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What Is Causing Active Trachoma? The Role of Nonchlamydial Bacterial Pathogens in a Low Prevalence Setting

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PURPOSE. In low prevalence settings, clinically active follicular trachoma (TF) is often found in the absence of detectable *Chlamydia trachomatis*. The reasons for this persistent follicular phenotype are not well understood; one possible explanation is that other bacterial species are provoking the inflammatory response. This study investigated the relationship between TF, *C. trachomatis*, and nonchlamydial bacterial infection.

METHODS. A cross-sectional survey was conducted in a trachoma endemic village in Tanzania. All available children were examined for trachoma and swabs were collected for microbiologic culture (blood and chocolate agar) and *C. trachomatis* PCR (Amplicor).

RESULTS. Four hundred seventy-three children under 10 years of age were recruited for this study. The prevalences of TF and *C. trachomatis* were 13.7% and 5.3%, respectively, and were not associated. Bacteria were cultured from 305 (64.5%) swab samples; 162 (34.3%) grew a pathogen (with or without a commensal organism) and 143 (30.2%) grew commensal bacteria only. The most common pathogens were *Streptococcus pneumoniae* and *Haemophilus influenzae* (type B and non–type B). The presence of bacterial pathogens was associated with TF (odds ratio, 4.68; 95% confidence interval, 2.31–9.50; $P < 0.001$).

CONCLUSIONS. In regions with low levels of endemic trachoma, it is possible that much of the TF that is observed is attributable to nonchlamydial bacterial pathogens. It is plausible that individuals who have previously developed a follicular conjunctivitis in response to *C. trachomatis* may more readily reform conjunctival follicles when challenged with certain other bacterial species. (*Invest Ophthalmol Vis Sci.* 2011;52:6012–6017) DOI:10.1167/iovs.11-7326

Trachoma remains a leading cause of blindness in many of the world's poorest regions.[1] It is caused by the obligate intracellular bacterium *Chlamydia trachomatis*, and is charac-terized by episodes of recurrent, chronic follicular conjunctivitis. In some individuals, this inflammation results in progressive scarring of the tarsal conjunctiva, leading to the blinding complications of trichiasis and corneal opacification.

The control of blinding trachoma focuses on the implementation of the surgery, antibiotics, facial cleanliness, and environmental improvement (SAFE) strategy.[2] Current World Health Organization (WHO) guidelines recommend annual mass drug administration (MDA) with oral azithromycin or topical tetracycline for 3 years to entire communities where the prevalence of trachomatous inflammation–follicular (TF; Simplified WHO Trachoma Grading System[3]) in children 1 to 9 years of age ($TF_{\%1-9}$) is greater than 10%.[2] However, it has been recognized for some time that in low prevalence settings, the relationship between the signs of TF and the detection of *C. trachomatis* infection is variable and at times very weak.[4–7] This relationship becomes even less consistent after the introduction of antibiotic control programs.[8–10]

The discordance between disease and chlamydial infection is an increasingly important issue for trachoma control programs as the prevalence of trachoma declines. When deciding to initiate or stop MDA, programs currently have no practical alternative to assessing the prevalence of clinical signs of active trachoma. There are probably several factors that contribute to the mismatch in signs and infection. First, the temporal sequence for these two events differs: infection probably starts and finishes before the inflammatory response, which can persist for many weeks after the resolution of infection.[11] At a population level, the prevalence of TF appears to take very much longer to decline after the initiation of MDA than the prevalence of chlamydial infection.[8–10] It has been found to stay above the 10% TF treatment threshold for months or years in the absence of detectable chlamydial infection. Second, there are other recognized causes of a follicular conjunctivitis, such as other bacteria and certain viruses. It is plausible that, in an individual who has previously developed a follicular response to *C. trachomatis*, subsequent nonchlamydial infections causing conjunctival inflammation might be more likely to elicit a follicular reaction that mimics TF.

To investigate the relationship between the signs of TF and *C. trachomatis* and other bacterial species, we conducted a cross-sectional survey of the children living in a trachoma-endemic community, relating the clinical phenotype to laboratory evidence of infection.

METHODS

Ethical Approval

This study adhered to the tenets of the Declaration of Helsinki. It was approved by the Tanzanian National Institute of Medical Research

Ethics Committee, the Kilimanjaro Christian Medical Centre Ethics Committee, and the London School of Hygiene and Tropical Medicine Ethics Committee. The study was explained to the parents/guardians of potential study subjects. Informed consent was documented in writing by the parent/guardian on behalf of each child before recruitment.

Study Participants

The study was conducted in a single village in Siha District, Kilimanjaro Region, Northern Tanzania. We carried out a census of the village. All children under 10 years of age who were present and for whom consent was given were enrolled into the study. This district had never received MDA for trachoma control.

Clinical Assessment and Sample Collection

The left eye of each subject was examined by a single ophthalmologist (MJB) using 2.5× loupes and a bright torch. Clinical signs were graded using the 1981 WHO Trachoma Grading System (FPC).[12] Clinically active trachoma was defined as the presence of either a follicular score of 2 or 3 (F2/3) or a papillary score of 3 (P3), equivalent to TF and trachomatous inflammation–intense (TI) of the WHO Simplified Trachoma Grading System, respectively.[3] The conjunctiva was anesthetized with preservative-free proxymetacaine 0.5% eye drops (Minims; Chauvin Pharmaceuticals, Surrey, UK). A rayon-tipped swab sample was collected from the inferior fornix, placed immediately into Amies–charcoal transport media (Sterilin, Caerphilly, UK) and kept at ambient temperature until processing in the laboratory later the same day. A second, Dacron polyester–tipped swab (Hardwood Products Company, Guilford, Maine) was collected from the left upper tarsal conjunctiva for the detection of *C. trachomatis* in a standardized manner (passed firmly four times across the conjunctiva with a quarter turn between each pass). The samples for PCR were kept on ice packs until transfer to a –80°C freezer later the same day for storage until processing. The examiner changed gloves before examining and collecting swabs from each child. "Negative field controls" were collected after every 50 subjects by passing the swab through the air a few centimeters in front of a seated study subject. The village was mass treated with single dose oral azithromycin immediately after the survey.

Laboratory Tests

Microbiology testing was performed at the KCMC Biotechnology Laboratory, Moshi, Tanzania. Microbiology samples were inoculated onto blood and chocolate agar later the same day (usually <6 hours from the collection time) and incubated at 37°C for 48 hours. Culture isolates were identified by standard microbiologic techniques. Testing for *C. trachomatis* by PCR was performed at the MRC Laboratories, Gambia; samples were transferred there on dry ice. DNA was extracted from the dry swab using an isolation kit (QIAmp DNA mini kit; Qiagen, Crawley, UK). *C. trachomatis* was detected using a test kit (Amplicor CT/NG kit; Roche Molecular Systems, Branchburg, NJ), with previously described modifications.[5,13]

Data Analysis

Data were entered into a database (Access 2007; Microsoft, Redmond, WA) and analyzed using software (STATA, v 11.0; StataCorp LP, College Station, TX). A nonparametric test for trend was used to examine the relationship between bacterial culture results and the ordered categories of follicular and papillary inflammation severity. χ^2 tests were used to determine strength of association for individual bacterial isolates with the TF status, with an exact test used if there were fewer than five expected events in a cell. Odds ratios (ORs) and 95% confidence intervals (CIs) for the univariate associations between TF and each factor were estimated using logistic regression, and *P* values were estimated using likelihood ratio tests. Factors associated with TF (*P* < 0.10) were included in a multivariable logistic regression model. Age was considered an a priori confounder because of the known associ-

ation with TF. *Staphylococcus epidermidis*, *Corynebacterium* spp., viridans group streptococci, and *Bacillus* spp. were designated as commensal organisms for the purposes of this analysis.

RESULTS

Study Participants and Samples

A total of 700 children under 10 years of age were recorded as living in the study village at the time of this survey. We were able to examine 571 (81.5%) children. Of the 129 children not examined, 58 (45%) had traveled away, 29 (23%) refused, 25 (19%) were too young, and 17 (2%) were not found despite several visits. Bacteriology and *C. trachomatis* PCR samples were collected from 484 (84.8%) and 557 (97.5%) of the 571 children who were examined, respectively. Both bacteriology and *C. trachomatis* PCR results were available on a total of 473 of 571 (82.8%) children. Comparing the 473 children for whom results were obtained and all the other 227 children living in the village, there was no difference in either the mean age (*P* = 0.92) or the proportion who were of male sex (47.6%; *P* = 0.20). The 98 children who were examined but did not have both microbiology and chlamydial PCR results were slightly older (5.8 vs. 5.0 years; *P* = 0.01); the proportion that was male was comparable (*P* = 0.13). All subsequent analyses are limited to the 473 children with both laboratory results.

Clinical Signs and *C. trachomatis* Infection

TF was diagnosed in 65 (13.7%) children. The frequencies of the FPC Grading System follicular (F) and papillary (P) inflammation scores are shown in Table 1. *C. trachomatis* DNA was detected by Amplicor PCR in 25 (5.3%) samples. The frequency of PCR positive samples by clinical grade is shown in Table 1. There was no association between the presence of TF and the detection of *C. trachomatis* (OR, 1.21; 95% CI, 0.40–3.64; *P* = 0.74). All "negative field controls" tested negative by Amplicor *C. trachomatis* PCR.

Conjunctival Bacterial Culture

Bacteria were cultured and identified from 305 (64.5%) swab samples, of which 162 (34.3%) grew a pathogen (with or without a commensal organism) and 143 (30.2%) grew commensal bacteria only. A wide range of organisms was cultured (Table 2). Double infections were found in 107 and triple infection in 20 eyes. Only 11 of these involved combinations of

TABLE 1. Clinical Disease and *C. trachomatis* Infection

Follicular Inflammation			Papillary Inflammation		
	n (%)	Infected (%)*		*n* (%)	Infected (%)*
FPC score			FPC score		
F0	323 (68.3)	13 (4.0)	P0	372 (78.6)	16 (4.3)
F1	85 (18.0)	8 (9.4)	P1	69 (14.6)	5 (7.3)
F2	35 (7.4)	2 (5.7)	P2	26 (5.5)	4 (15.4)
F3	30 (6.3)	2 (6.7)	P3	6 (1.3)	0 (0.0)
TF			TI		
No	408 (86.3)	21 (5.1)	No	467 (98.7)	25 (5.4)
Yes	65 (13.7)	4 (6.1)	Yes	6 (1.3)	0 (0.0)

The frequency of *C. trachomatis* infection for the different follicular (F) and papillary (P) inflammation grades of the FPC system and for the trachomatous inflammation—follicular (TF) and trachomatous inflammation—intense (TI) scores of the Simplified World Health Organization system.

* This percentage value is for the number infected within each clinical disease grade.

TABLE 2. Bacteria Cultured from Conjunctival Swabs

Name	All Eyes ($n = 473$) n (%)	No TF ($n = 408$) n (%)	TF ($n = 65$) n (%)	P^*
Commensal organisms				
Viridans group streptococcus	153 (32.4)	131 (32.1)	22 (33.9)	0.78
Staphylococcus epidermidis	70 (14.8)	61 (14.9)	9 (13.8)	0.82
Corynebacterium spp.	45 (9.5)	40 (9.8)	5 (7.7)	0.59
Bacillus spp.	8 (1.7)	8 (2.0)	0 (0.0)	0.26
Pathogenic organisms				
Streptococcus pneumoniae	48 (10.2)	34 (8.3)	14 (21.5)	0.001
Haemophilus influenzae, type B	66 (14.0)	50 (12.6)	16 (24.6)	0.008
Haemophilus influenzae, non–type B	43 (9.1)	28 (6.9)	15 (23.1)	<0.001
Micrococcus spp.	8 (1.7)	8 (2.0)	0 (0.0)	0.30
Moraxella catarrhalis	3 (0.6)	3 (0.7)	0 (0.0)	1.00
Haemophilus parainfluenza	2 (0.4)	2 (0.5)	0 (0.0)	1.00
Branhamella catarrhalis	2 (0.4)	2 (0.5)	0 (0.0)	1.00
Neisseria spp.	1 (0.2)	1 (0.3)	0 (0.0)	1.00
Enterobacter spp.	1 (0.2)	1 (0.3)	0 (0.0)	1.00
Klebsiella spp.	1 (0.2)	1 (0.3)	0 (0.0)	1.00

Frequency of bacterial species cultured in all eyes and by presence or absence of trachomatous inflammation—follicular (TF).

* P values are for χ^2, comparing the no TF with the TF group. The Fisher's exact test was used when there were fewer than five events in a cell.

the more common pathogenic organisms. There was no significant difference between the three bacterial infection categories (no growth, commensal only, and pathogen) in the proportion of eyes with *C. trachomatis* detected ($P = 0.21$).

Clinical Signs and Bacterial Infection

Pathogenic bacteria were grown from samples from 61.1% of eyes with TF compared to 29.9% of eyes without TF. There was no difference in the proportion of eyes with or without TF that had commensal bacteria (Table 2). *Streptococcus pneumoniae*, *Haemophilus influenzae* type B, and *Haemophilus influenzae* non–type B were significantly more frequent in eyes with TF (Table 2). There was an increasing trend in the proportion of eyes with bacterial pathogens cultured with increasing FPC follicular score ($P < 0.001$; Table 3). There was a similar but less marked increase for FPC papillary inflammation (Table 3). There were also significant univariate associations between TF and being younger than 3 years of age and with having pathogenic bacteria cultured (Table 4). In a multivariable logistic regression model, *S. pneumoniae*, *H. influ-*

enzae type B, and *H. influenzae* non–type B were all independently associated with TF (Table 5).

DISCUSSION

In this study, the prevalence of $TF_{\%1-9}$ was relatively low (13.7%) but was still above the 10% treatment threshold for initiating community level MDA.[2] An additional 18% of the children in this population had a mild follicular conjunctivitis (FPC grade F1). The prevalence of *C. trachomatis* detected by Amplicor PCR was lower (5.3%) than the prevalence of TF. Overall, we found no association between the signs of active trachoma and chlamydial infection in this community. These observations are consistent with findings from other low prevalence settings and illustrate the difficulty control programs face in determining where to invest resources to distribute antibiotic for trachoma control.[6–9] The weak relationship between the signs of active trachoma and *C. trachomatis* infection is likely to lead to many communities receiving unnecessary antibiotic treatment. In regions with an initially higher

TABLE 3. Clinical Signs of Trachoma and Type of Conjunctival Bacterial Isolates

	Follicular Inflammation				Papillary Inflammation		
	No Growth n (%)	Commensal n (%)	Pathogen n (%)		No Growth n (%)	Commensal n (%)	Pathogen n (%)
FPC score				FPC score			
F0	130 (40.3)	99 (30.7)	94 (29.1)	P0	145 (39.0)	114 (30.7)	113 (30.4)
F1	27 (31.8)	30 (35.3)	28 (32.9)	P1	16 (23.2)	21 (30.4)	32 (46.4)
F2	6 (17.1)	7 (20.0)	22 (62.9)	P2	6 (23.1)	6 (23.1)	14 (53.9)
F3	5 (16.7)	7 (23.3)	18 (60.0)	P3	1 (16.7)	2 (33.3)	3 (50.0)
TF				TI			
No	157 (38.5)	129 (31.6)	122 (29.9)	No	167 (35.8)	141 (30.2)	159 (34.0)
Yes	11 (17.0)	14 (21.5)	40 (61.5)	Yes	1 (16.7)	2 (33.3)	3 (50.0)

The frequency of bacterial infection for the different follicular (F) and papillary (P) inflammation grades of the FPC System and for the TF and TI scores of the Simplified WHO system. TF, trachomatous inflammation—follicular; TI, trachomatous inflammation—intense.

TABLE 4. Univariate Associations with Trachomatous Inflammation-Follicular

Variable	OR	95% CI	*P**
Sex, female	1.33	0.79–2.26	0.28
Age group, y			
0–3	1	—	0.06
4–6	0.68	0.37–1.25	—
7–10	0.46	0.23–0.90	—
Chlamydia trachomatis	1.21	0.40–3.64	0.74
Bacterial infection			
None	1.00	—	<0.001
Commensal only	1.54	0.68–3.53	—
Pathogen	4.68	2.31–9.50	—
Bacterial species			
Viridans group streptococcus	1.08	0.62–1.88	0.78
Staphylococcus epidermidis	0.91	0.43–1.94	0.81
Corynebacterium spp.	0.77	0.29–2.02	0.58
Streptococcus pneumoniae	3.02	1.52–6.01	0.003
Haemophilus influenzae, type B	2.34	1.24–4.42	0.01
Haemophilus influenzae, non–type B	4.07	2.04–8.14	<0.001

  * *P* values are derived from likelihood ratio testing. For categorical variables (age group and bacterial infection), overall *P* values are shown.

prevalence of disease and chlamydial infection, the relationship between the two weakens markedly after the initiation of MDA.[10]

To develop rational strategies for managing MDA in low and medium prevalence settings, it is necessary to have a better understanding of the causes of follicular conjunctivitis in trachoma endemic communities. Probably part of the explanation for the discordance between episodes of active disease and *C. trachomatis* infection is their different time course.[11,14] Follicles in children can persist for weeks or months after the chlamydial infection is no longer detectable. In low prevalence settings, *C. trachomatis* infection prevalence is often so low that it is difficult to imagine that this alone is sufficient to sustain a prevalence of TF above the treatment threshold, and other factors may contribute.[7]

In this population-based survey, we examined the potential contribution of nonchlamydial bacterial species to the presence of a "TF" phenotype. In contrast to *C. trachomatis*, nonchlamydial bacteria were frequently cultured from the conjunctiva of children. The range of organisms included some that are generally considered commensal and others normally considered to be pathogens. We found no association between the presence of TF and the presence of a commensal organism alone. However, we did find a clear association between TF and pathogenic bacteria, specifically *S. pneumoniae* and *H. influenzae*. There was no significant difference in the frequency of bacterial pathogens between individuals with no follicles (F0) and those with very few follicles, below the diagnostic threshold for TF (F1).

There are little published data on the normal conjunctival bacterial flora in children in Africa. The only recent study comes from a village in Sierra Leone, a country that does not have endemic trachoma, which tested people of all ages.[15] This study found 86% had positive cultures (*S. epidermidis* 28%, *S. aureus* 20%, *P. aeruginosa* 6%, *Klebsiella* 4%, and *H. influenzae* 2%). However, there were a number of differences in the range and relative frequencies of organisms cultured in these two studies. For example, the study from West Africa did not identify any *S. pneumoniae* and only relatively few *H. influenzae*. These differences could be attributable to differences in sample collection and processing (performed in the United States), population demographics (only 16% under 18

years of age), and the environment (more humid) in the Sierra Leonean study.

A number of studies have investigated bacterial infection in children living in trachoma-endemic regions (Table 6).[16–21] However, these were mostly conducted before the development of sensitive PCR-based techniques for *C. trachomatis* detection and the current trachoma grading systems.[3,12] In addition, a number of methodologic variations make it difficult to draw definite conclusions about the contribution of other bacteria to follicular conjunctivitis in trachoma-endemic environments. Several studies were not population-based, only including cases with active trachoma or with a limited selection of unaffected individuals.[16,17,20] Two studies present microbiology results based on microscopy alone (no culture performed).[18,20] In these earlier studies, the range of organisms identified by culture was generally similar to those we found, albeit with some differences in the relative frequency. In the most methodologically comparable studies to ours, *S. pneumoniae* and *H. influenzae* were prominent among the pathogens.[16,19,21] In two studies, it is possible to partially evaluate the relationship between active trachoma and bacterial infection.[16,17] In the larger of these, reanalysis of the available data suggests a significant association between active trachoma and conjunctival pathogens, when compared to normal healthy controls.[16] Surprisingly, the authors reached the opposite conclusion—that individuals with trachomatous conjunctivitis were no more likely to grow a pathogen than controls. However, in their analysis, they included within the control group a large number of individuals with "simple bacterial conjunctivitis," which added to the number of pathogens identified in the control group and probably should not have been regarded as clinically normal.

We have previously found that individuals with established trichiasis and conjunctival scarring are more likely to have nonchlamydial bacterial infections.[22–24] This is often associated with a marked clinically apparent inflammatory reaction in the conjunctiva in the absence of detectable *C. trachomatis* infection.[22] In addition, after trichiasis surgery, individuals with bacterial infection had significantly increased expression of various factors that could plausibly be involved with the scarring process (interleukin-1β, tumor necrosis factor–α, and matrix metalloproteinases-1 and -9).[25] This raises the possibility that these other bacteria could contribute to stimulating progressive cicatricial disease in conjunctiva that has previously been damaged by the immune response to *C. trachomatis*.

This study, from an area with low prevalence trachoma, indicates the potential importance of nonchlamydial bacterial pathogens in the production of a follicular phenotype. The possibility of reverse causality in the association between bacterial pathogens and follicular conjunctivitis (namely, that eyes with TF are more susceptible to being infected with bacteria) cannot be ruled out in a cross-sectional study. However, even

TABLE 5. Multivariable Logistic Regression Model for Trachomatous Inflammation-Follicular

Variable	OR	95% CI	*P**
Age group, y			
0–3	1	—	0.25
4–6	0.80	0.42–1.52	—
7–10	0.66	0.33–1.35	—
Bacterial species			
Streptococcus pneumoniae	3.22	1.56–6.66	0.003
Haemophilus influenzae, type B	2.92	1.47–5.81	0.003
Haemophilus influenzae, non-type B	5.34	2.57–11.3	<0.001

  * *P* values are derived by likelihood ratio testing. For age group, *P* value is for trend.

TABLE 6. Studies of Conjunctival Bacterial Infection in Children in Trachoma Endemic Communities

Country (Year)	Study Population and Design	Findings	Comments
Taiwan (1962)[16]	Three separate trachoma endemic areas; conjunctival swab samples from preschool and first-grade children; about half had active trachoma; cultured (blood and chocolate agar)	Culture positive; normal, 42/144 (29%); active trachoma, 74/201 (37%); organisms: *Staphylococcus pneumoniae*, 15.6%; α-streptococci, 11.6%; Haemophilus, 6.4%; *Staphylococcus* spp., 5.0%	Sampling frame not specified, drawn from a number of different settings; variation of MacCallan's trachoma grading system used, making it difficult to relate to current clinical grades (to derive an approximation to active trachoma, Tr-D, Tr-I Tr-II, Tr-III, and CFC have been combined here); no *Chlamydia trachomatis* test data presented; reanalysis of the data suggests a significant association between active trachoma and bacterial infection (OR, 2.58; 95% CI, 1.6–4.0; $P < 0.0010$)
USA (1967)[17]	School children (140) enrolled in a treatment trial for active trachoma; cultured (blood agar); microbiology results from before and after treatment combined	Culture positive; normal/Tr-4, 41%, and Tr-I, Tr-II, and Tr-III, 43%	Sampling frame not specified; MacCallan's trachoma grading system used; microbiology results from before and after treatment combined; no *C. trachomatis* test data presented.
Morocco (1968)[18]	Sample from 16 communities enrolled in a trachoma control study; in each community, 160–180 children 0–8 years of age were randomly selected; conjunctival scrapings were Gram stained; no culture	Positive slide: Haemophilus, 81%; Moraxella, 20%; *S. pneumoniae*, 19%	MacCallan's trachoma grading system used; denominator not stated; no *C. trachomatis* test data presented; no analysis of bacterial infection in relation to active trachoma
Tunisia (1974)[19]	Two villages—(A) 151 children 6–9 years with active trachoma; (B) 44 children <15 years, randomly selected; conjunctival swab (cultured blood agar); conjunctival smear, Giemsa stain for chlamydial inclusions	Culture positive: *S. viridans*, 65%; Diphtheroids, 52%; *Haemophilus* spp., 40%; *S. epidermidis*, 13%	The number of children contributing data to the reported culture results was 277, and this is higher than the 195 children described in the subject description; the age and clinical status of the additional 82 children is not presented; Haemophilus was found to be the major cause of mucopurulent conjunctivitis; no analysis of bacterial infection in relation to active trachoma
Tunisia (1975)[20]	Single village—151 children initially having active trachoma were enrolled into a treatment trial; conjunctival scraping with Giemsa staining; no culture; each child had both eyes sampled on three occasions	Results of 927 slides presented; slides positive for bacteria: 48% (Haemophilus, 25% and Moraxella, 16%)	Difficult to interpret, because multiple data from both eyes are presented together; no analysis of bacterial infection in relation to active trachoma
Nepal (1999)[21]	Single village—122 children 1–10 years of age; conjunctival swab (cultured blood agar)	Active trachoma in 38%; *S. pneumoniae*, 22%; *Haemophilus* spp., 7%; Moraxella, 16%	The focus of this study was the change in bacterial antibiotic sensitivity patterns after azithromycin treatment; no *C. trachomatis* test data presented; no analysis of bacterial infection in relation to active trachoma

if this is part of the explanation for the observed association, it remains probable that these other bacteria contribute to the inflammatory response. It has long been recognized that various viral and bacterial pathogens can cause a follicular conjunctivitis. It is conceivable that these effects are amplified in a trachoma-endemic population: individuals who have previously developed a follicular conjunctivitis in response to *C. trachomatis* may more readily reform conjunctival follicles when challenged with certain other bacterial species. This may provide part of the explanation why the community prevalence of TF declines more slowly than chlamydial infection

after the successful introduction of MDA.[8,9] A rapid, inexpensive point of care (POC) test would potentially be very useful to control programs, by providing an indication of whether *C. trachomatis* is no longer endemic in the face of persisting TF, allowing MDA to be stopped at an earlier stage.[26] Unfortunately, because there is not currently a POC test available, control programs have to base the decision of whether to continue treating on the community prevalence of TF. There is probably some potential to refine the treatment algorithm further as more empiric data on the relationship between infection and disease at different prevalence levels becomes available.

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