Etiologic and Therapeutic Pitfalls of Newborn Conjunctivitis

Stan L. Block, MD, FAAP

With some trepidation, a bleary eyed, pallid-looking, young mother brings her 7-day-old infant boy into my office. Baby care is all so new to her that she reports relying heavily upon her grandmother for advice. The child developed purulent drainage from the right eye yesterday. The grandmother, who was afflicted by some eye discharge 3 days earlier, remarked that the baby should be "checked out" by a doctor. A 2-year-old sibling at home has been well. Incidentally, the baby was born at 38 weeks gestation by emergency caesarean-section after placental rupture during a motor vehicle accident. Fortunately, no other serious injuries were sustained by the mother or newborn.

Upon examination, the newborn appears to be well-fed, growing, and robust. The right eye has obvious green, purulent discharge exuding from it (see Figure 1, page 311). Upon a careful and technically very difficult examination of the tympanic membranes (TM), they appear flat and dark gray. The usual TM landmarks observed in older children are virtually never discernible at this age. Similar to many pediatricians,[1] the 4th-year medical student on his outpatient rotation in my office apparently was unable to adequately visualize the appearance of the TMs. He was using those poorly designed disposable speculum that he was given at the hospital. The remainder of the newborn's examination was normal.

"PINK EYE"

"Pink eye" is a misnomer for young children, because very few children younger than 24 months have a pink or red bulbar conjunctiva when it becomes infected. Typically, it remains white or merely somewhat injected looking. The salient manifestation of childhood "pink eye," or bacterial conjunctivitis, is heavy green or yellow discharge on the eyelids or in the conjuctival sac (see Figure 1, page 311).

Because of his very young age, the infant's conjunctival sac was cultured for aerobic bacteria. Polymixin-trimethoprim ophthalmic solution was prescribed four times daily for 7 days. When the patient returned to the office after 48 hours of treatment, his eye had cleared completely. Three days later, his eye culture grew beta-lactamase–negative *Haemophilus aphrophilus*, possibly a genital tract isolate, or a mistakenly identified nontypeable *Haemophilus influenzae* strain, in light of the grandmother's infection, which was likely infectious conjunctivitis. In most children, *H. influenzae* accounts for 50% to 70% of bacterial conjunctivitis pathogens.[2-4]

PREDOMINANT PATHOGENS OF NEONATAL CONJUNCTIVITIS

Many pediatricians consider *Chlamydia trachomatis* to be the true pathogen of newborn acute purulent conjunctivitis in the United States. But does the literature after the advent of universal topical antibiotic prophylaxis truly support this notion? Emphatically: No.

At birth, prophylactic topical erythromycin ointment is administered into the conjunctiva of all newborns. During an erythromycin shortage, silver nitrate, tetracycline, or azithromycin ointment can be substituted. But all prophylactic ophthalmic antibiotics are intended only to prevent gonococcal conjunctivitis. According to the *2012 AAP Red Book*,[5] conjunctival prophylaxis at birth will not eradicate *C. trachomatis* conjunctivitis. I assume this is because of its lack of deeper conjunctival tissue penetration, and, critically, the ointment will also not eradicate the nasopharyngeal infection.[5]

Furthermore, most studies have reported a very low rate of chlamydial infection in neonatal conjunctivitis – usually in the range of 2%, and rarely as high as 20%. Why?

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The low level of neonatal chlamydial infection makes sense statistically when one calculates each level of risk, because only about 50% of babies with vaginal deliveries will acquire the infection; an even lower rate of acquisition is observed with cesarean delivery. In studies of women 15 to 24 years old attending a perinatal clinic, the rate of *C. trachomatis* detection with polymerase chain reaction (PCR) in the genital tract similarly averaged about 7%, with a range of 2% to 20%. Next, the risk of developing chlamydial conjunctivitis during an infection is only about 25% to 50%.[5] Thus, I calculate that 7% times 50% times 50% equals 1.75%, or about a rate of 2%. Furthermore, the risk of developing chlamydial pneumononitis in these same babies with conjunctivitis is only 5% to 20%, meaning we may see a rate of chlamydial pneumononitis in a range of 2 to 8 babies per thousand.

Note also that the rate of infection with *C. trachomatis* is much lower in mothers older than 25 years.

About 65% to 80% of purulent conjunctivitis infections in children older than 2 months grow a single typical bacterial otopathogen that is predominantly beta-lactamase–producing, nontypeable *H. influenzae*, and less frequently *Streptococcus pneumoniae*. Likewise, I have reported earlier that 60% of eye cultures in a subset of infants younger than 2 months old similarly grew these same typical otopathogens.[2]

Although many clinicians allege that *Staphylococcus aureus* and *Staphylococcus epidermidis* are conjunctival pathogens, most microbiologic studies have found *Staphylococcus* with the same frequency in asymptomatic children as in those who have conjunctivitis. Other potential conjunctival pathogens include bacteria from the maternal genital flora, such as *Escherichia coli*, and other gram-negative bacilli.[6]

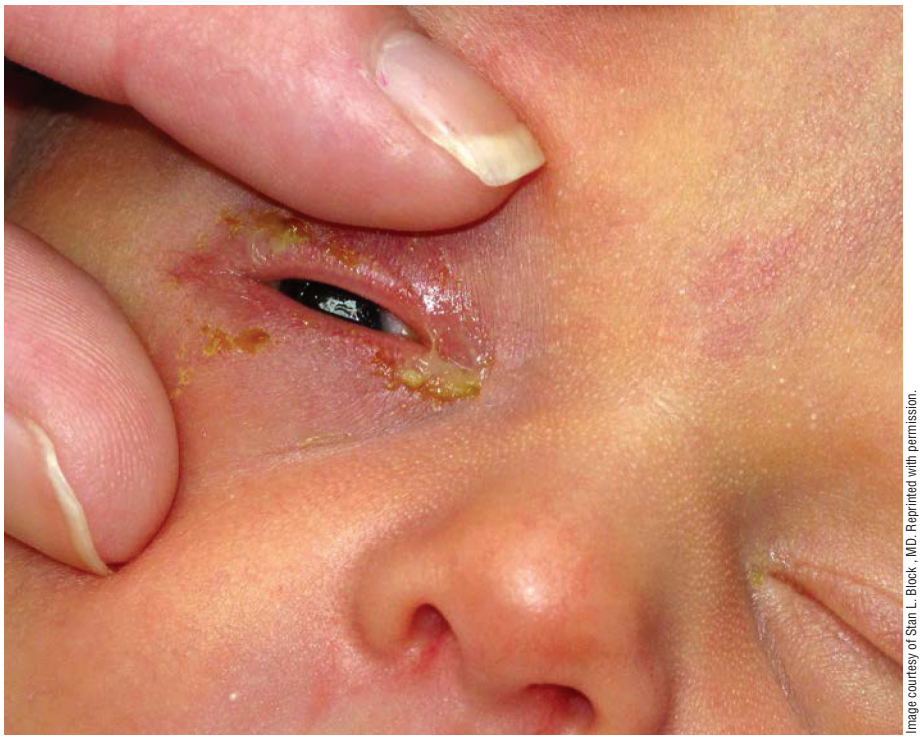

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Figure 1. A 7-day-old infant with abrupt onset of unilateral acute purulent conjunctivitis.

Neisseria gonorrhoeae, an extremely rare cause of newborn conjunctivitis, presents with continuous severe and profuse purulent discharge within days after birth. On the other hand, manifestations of chlamydial conjunctivitis are more similar to a typical purulent conjunctivitis caused by the oto-pathogens, but symptoms usually develop by 5 to 14 days of life. It is still very rarely identified.

Viruses are alleged to be a very common cause of "pink eye." However, most recent North American studies that evaluated young children (< 5 years old) with true purulent conjunctival discharge by history or by clinical assessment have reported a bacterial otopathogen in 65% to 80% of cultures (see Table, page 312).[3,4]

IDENTIFYING BACTERIAL AND CHLAMYDIAL CONJUNCTIVITIS

The most likely method used to detect *Chlamydia* is the nucleic acid amplification test (NAAT), such as PCR, of the eye discharge. However, these tests are not approved by the US Food and Drug Administration (FDA) for neonatal samples from conjunctiva or nasopharynx. Culture techniques are probably as sensitive as NAAT, but they require a much longer time period for results, and are not commonly available.

A routine bacterial conjunctival culture should be performed when the infant: 1) is younger than 14 days old; 2) has failed a second round of topical antibiotics; 3) has had recurrent conjunctivitis, even if dacryostenosis is assumed; and 4) has hyperacute severe discharge from the conjunctiva.

TREATMENT OF NEWBORN CONJUNCTIVITIS

I recommend the following approaches for treatment of acute purulent conjunctivitis in the newborn from birth

TABLE.

Pediatric Acute Conjunctivitis: Bacteria versus Virus

Study (location)	Year	Bacteria	% of Conjunctivitis with AOM	Virus
Gigliotti et al[9]	1981	65%	NA	20%
Weiss et al[10]	1993	78%	NA	13%
Block et al[2] (rural Kentucky)	1997-1998	68%	39%	NA
Jackson et al[3] (Ottawa)	2003	80%	NA	NA
Patel et al[4] (Delaware)	2007	78%	NA	NA

NA = not applicable.

Source: Block, SL.

to 2 months old. First, ensure that the patient has indeed received antibiotic prophylaxis at birth, and that a hyperacute profuse purulent conjunctivitis is NOT present. This latter condition would require evaluation for systemic infection, empiric hospitalization, and treatment with parenteral ceftriaxone for presumptive gonococcal conjunctivitis, at least until the eye culture results return in about 4 to 5 days. Personally, I have never seen such a case in 33 years of practice.

Newborns should receive multiple daily doses of topical antibiotic drops or ointment for at least 5 to 7 days. First line topical antibiotics should cover the typical otopathogens, especially *H. influenzae*, and the usual urogenital tract commensals such as *E. coli*.[2,7,8] My first line options (depending on formulary coverage) are polymixin-trimethoprim, combination neomycin-polysporin ointment, or possibly generic quinolone drops which may also provide partial chlamydial coverage. Topical fluoroquinolones in the newborn period are prescribed with some trepidation due to concern about the theoretical risk of arthropathy; thus, I prefer to use them as second-line agents. Topical aminoglycosides and sulfacetamide are probably best avoided because of their weak coverage of of conjunctival pathogens.[2] All topical antibiotic drops for newborns are currently considered off-label use by the US Food and Drug Administration.

For the infant younger than 4 weeks, ideally, you should request follow-up phone contact within 48 to 72 hours after treatment is initiated. If the infection has not improved, I would then obtain chlamydial NAAT (PCR) testing of the eye discharge if your laboratory has this capability. Sometimes a component of concomitant dacryostenosis is present, which may be quite confusing for the clinician, and which may be a common cause of persistent and recurrent conjunctivitis.

Erythromycin Ointment

In my opinion, topical erythromycin should not be prescribed to newborns (or any age child) any more. I believe this for following reasons: 1) the rate of chlamydial conjunctivitis is probably less than 1% to 2%; 2) the drugs of choice for chlamydial conjunctivitis are oral erythromycin or oral azithromycin; and 3) topical erythromycin does not eradicate *Chlamydia* in either conjunctiva or nasopharynx, nor in pneumonitis, which occurs concomitantly in 5% to 20% of children with chlamydial conjunctivitis.[5] Although data in newborn infections are limited for both antibiotics, I prefer to use oral azithromycin (10 to 20 mg/kg daily) instead of oral erythromycin (50 mg/kg/day divided four times daily).

Oral azithromycin is much better tolerated, has much better adherence because it is dosed once daily instead of 4 times daily; and it requires only 3 to 5 days total therapy versus 14 days therapy. It also probably has much less risk of secondary pyloric stenosis in infants younger than 6 weeks.[5] Plus, the high level and frequency of gastrointestinal distress caused by oral erythromycin is legendary for an old timer like me. It's also important to note that coverage of topical erythromycin for the two most common conjunctival pathogens, *H. influenzae* and drug-resistant pneumococcus, is minimal.[2] Also, remember that: 1) *Chlamydia* treatment failure rates are up to 20%; and 2) to have the mother and her partner treated.[5]

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REFRACTORY PURULENT CONJUNCTIVITIS

However, practitioners face another complex therapeutic dilemma: when the purulent conjunctivitis persists despite two courses of topical antibiotic therapy (See Figure 2, page 313). Refractory conjunctivitis is often caused by penicillin-susceptible or penicillin-resistant pneumococcus, and occasion-

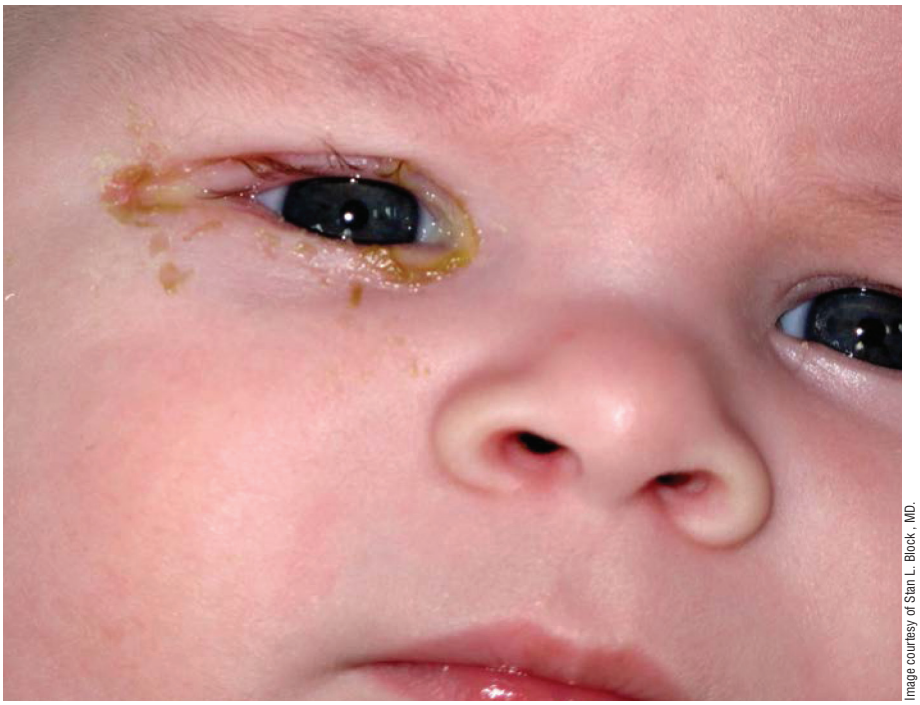

Image courtesy of Stan L. Block, MD.

Figure 2. An 8-week-old infant with persistent purulent conjunctivitis despite topical therapy with polymixin-trimethoprim, ocufloxin, and moxifloxacin over a 2-week interval. His culture grew penicillin-resistant pneumococcus, requiring additional oral therapy with oral clindamycin for 10 days to eradicate the infection. Note the bulbar conjunctiva is not red or pink.

ally by methicillin-resistant *S. aureus*. Chlamydial infection is still very rare in this scenario. I suggest starting empiric oral antibiotic therapy, with the adjustment of therapy based on culture results (see below).

Oral Antibiotics in Healthy Neonates

Similar to older children with conjunctivitis, oral antibiotics should not routinely be prescribed in isolated, typical neonatal conjunctivitis. However, because of the high rates of *H. influenzae*, the oral antibiotics cefdinir and amoxicillin-clavulanate should be used empirically if persistent purulent conjunctivitis persists after two courses of topical antibiotics (a routine conjunctival culture should be obtained first) with a culture proved pathogen; or if concomitant acute otitis media or sinusitis (purulent rhinorrhea for over 10 days) is diagnosed.

By contrast, if penicillin-resistant pneumococcus or *S. aureus* is recovered, then prescribe oral clindamycin or intramuscular ceftriaxone (for 2 or 3 days), or oral clindamycin or trimethoprim/sulfamethoxazole, respectively (see Figure 2).

CONCLUSION

Please note the following concepts about neonatal conjunctivitis: the conjunctiva is rarely pink, rather it will have purulent discharge by history or by examination. *C. trachomatis* is a very rare causative pathogen in this age group. When you are truly treating presumptive or confirmed chlamydial conjunctivitis, you should use an oral macrolide, and I prefer oral azithromycin. Most neonatal conjunctivitis is caused by *H. influenzae, S. pneumoniae,* or gram-negative commensals; initially treat accordingly with appropriate topical drops (not erythromycin) for at least 5 to 7 days. ■

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