ARTICLE

Identifying Children at Low Risk for Bacterial Conjunctivitis

James A. Meltzer, MD; Sergey Kunkov, MD, MS; Ellen F. Crain, MD, PhD

Objective: To identify a population of children at low risk for bacterial conjunctivitis on the basis of history and physical examination findings.

Design: Prospective observational cohort study.

Setting: Urban pediatric emergency department.

Participants: Children aged 6 months to 17 years with conjunctival erythema, eye discharge, or both. The exclusion criteria were eye trauma, exposure to a noxious chemical, contact lens use, and antibiotic drug use in the past 5 days.

Interventions: Clinicians completed a checklist of signs and symptoms and collected a conjunctival swab for bacterial culture.

Main Outcome Measures: The χ^2 test, the Mann-Whitney test, and logistic regression were used to create a prediction model for a negative bacterial culture.

Results: Of 368 patients enrolled, 194 (52.7%) were males. The median patient age was 3 years (interquartile range, 1-5 years). Conjunctival cultures were negative in 130 patients (35.3%). Age 6 years or older, presentation in April through November, no or watery discharge, and no glued eye in the morning were the clinical factors found to be independently associated with a negative conjunctival culture. If 3 factors were present, 76.4% (95% confidence interval, 63.6%-85.6%) of patients had a negative culture. If all 4 factors were present, 92.3% (95% confidence interval, 66.1%-98.2%) of patients had a negative culture.

Conclusion: The combination of 4 clinical factors may enable clinicians to identify children at low risk for bacterial conjunctivitis and may reduce routine antibiotic drug administration.

Arch Pediatr Adolesc Med. 2010;164(3):263-267

ACUTE CONJUNCTIVITIS IS A common condition responsible for more than 5 million outpatient and emergency department visits in the United States each year.[1] Previous research[2-4] has suggested that approximately 50% to 80% of cases of conjunctivitis in children are caused by bacteria. However, the validity of classic signs and symptoms thought to differentiate bacterial from nonbacterial causes of acute conjunctivitis has not been supported by the literature.[5] Therefore, most clinicians (ie, physicians, nurse practitioners, physician assistants, etc, all who have licenses, care for children, and can prescribe antibiotics) prescribe topical antibiotics to all children with acute conjunctivitis.[6]

Bacterial resistance to antibiotic drugs is an ever-increasing problem, and there is a nationwide effort to find conditions for which antibiotic drug use can be restricted. No guidelines exist to help clinicians differentiate bacterial from nonbacterial conjunctivitis with confidence. The objective of this study was to identify a population of children at low risk for bacterial conjunctivitis on the basis of history and physical examination findings.

METHODS

We conducted a prospective observational cohort study of children aged 6 months to 17 years presenting to the pediatric emergency department at Jacobi Medical Center, Bronx, New York, with acute conjunctival erythema, eye discharge, or both between April 2007 to March 2008. Patients were excluded if they had used contact lenses or antibiotic drugs (topical or oral) or had had eye trauma or exposure to a noxious chemical in the previous 5 days. Before study implementation, all attending physicians, nurse practitioners, and house staff received training on the proper collection of conjunctival specimens for culture.

Attending physicians enrolled eligible patients after obtaining written consent from the caregiver and assent from children 7 years and older. Patients were enrolled 24 hours a day and 7 days a week. Clinicians completed a checklist of signs and symptoms and obtained a bacterial conjunctival swab for culture. The affected lower palpebral conjunctiva was sampled using a cotton swab that was then inserted into transport media and immediately sent to the microbiology laboratory. Conjunctival swabs were processed using standard microbiologic techniques.

The primary outcome was the result of the conjunctival culture. Cultures were considered to be negative if they grew normal flora or if there was no growth after 3 days. The microbiology laboratory defined normal conjunctival flora as

Author Affiliations: Lewis M. Fraad Department of Pediatrics (Emergency Medicine), Jacobi Medical Center and Albert Einstein College of Medicine, Bronx, New York.

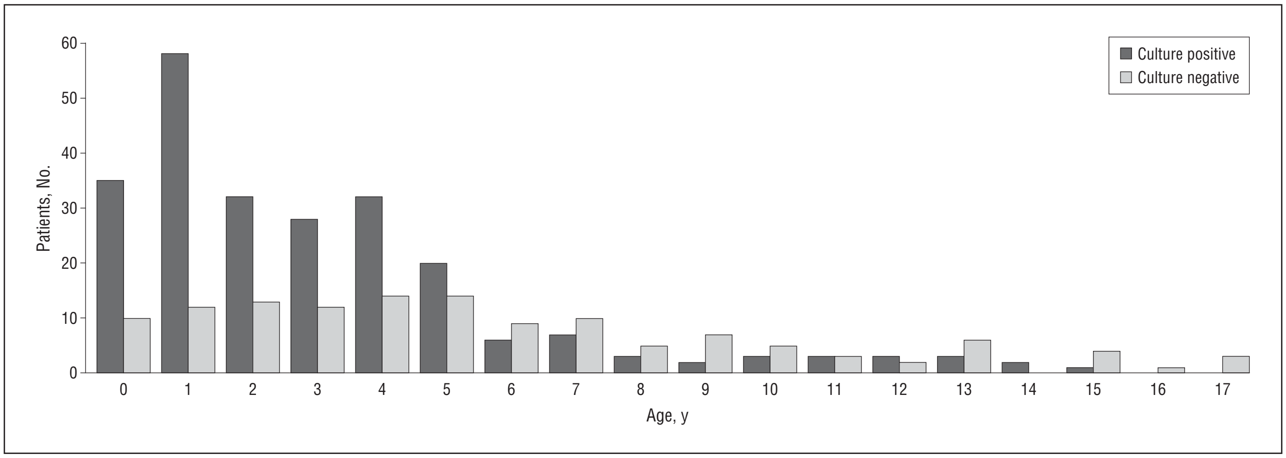

Figure 1. Conjunctival culture results by patient age.

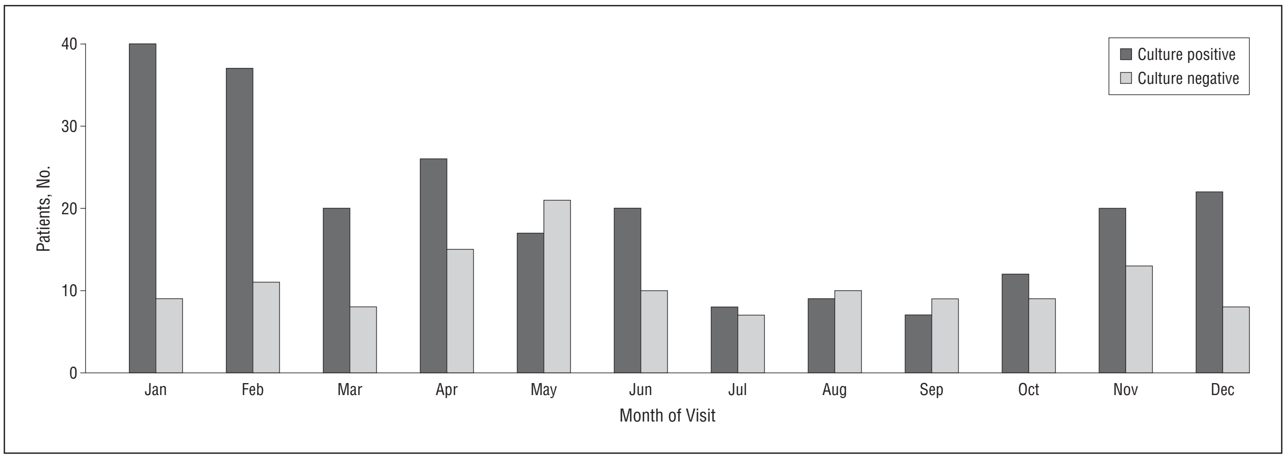

Figure 2. Conjunctival culture results by month of emergency department presentation.

coagulase-negative *Staphylococcus*, *Streptococcus viridans*, and *Diphtherioid* species. Conjunctival culture results were considered positive when the laboratory reported the growth of any bacteria other than normal flora.

Power analysis was conducted using statistical and power analysis software (PASS 2005; NCSS, Kaysville, Utah). The null hypothesis was that there was no relationship between any potential predictor and the baseline probability of having a negative bacterial conjunctival culture. We decided a priori that to consider a variable significant, a negative bacterial culture should be approximately 3 times as likely in the presence of that variable. Using this assumption, a sample size of 353 would be required ($P = .05$, power of 80%).

Data analysis was performed using a statistical software program (SPSS 14.0 for Windows Graduate Student Version; SPSS Inc, Chicago, Illinois). The χ^2 and Mann-Whitney tests were used for bivariate analysis. For the continuous variable of age, a receiver operating characteristic curve was constructed. The age affording optimal discrimination was then used to dichotomize the variable. Variables showing an association of $P < .10$ with the outcome variable in bivariate analysis were then tested in a multivariate logistic regression model. A prediction model was created using combinations of the multivariate predictors.

Subanalyses of children above and below the cutoff age were performed to determine whether subjective factors (ie, eye itch, foreign body sensation, eye burning, eye pain, photophobia, and sore throat) had a greater effect on predicting a negative culture for older children. Separate prediction models were then constructed for each of these 2 age groups. This study was approved by the institutional review boards of the Albert Einstein College of Medicine, Bronx, New York, and Jacobi Medical Center.

RESULTS

A total of 402 children aged 6 months to 17 years with acute conjunctivitis were eligible for enrollment. Of these, 23 parents declined to have their children participate in the study. For 11 children who were enrolled, the laboratory did not receive a culture specimen. The remaining 368 children formed the study population.

One hundred ninety-four patients (52.7%) were males. The median patient age was 3 years (interquartile range [IQR], 1-5 years). Children with positive cultures were significantly younger than children with negative cultures: 2 years (IQR, 1-4 years) vs 5 years (IQR, 2-8 years) ($P < .001$) (**Figure 1**). Using a receiver operating characteristic curve, 6 years provided the optimal discrimination cutoff point for age. Overall, conjunctival cultures were negative in 130 patients (35.3%). Conjunctival culture specimens were obtained throughout the year. Patients presenting to the emergency department in April through November were significantly more likely to have a negative culture ($P < .001$) (**Figure 2**). In patients with

Table 1. Causes of Bacterial Conjunctivitis in 238 Culture-Positive Patients

Bacteria	Patients, %
Haemophilus influenzae	67.6
Streptococcus pneumoniae	19.7
Staphylococcus aureus	8.0
Haemophilus parainfluenzae	2.5
Other bacteria	2.2

positive cultures, *Haemophilus influenzae* and *Streptococcus pneumoniae* accounted for most of the bacteria cultured (**Table 1**).

Associations between demographic and clinical variables and results of the conjunctival cultures are listed in **Table 2**. Sixteen predictor variables qualified for entry into the multivariate regression analysis; 5 of these variables were independently associated with a negative conjunctival culture: age 6 years and older, presentation in April through November, no or watery discharge, absence of a glued eye in the morning, and photophobia. However, photophobia was reported to be unobtainable in 99 patients (26.9%), all of whom were younger than 6 years. Because the median age of the sample was 3 years and because photophobia is an unreliable predictor in young children, we removed this infrequently reported symptom and repeated the analysis, yielding the 4 variables given in **Table 3**. A model was created using combinations of these 4 variables to predict the probability of a negative conjunctival culture (**Table 4**). Using this model, a child with no predictors would have a negative culture 11.8% of the time, whereas a child with all 4 predictors would have a negative culture 92.3% of the time.

The results of the subanalyses for children above and below the cutoff age of 6 years are noted in **Table 5**. In children 6 years and older, "no sore throat" emerged as an additional predictor variable. In children younger than 6 years, only 2 variables were found to be independently associated with a negative culture. Prediction models for both age groups are given in **Table 6**.

Table 2. Bivariate Analysis of Clinical and Demographic Features[a]

Predictor Variable	Patients, No. (%) Positive Culture	Patients, No. (%) Negative Culture	*P* Value
Male sex	133 (56)	61 (47)	.10
Age ≥6 y	33 (14)	55 (42)	<.001
Presentation in April-November	119 (50)	94 (72)	<.001
History of			
Eye itch	132 (67)	94 (78)	.04
Foreign body sensation	11 (9)	17 (19)	.06
Photophobia	12 (8)	17 (15)	.08
No eye discharge	5 (2)	24 (19)	<.001
No glued eye in the morning	23 (10)	45 (35)	<.001
Absence of fever	148 (63)	99 (77)	.005
Cough	133 (56)	49 (38)	.001
Seasonal allergies	38 (16)	32 (25)	.05
Previous conjunctivitis	57 (24)	47 (36)	.02
Burning sensation	26 (21)	23 (24)	.63
Eye pain	42 (27)	38 (35)	.18
Sore throat	29 (16)	15 (14)	.62
Rash	14 (6)	4 (3)	.31
Attendance at day care	65 (28)	33 (27)	.81
Asthma	61 (26)	39 (30)	.39
Eczema	44 (19)	27 (21)	.68
Household member with conjunctivitis	41 (18)	20 (15)	.66
Physical examination			
Temperature ≥100.4°F in ED	61 (27)	16 (13)	.004
Bilateral	162 (68)	65 (50)	.001
No or watery discharge	66 (28)	85 (65)	<.001
Otitis media	51 (22)	11 (9)	.001
Nasal discharge	138 (59)	46 (36)	<.001
Erythema	205 (86)	114 (89)	.51
Chemosis	26 (11)	18 (14)	.40
Periorbital edema	46 (19)	27 (21)	.79
Preauricular lymph node	17 (7)	6 (5)	.50
Pharyngitis	27 (11)	9 (7)	.20
Wheezing	10 (4)	5 (4)	>.99

Abbreviation: ED, emergency department.
[a] The denominator differs for each variable depending on the number of responses received.

Table 3. Results of Multivariate Analysis in 360 Patients With Acute Conjunctivitis

Variable	Adjusted Odds of a Negative Culture (95% CI)
Age ≥6 y	3.1 (1.7-5.4)
Presentation in April-November	2.7 (1.6-4.5)
No or watery discharge	3.2 (1.9-5.3)
No glued eye in the morning	3.3 (1.8-6.1)

Abbreviation: CI, confidence interval.

COMMENT

Although acute conjunctivitis is one of the most common conditions for which patients seek care, few studies have focused on its clinical diagnosis.[7,8] Moreover, although the patients most likely to have this condition are children, there are even fewer studies involving pediatric patients.[9] Previous research[9] has demonstrated that pediatricians correctly diagnose conjunctivitis as bacterial or nonbacterial only approximately half of the time but prescribe topical antibiotics to most children.

Patel et al[9] studied 111 children with acute conjunctivitis in search of clinical factors to distinguish bacterial from nonbacterial causes. The baseline prevalence of bacterial conjunctivitis in their group was 78%. They found 2 variables, a history of glued or sticky eyelids and physical findings of mucoid or purulent discharge, to be most predictive of a bacterial cause. However, there were several important limitations to their study. By excluding children with a "history of allergy, diagnosis of allergic conjunctivitis, or other symptoms of allergy,"[10(p760)] they may have eliminated a significant portion of those without disease, biasing their prediction model. Moreover, they used a convenience sample and may have sampled children in certain parts of the year when the incidence of bacterial disease is more common.

Table 4. Number of Predictors and Probability of a Negative Culture

No. of Predictors	Positive Culture, % (n=231)	Negative Culture, % (n=129)	Probability of a Negative Culture, % (95% CI)
0	29.0	7.0	11.8 (6.4-21.0)
1	45.5	21.7	21.1 (15.0-28.8)
2	19.5	29.5	45.8 (35.5-56.5)
3	5.6	32.6	76.4 (63.6-85.6)
4	0.4	9.2	92.3 (66.1-98.2)

Abbreviation: CI, confidence interval.

Table 5. Results of Multivariate Analysis by Age Group

Variable	Adjusted Odds of a Negative Culture (95% CI)
Age ≥6 y (n=88)	
Presentation in April-November	3.5 (1.1-10.9)
No or watery discharge	4.8 (1.6-14.5)
No glued eye in the morning	7.9 (1.9-32.2)
No sore throat	4.1 (1.2-14.5)
Age <6 y (n=272)	
No or watery discharge	2.8 (1.6-4.9)
No glued eye in the morning	3.0 (1.5-6.3)

Abbreviation: CI, confidence interval.

The literature involving adults suggests that the prevalence of bacterial conjunctivitis is approximately 35%,[8] implying that as children get older, the likelihood of a positive culture decreases. The study by Patel et al[9] included children up to 18 years old but found no significant difference in the mean age of children with and without positive cultures. This may have been due to their relatively small sample size and the fact that most patients presenting with acute conjunctivitis were infants and toddlers.

We sought to identify children at low risk for bacterial conjunctivitis on the basis of history and physical examination findings. We chose to define low risk as a high probability of having a negative culture because we believed that this definition would be most useful to the clinician. Children with negative cultures most likely have viral or allergic conjunctivitis and do not need topical antibiotics. Patients were enrolled consecutively for an entire year to determine the true incidence of disease and to determine the role that time of year might play in prediction.

Age 6 years and older, absence of a glued eye in the morning, no or watery discharge, and presentation in April through November were the variables found to be most associated with having a negative bacterial culture. We combined these 4 predictors and created a simple decision rule. When 3 of the 4 predictors were present, the probability of the child having a negative culture was high. When all 4 predictors were present, the probability was greater than 90%. The rule is user specific and allows the clinician to decide how many variables need to be present before he or she withholds antibiotics. Consisting of

Table 6. Number of Predictors and Probability of a Negative Culture

No. of Predictors	Positive Culture, %	Negative Culture, %	Probability of a Negative Culture, % (95% CI)
Age ≥6 y[a]	(n=33)	(n=55)	
0	3.0	0	0 (NA)
1	51.5	7.3	19.0 (7.8-40.2)
2	27.3	21.8	57.7 (36.4-75.6)
3	15.2	52.7	85.3 (69.7-93.4)
4	3.0	18.2	90.9 (61.5-97.9)
Age <6 y[b]	(n=198)	(n=74)	
0	68.7	39.2	17.6 (12.5-24.1)
1	27.3	39.2	34.9 (25.6-45.7)
2	4.0	21.6	66.7 (46.5-82.0)

Abbreviations: CI, confidence interval; NA, not applicable.
[a]The 4 predictors were presentation in April through November, no or watery discharge, no glued eye in the morning, and no sore throat.
[b]The 2 predictors were no or watery discharge and no glued eye in the morning.

only 4 predictors, the rule is not cumbersome and is easy to remember.

Despite the fact that most cases of conjunctivitis occur in younger children, many factors classically associated with nonbacterial conjunctivitis (ie, eye itch, foreign body sensation, eye burning, eye pain, photophobia, and sore throat) could not reliably be recorded in younger children. We found that this model performed better in older children than in the overall sample. Moreover, when analyzing only older children, only 1 additional subjective variable, no sore throat, aided in the prediction of a negative culture.

There were some limitations associated with this study. Although all clinicians received training about collection of specimens for culture at study implementation, technique may have changed across time, and retraining was variable. It is also possible that clinicians may not have obtained adequate specimens owing to lack of patient cooperation. However, the largest percentage of positive cultures was obtained in younger children, who are often uncooperative. In addition, the patient population is located in the northeastern United States, where there is a seasonal variation in causes of conjunctivitis. Regions that experience less seasonal variation may find the prediction rule less useful.

Another limitation is that we did not specify the exact duration of symptoms that was required to define a patient's conjunctivitis as acute. It is possible that practitioners may have excluded some patients whose symptoms they did not feel were acute. However, a post hoc analysis of these data showed that only 2 patients (0.5%) presented with symptoms lasting longer than 14 days.

This study was designed to assist clinicians in making the diagnosis of nonbacterial conjunctivitis. It is still unclear whether all children with bacterial conjunctivitis need to be treated initially with topical antibiotics or whether a wait-and-see approach, as suggested by Everitt et al,[11] is a better strategy. Whereas a few studies[2,3] have shown that most children with bacterial conjunctivitis will demonstrate clinical cure after a week regardless of treatment, others[2,12,13] have suggested that children with bacterial conjunctivitis are cured more rapidly when treated with antibiotics.

In conclusion, the medical community is concerned about the excessive use of antibiotic drugs and the rapidly growing rate of bacterial resistance. These data suggest that the combination of 4 clinical factors (age ≥6 years, presentation in April-November, no or watery discharge,[11] and the absence of glued eyes in the morning) may aid clinicians in identifying children at low risk for bacterial conjunctivitis. If these findings are validated in other populations, we may be able to limit routine antibiotic drug administration for children with acute conjunctivitis.

Accepted for Publication: September 4, 2009.

Correspondence: James A. Meltzer, MD, Lewis M. Fraad Department of Pediatrics (Emergency Medicine), Jacobi Medical Center, 1400 Pelham Pkwy S, Bronx, NY 10461 (jamesmeltzer@yahoo.com).

Author Contributions: Drs Meltzer and Kunkov had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Meltzer, Kunkov, and Crain. *Acquisition of data:* Meltzer. *Analysis and interpretation of data:* Meltzer and Kunkov. *Drafting of the manuscript:* Meltzer, Kunkov, and Crain. *Critical revision of the manuscript for important intellectual content:* Meltzer, Kunkov, and Crain. *Statistical analysis:* Kunkov. *Administrative, technical, and material support:* Meltzer and Crain. *Study supervision:* Kunkov and Crain.

Financial Disclosure: None reported.

Additional Contributions: Ellen J. Silver, PhD, provided thoughtful suggestions regarding the presentation of results.

REFERENCES

1. Schappert SM, Burt CW. Ambulatory care visits to physician offices, hospital outpatient departments, and emergency departments: United States, 2001–02. *Vital Health Stat 13*. 2006;159(159):1-66.
2. 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(4):623-626.
3. Rose PW, Harnden A, Brueggemann AB, et al. Chloramphenicol treatment for acute infective conjunctivitis in children in primary care: a randomised double-blind placebo-controlled trial. *Lancet*. 2005;366(9479):37-43.
4. 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(9):823-828.
5. Rietveld RP, van Weert HC, ter Riet G, Bindels PJ. Diagnostic impact of signs and symptoms in acute infectious conjunctivitis: systematic literature search [abstract]. *BMJ*. 2003;327(7418):789.
6. Everitt H, Little P. How do GPs diagnose and manage acute infective conjunctivitis? a GP survey. *Fam Pract*. 2002;19(6):658-660.
7. Leibowitz HW, Pratt MV, Flagstad IJ, Berrospi AR, Kundsin R. Human conjunctivitis, I: diagnostic evaluation. *Arch Ophthalmol*. 1976;94(10):1747-1749.
8. Rietveld RP, ter Riet G, Bindels PJ, Sloos JH, van Weert HC. Predicting bacterial cause in infectious conjunctivitis: cohort study on informativeness of combinations of signs and symptoms. *BMJ*. 2004;329(7459):206-210.
9. Patel PB, Diaz MC, Bennett JE, Attia MW. Clinical features of bacterial conjunctivitis in children. *Acad Emerg Med*. 2007;14(1):1-5.
10. Pelletier J, Haim L, Patel NS. Comment on "Clinical features of bacterial conjunctivitis in children." *Acad Emerg Med*. 2007;14(8):759-760, author reply 760.
11. Everitt HA, Little PS, Smith PW. A randomised controlled trial of management strategies for acute infective conjunctivitis in general practice [published correction appears in *BMJ*. 2006;333(7566):468]. *BMJ*. 2006;333(7563):321.
12. Granet DB, Dorfman M, Stroman D, Cockrum P. A multicenter comparison of polymyxin B sulfate/trimethoprim ophthalmic solution and moxifloxacin in the speed of clinical efficacy for the treatment of bacterial conjunctivitis. *J Pediatr Ophthalmol Strabismus*. 2008;45(6):340-349.
13. Sheikh A, Hurwitz B. Antibiotics versus placebo for acute bacterial conjunctivitis [update of: *Cochrane Database Syst Rev*. 2000;(2):CD001211]. *Cochrane Database Syst Rev*. 2006;(2):CD001211.

"You do not really understand something unless you can explain it to your grandmother."

—Dave Barry