media.[15] Use of an antibiotic resistant to ß-lactamase is recommended for conjunctivitis-otitis syndrome, as ß-lactamase is common in *H influenzae*, the predominant etiologic agent of this highly contagious infection.[9,15] The concomitant use of a topical antibiotic will allow for quick eradication of the organism from the eye and help prevent contagious spread.

PINK EYE AND THE ELUSIVE DIAGNOSIS

Case History #1: Matthew



Courtesy of Rudolph S. Wagner, MD

The physician examines 3-year-old Matthew's red eye and takes a history. Only the left eye is red, and the history is unclear. Thinking Matthew probably has bacterial conjunctivitis that has not yet manifested in the right eye, he prescribes topical tobramycin and asks Matthew's mother to report back in a few days. Three days later, Matthew's mother calls to say that the child's eye is still red, but still only the left one. The physician rules out trying another antibiotic. Tobramycin is bactericidal and covers the usual etiologic pathogens for conjunctivitis; also, the redness has remained unilateral. Clearly, another office visit and consideration of another diagnosis is in order. At the visit, Matthew exhibits some light sensitivity and rubs his eye, saying something "is in it."

The physician wets a fluorescein strip with anesthetic and applies it to the eye. He then uses a penlight, fitted with a cobalt blue filter cap, to examine the eye. The cornea exhibits a dendritic pattern. Is this a corneal abrasion that is healing or the dendritic pattern of a herpes simplex virus? He suspects herpes simplex infection and refers Matthew to a pediatric ophthalmologist for further evaluation. The ophthalmologist confirms the diagnosis of herpes simplex with corneal involvement and prescribes a topical antiviral agent.

Macrolides. Erythromycin is active against gram-positive organisms as well as some atypical pathogens, such as *Mycoplasma*, *Legionella*, *Chlamydia*, and *Mycobacteria*. Erythromycin ointment, applied four times a day for 7 days, is well tolerated—very young children find ointments more comfortable than drops—and is not toxic, but it does not have good penetration into ocular tissue.[17] Older children may not tolerate ointments as well if their vision is blurred by the treatment. In addition, the ointment has been associated with hypersensitivity reactions and staphylococcal resistance.[17,18]

In 2007, the US Food and Drug Administration (FDA) approved a 1% topical ophthalmic solution of azithromycin.[19,20] A slightly viscous product, it has bioadhesive properties that tend to keep the medication on the surface of the eye longer than with conventional drops, increasing bioavailability to the ocular surface. In addition, the agent has reduced dosing frequency compared with other treatments (one drop twice daily 8 to 12 hours apart, for the first 2 days, followed by one drop daily for the next 5 days). The product is bacteriostatic, and effectiveness is time-dependent: Skipping doses or not completing the full course of therapy decreases the effectiveness of treatment and increases the likelihood that bacterial resistance will develop.[19]

Sulfonamides. Topical sulfa drugs, formerly the primary medications for treating bacterial conjunctivitis, have been used with less frequency in recent years. These

PINK EYE AND THE ELUSIVE DIAGNOSIS

Case History #2: Lila

Coutesy of Rudolph S. Wagner, MD

Lila's mother has brought her daughter to the clinic because the 4-month-old has recurrent episodes of what her mother fears could be chronic conjunctivitis. Lila frequently has a discharge that accumulates in the medial area and the lower eyelid and wakes up in the morning with the lashes matted together. Some days are better than others, Lila's mother says. She had been giving Lila an antibiotic, which seemed to help, but now that the medicine is gone the discharge is back. Should Lila be getting another antibiotic?

Examination reveals that the conjunctiva is white, not red, and Mom confirms that one eye, not both, has the discharge. These diagnostic clues suggest that Lila does not have conjunctivitis and most likely has a nasolacrimal duct obstruction, although bilateral involvement is not unusual in that condition. To verify the diagnosis, the pediatrician massages the child's eye. This produces reflux, providing the confirmation.

Lila's mother wants to know why the obstruction first manifested when Lila was 2 months old instead of soon after birth. The pediatrician explains that while the blocked duct sometimes is evident right away, some children do not produce enough tears to cause a discharge until they are a bit older. She also notes that although the antibiotics can treat the discharge, they can not open the blocked tear duct. If the problem had been bacterial conjunctivitis, it would have gone away with antibiotic treatment.

Next, the pediatrician explains that though most such obstructions resolve by the time a child is 1 year of age, massaging the eye a few times a day can speed the process and help avoid infection. She shows Lila's mother how to massage the area over the lacrimal sac, first making sure that the fingernail is clipped short. She tells her to massage the eye—after washing her hands—while feeding Lila because this is when the child is most likely to remain calm. The technique involves placing a small finger in the medial canthal area, where the upper and lower lid join. Then the finger is moved in a downward motion over the nasolacrimal sac.

Lila's signs and symptoms resolved abruptly one day when she was 6 months of age. Most likely, the obstruction in the distal valve of Hasner in the nasolacrimal duct opened spontaneously and remained open, thus avoiding the need for surgical intervention.

agents, which are bacteriostatic, are available in drop and ointment form. They have been associated with a variety of adverse effects, including allergic reactions and rare cases of Stevens-Johnson syndrome.[21] The drops may sting or burn, inhibiting compliance, and the drugs are subject to bacterial resistance.[22-24] An in vitro study in 2000 showed that sulfamethoxazole had no activity against either *H influenzae* or *S pneumoniae*.[24]

Aminoglycosides. Gentamicin, tobramycin, and neomycin provide excellent coverage of gram-negative pathogens;[17] however, increasing resistance has been noted.[24] In addition, aminoglycosides have been

WHEN TO RETURN TO SCHOOL?

The American Academy of Pediatrics *Red Book* has this to say about eye infections and school attendance: "Except when viral or bacterial conjunctivitis is accompanied by systemic signs of illness, infected children should be allowed to remain in school once any indicated therapy is implemented, unless their behavior is such that close contact with other students cannot be avoided."[1]

Some schools disagree with this policy, believing it necessary to exclude students with conjunctivitis to protect other children, and the community at large, from infection. Yet some officials claim that because students with certain respiratory infections are not kept home, youngsters with conjunctivitis should not be either. Given these disparate views, it's no wonder that state departments of health have a range of regulations about when students with conjunctivitis should be excluded from school.[2] Nevertheless, in cases of acute bacterial conjunctivitis, the use of an agent that provides rapid clinical and bacterial cure is desirable for getting the child back to school as soon as possible.

Of 43 states that responded to a survey, seven allow children with conjunctivitis to remain in school, eight permit them to return once antibiotic treatment is begun, 12 allow for their return 24 hours after antibiotics first are given, 13 exclude them until the infection is "noncommunicable," and 16 require a physician's approval to return to school.[2] This adds up to 56 responses because 17 of the states responding have multiple recommendations, often contradictory. In addition, 12 states have no official policy, though some provide guidance to school districts when asked.[2] Finally, policies in only three states differentiate between viral and bacterial conjunctivitis.

As the *Red Book* statement suggests (six states cited *Red Book* as the source of their policies), children with conjunctivitis should avoid contact with others to prevent contagion. This can be difficult, especially among younger children in day care or school, who spend most of their time in groups, not sitting at desks. Nonetheless, school nurses and teachers can help prevent the spread of bacterial conjunctivitis by instituting a hand washing program and supplying supplemental alcohol cleaning gels.[1]

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associated with hypersensitivity and severe allergic reactions.[17]

Antibacterial combinations. The ophthalmic solution of trimethoprim and polymyxin B sulfate has activity against many gram-negative and gram-positive organisms, and polymyxin B is bactericidal for many gram-negative organisms.[25] The agent also has been linked to increasing bacterial resistance, and because the solution is bacteriostatic, it may take several days to eradicate the infection.[24] The ointment polymyxin B-neomycin has a wide range of bactericidal action[26] but has shown increasing bacterial resistance.[24] Some children develop an allergic reaction to the neomycin in the ointment, making it difficult to determine if the child's symptoms are caused by the medication or the conjunctivitis.[22]

Antibiotic-corticosteroid combinations. Medications containing steroids generally have no place in treating primary conjunc-

tivitis because of the risks they pose. Topical steroids can exacerbate an underlying fungal or herpetic infection, resulting in irreversible ocular damage.[22] Used chronically, steroids can cause cataracts or increase intraocular pressure, heightening the risk of glaucoma.[22] Also note that some topical medications for treating allergy contain steroids and should be used with care.

Fluoroquinolones. The 1962 introduction of nalidixic acid marked the beginning of development of the quinolones, a family of synthetic broad-spectrum antibiotics that were first introduced for treatment of systemic infection in the 1980s.[27] Originally used only for treating urinary tract infections, these agents are now approved for a wide variety of indications. Flumequine, the first topical fluoroquinolone, was used only briefly because of its association with ocular toxicity. Development of second- and third-generation fluoroquinolones, such as ciprofloxacin, ofloxacin, lomefloxacin, and levofloxacin, followed in the 1990s and beyond.[27] These bactericidal agents have been used widely for treating bacterial conjunctivitis because of their broad coverage of both gram-positive and gram-nega-

KEY CONSIDERATIONS FOR TREATMENT

In selecting among treatment options for bacterial conjunctivitis, keep in mind the following parameters:

- **Spectrum of activity.** Because initial treatment is generally empiric, the chosen drug should be active against the most common etiologic bacteria, especially *Streptococcus pneumoniae* and *Haemophilus influenzae*, and therefore cover both gram-positive and gram-negative organisms.
- **Level of availability**. The agent of choice should have high bioavailability, achieved when drug content is slightly higher than the lowest concentration needed to inhibit growth of the causative bacteria and by good ocular tissue penetration.[1]
- **Rate of bacterial kill**. A rapid rate of bacterial kill shortens both the duration of the infection and period of infectivity, while preventing potential complications.[2]
- **Incidence of resistance**. Also important is to choose a drug with a low incidence of resistance. Though systemic agents are far more likely to lead to bacterial resistance than topical antibiotics, resistance to the topical agents used in treating conjunctivitis is increasing.[1]
- **Toxicity**. Many practitioners avoid medications that contain neomycin because of reported hypersensitivity reactions. Aminoglycosides are associated with corneal toxicity. Few physicians today would prescribe chloramphenicol because of its association with aplastic anemia.[3]
- **Comfort and convenience**. Choosing an agent that isn't associated with frequent administration or stinging or burning is particularly important for promoting adherence in children.

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tive pathogens and their lack of toxicity.

Fluoroquinolones, too, have been found to trigger bacterial resistance.[28,29] Partly for this reason, fourth-generation fluoroquinolones were developed. Moxifloxacin and gatifloxacin first became available in 2003; in 2009, the FDA approved another topical ocular fluoroquinolone, besifloxacin. The fourth-generation fluoroquinolones have an 8-methoxy substitution on the basic quinolone molecule, which provides better coverage against gram-positive organisms, including resistant strains, than earlier-generation fluoroquinolones. At the same time, coverage of gram-negative organisms is comparable to that of earlier-generation fluoroquinolones.[11] In general, fourth-generation fluoroquinolones provide broad coverage with rapid bacterial eradication. They have low toxicity and are associated with low levels of bacterial resistance. Supporting evidence comes from investigations that compare fourth-generation fluoroquinolones with their predecessors, other contemporary treatments, and one another.

ANTIBIOTIC RESISTANCE

Development of antibiotic resistance is thought to result from slowly decreasing levels of drug in tissue, exposing remaining bacteria to antibiotic levels below the concentration needed to prevent mutated strains. This mutant prevention concentration is defined as the range between the MIC_{90} (MIC necessary to inhibit growth of 90% of organisms) and the MIC of the least susceptible, but not resistant, mutant.[30] Ocular therapy is considered less likely than systemic therapy to result in resistance because eye drops deliver a significant amount of drug to the affected surface. In addition, ocular infections involve far fewer organisms than systemic infections and are treated for a shorter time, which also makes development of resistance less likely.

Fluoroquinolones inhibit development of resistance by binding with bacterial nuclear enzymes, disrupting their activity. Early-generation fluoroquinolones hamper bacterial DNA synthesis by inhibiting DNA gyrase, an enzyme required for DNA replication, in gram-negative organisms. In gram-positive organisms, the drugs interrupt the enzymatic pathway by inhibiting topoisomerase IV. Because fourth-generation fluoroquinolones attack both DNA gyrase and topoisomerase IV in gram-positive organisms, two spontaneous mutations of bacterial DNA, rather than one, are required to trigger gram-positive bacterial resistance to these agents.[33]

A recent investigation explored the question of whether use of fourth-generation fluoroquinolones leads to bacterial resistance.[31] Given that instillation of topical ocular fluoroquinolones results in drug overflowing to skin around the eyes and other nearby sites, the authors set out to determine if diluted drug at these sites selects for bacteria with decreased fluoroquinolone susceptibility. They took swabs of the eyes, cheeks, nostrils, and throats of 105 children from 8 months to 12 years of age with bacterial conjunctivitis as well as 57 healthy control subjects. Children with conjunctivitis received topical moxifloxacin three times a day for 7 days. Investigators

Table 5. Fourth-generation fluoroquinolones

Name	Concentration	Dosing/schedule	Other features
Besifloxacin[1]	0.6%	1 drop 3 times a day, 4-12 hours apart for 7 days	Formulated with DuraSite®, a mucoadhesive polymer delivery system Contains BAK.* pH 6-7
Gatifloxacin[2]	0.3%	Days 1, 2: 1 drop every 2 hours up to 8 times daily Days 3-7: 1 drop up to 4 times daily while awake	May contain hydrochloric acid or sodium hydroxide to adjust pH to about 6. Contains BAK.*
Moxifloxacin[3]	0.5%	1 drop 3 times a day for 7 days	May contain hydrochloric acid or sodium hydroxide to adjust pH to about 6.8. Has bicyclic C-7 side chain to inhibit efflux pump mechanism.

*BAK= Benzalkonium chloride, a preservative.

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again took swabs after the treatment period and 5 weeks later and looked for changes in the susceptibility of *S aureus*, *S pneumoniae*, and *H influenzae* in the eye, nose, and throat to 20 different antibiotics. The three organisms' susceptibility to moxifloxacin did not change in the eye or other body sites, and the drug's MIC did not increase. Also significant, even before treatment the children with conjunctivitis were found to have some drug-resistant bacteria—principally species that colonize the throat. Investigators therefore concluded that the resistance probably was attributable to systemic, not topical, antibiotics.[31]

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