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Association of Pharyngitis With Oral Antibiotic Use for the Treatment of Acne

A Cross-sectional and Prospective Cohort Study

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Objective: To prospectively evaluate the association between antibiotics used to treat acne and pharyngitis.

Design: Cross-sectional and 9-month prospective cohort.

Setting: Urban university setting.

Participants: University students.

Intervention: Participants were asked to fill out a survey form, were swabbed for culture, and had a visual examination for acne.

Main Outcome Measure: Report of pharyngitis.

Results: In the cross-sectional study, 10 of the 15 students receiving oral antibiotics for acne reported an episode of pharyngitis in the previous 30 days, whereas 47 of the 130 students not receiving oral antibiotics, but who had acne, reported an episode of pharyngitis in the prior month. The unadjusted odds ratio (OR) (95% CI) associating current oral antibiotic use in acne patients with a self-reported episode of pharyngitis was 3.53 (95% CI, 1.14-10.95). In the cohort study, there were 358 female and 218 male participants; 36 (6.2%) received oral antibiotics for acne during the study, and 96 (16.6%) received topical antibiotics for acne. Using mixed model logistic regression, the OR was 4.34 (95% CI, 1.51-12.47) associating oral antibiotic use with pharyngitis. Less than 1% of participants were colonized by group A streptococcus, which was not associated with pharyngitis.

Conclusions: Our studies show that that the odds of reporting pharyngitis is more than 3 times baseline in patients receiving oral antibiotics for acne vs those who are not receiving oral antibiotics. The true clinical importance of these findings needs to be evaluated further by prospective studies, but this finding is not associated with group A streptococcus.

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MANY INCONSISTENT concerns have been voiced about the safety of long-term use of antibiotics.[1-4] Because of the high prevalence of acne and the frequent use of antibiotics to control acne, individuals undergoing therapy to treat their acne are an ideal group in which to study the effects of long-term antibiotic use. Both topical and oral antibiotics are used in the treatment of these patients, and the most commonly used are clindamycin phosphate and erythromycin as topical therapies and the tetracyclines (tetracycline, doxycycline, and minocycline) as oral therapy.[5,6]

Previous studies have shown an association between the use of oral antibiotics in those with acne and the development of pharyngitis.[7-10] For example, a recent retrospective cohort study using a general medical database in the United Kingdom showed an association between pharyngitis and individuals using antibiotics for acne vs those not using antibiotics.[8] The hazard ratio for this association was 2.15 (95% CI, 2.05-2.23).[8] The reason for this increased risk was not apparent. One study showed that for patients receiving oral antibiotics for acne, there was a higher colonization rate of group A streptococcus (GAS) than for those who were not receiving oral antibiotics (33% vs 10%, respectively).[11] As such, it could be possible that oral antibiotics used to treat acne result in an increase in the colonization rates of GAS, with a resulting increase in the frequency of symptomatic infection. One hypothesis surmised that the increased colonization could be due to a decreased prevalence in organisms known to prevent the colonization of GAS, such as *Streptococcus salivarius*.[12,13] It is important, however, to realize that most upper respi-

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ratory tract infections (URTIs) are not of bacterial origin and are likely due to viral illnesses[14]; specifically, only about 10% of pharyngitis is due to bacterial infections, and of those, 90% are caused by GAS.[14,15] It is, however, possible that bacterial colonization could facilitate infection by viral organisms. Unfortunately, these previous studies were not prospective and longitudinal, so establishing a direct relationship between URTIs and GAS in those using antibiotics for acne was not possible.

Based on our prior studies, using better designs, our goal was to more directly establish the relationships among antibiotic use, bacterial colonization patterns, and URTIs among patients with acne. To that end, we first attempted to replicate the finding that individuals receiving antibiotics for acne are more likely to report pharyngitis in a cross-sectional study of a group of college students. We then conducted a prospective cohort study of college students in order to validate this observation. We further hypothesized that these changes might include increased colonization of the throat by GAS and decreased colonization with *S salivarius*, a natural inhibitor of GAS growth. Specifically, we followed a cohort of students over a school year and queried them about the development of pharyngitis and their use of antibiotics for acne, both oral and topical; examined them for the presence of acne; and obtained samples for oral and pharyngeal cultures. These cultures were used to assess whether the students were colonized with GAS or *S salivarius*. *Streptococcus salivarius* was selected because it is an organism that is known to produce a substance that is toxic to GAS and is found in the same microflora. It is also thought to be sensitive to the tetracycline antibiotics, while GAS is not. Our hypothesis was that prolonged use of oral antibiotics for acne is responsible for changes in the microbial flora of the throat leading to an increased risk of developing pharyngitis.

METHODS

POPULATION AND DATA COLLECTION

Participants were recruited throughout the campus of the University of Pennsylvania, Philadelphia, an urban campus of about 10 000 students. All individuals were fulltime undergraduate or graduate students with access to student health services. The university population offers many advantages for this research because, by age, these individuals have a high prevalence of acne, they are frequently prescribed antibiotics for the treatment of their acne, they are generally otherwise healthy, and they are geographically concentrated near the study team. Students with and without acne were eligible for this study. Participants were defined as having acne based on 1 of 3 criteria: (1) if they were determined by a trained expert on the day of the visit to have acne, (2) if they were currently using oral or topical treatments specifically for acne, or (3) if they had evidence of acne elsewhere on the body (eg, chest) besides the face. Because of the effect that isotretinoin has on acne and epidermal differentiation, participants using isotretinoin for acne were excluded from the study.

Informed consent approved by the University of Pennsylvania institutional review board was obtained from all students. In addition, the study was approved by the Office of Student Life of the University of Pennsylvania. We conducted 2 studies: 1 was cross-sectional, and 1 was a longitudinal cohort study. The cross-sectional study consisted of a single study visit in January and February of 2007. Evaluations for this study were similar to those described herein for the first visit of the longitudinal study (albeit the survey information was briefer). For the longitudinal study, participants were followed for up to 3 visits (the beginning of fall semester, the end of fall semester, and near the end of spring semester) over a single school year (2007-2008). On each visit, the student completed a self-administered survey, underwent a visual examination for acne using the Allen and Smith grading scale, had his or her throat swabbed to obtain a culture specimen for GAS, and had a distal tongue swab to obtain a culture specimen for *S salivarius*. None of the participants enrolled in the cross-sectional study were enrolled in the longitudinal study, and none were enrolled our previous studies. The survey consisted of questions asking about their acne history, their treatments for acne, whether they were currently or had recently (within the past 60 days for the first survey and then since the last survey) used antibiotics, and if they had been recently evaluated for pharyngitis (ie, "Have you seen a health care provider because you were sick with a sore throat or have you been evaluated for a sore throat within the last 30 days?"). At each visit, each participant had his or her throat (GAS) and distal tongue (*S salivarius*) swabbed in duplicate for culture using Copan rayon swabs in Amies transport medium (Copan Diagnostics, Corona, California). The biologic material was placed in the eSwab transport solution (Copan Diagnostics) and hand delivered to the laboratory within 4 hours of collection. The swab in the transport system was then vortexed to produce a homogenous suspension. Selective and differential media were used to grow GAS and *S salivarius* (SXT blood agar and *Mitis-Salivarius* agar with 1% tellurite media, respectively [BD BBL, Franklin Lakes, New Jersey]). Two culture plates for GAS were set up for each patient specimen, 1 from each of the 2 oropharyngeal swabs. The bacteria of interest were identified using conventional microbiologic criteria.[16] *Streptococcus salivarius* was identified using an immunodiagnostic method.[16,17] A pilot study showed that 98.6% of 223 *S salivarius* isolates identified by conventional methods were correctly identified using a polymerase chain reaction method.[17] Bacteriocin-like inhibiting substance (BLIS) production of all *S salivarius* isolates was determined as described previously, using both direct and indirect assays, using 3 different GAS indicator strains.[18-20] Antimicrobial susceptibility of a selected sampling of *S salivarius* isolates was by disk diffusion testing, as previously described.[21]

EXPOSURE DEFINITION

Exposure to an antibiotic was defined as a participant's report of current oral or topical antibiotic use (eg, tetracyclines, erythromycin, clindamycin) for acne treatment that had been ongoing for at least 1 month. For the longitudinal study, antibiotic exposure had to be documented on the survey prior to the report of pharyngitis. Other exposures were also evaluated, as listed in the next subsection as confounding variables.

OUTCOME AND CONFOUNDING VARIABLES

As noted, our outcome of interest initially was the participant's report of pharyngitis. For the cross-sectional study, the participants were asked if they currently had pharyngitis or had had it within the past 30 days. For the longitudinal study, this definition was modified. First, since this was a prospective study, to count as an outcome for this study, the symptoms of pharyngitis must have occurred after the first survey (ie, after enrollment), and, to mimic a previous retrospective cohort study[8] and to provide for a more specific outcome, pharyngitis was considered to

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Table 1. Cross-sectional Study: Basic Demographic and Exposure Information for All Participants, Those With Acne, and Those Without

Demographic or Exposure Information	No. (%)		
	All Participants (n=266)	Those With Acne (n=145)	Those Without Acne (n=121)
Antibiotics use			
Oral	15 (5.6)	15 (10.3)	0
Topical	41 (15.4)	41 (28.3)	0
Oral and/or topical	49 (18.4)	49 (33.8)	0
Male	205 (77.1)	112 (78.9)	93 (76.9)
Age, mean (SD), y	21.0 (2.1)	20.5 (2.0)	21.7 (2.2)
Smoker (any daily cigarette use)	67 (25.2)	45 (31.0)	22 (18.2)
Report of pharyngitis	92 (34.0)	61 (35.3)	31 (31.6)

have occurred if the participants noted that they had had pharyngitis and if they and their symptoms were evaluated by a health care provider. A priori confounding was evaluated with respect to age, sex, race/ethnicity, presence and severity of acne, topical antibiotic use for acne (when oral antibiotic use was the exposure of interest), teeth-flossing habits, teeth-brushing habits, face-washing habits, number of cavities, presence of diabetes mellitus, reported alcohol use, and reported tobacco use.

STATISTICAL ANALYSES

The initial analysis for every variable consisted of characterizing the distribution of that factor. Characterization depended on the data and consisted of estimating the means (SDs) for each evaluation. Initial univariate assessments of association, when appropriate, were performed using 2×2 tables and the Mantel-Haenszel statistic. For variables with more than 1 category, a χ^2 test was performed.

For the cross-sectional study, our primary question was to assess the effect of various risk factors, particularly the use of oral antibiotics for acne, on the development of pharyngitis. The selection of variables for the multivariable model was based on purposeful selection and a confounder that altered the effect estimate by more than 10%.[22] To assess the magnitude of association of a given risk factor with the outcome of interest, single variable and multivariable logistic regression models were created. Both unadjusted and fully adjusted (from a multiple variable logistic model) prevalence odds ratios (ORs) were reported with 95% CIs.

For the longitudinal study, to account for repeated measures in our longitudinal design we used a mixed-effect logistic regression, allowing the repeated measures from the study participants to be expressed as random effects.[22] Both unadjusted (from a single variable logistic model) and fully adjusted (from a multiple variable logistic model) ORs were evaluated with 95% CIs. The selection of variables for the multivariable model was based on purposeful selection (ie, variables thought to be clinically important) and a confounder that altered the effect estimate by more than 10%.[23] All statistical tests were 2 sided. Values were considered to be significant if $P < .05$. Statistical analyses were performed using Stata software (version 11.0; Stata Corp Inc, College Station, Texas).

RESULTS

FOR THE CROSS-SECTIONAL STUDY

The mean (SD) age was 21.0 (2.1) years, with a range of 18 to 27 years. There were 205 male participants and 57 female participants who provided culture samples in the winter or early spring. Four participants did not record their sex on the questionnaire. Of 266 total participants, 15 (5.6%) reported that they were currently using oral antibiotics for acne treatment, and 251 (94.4%) were not. Based on our diagnostic criteria, 145 students (53.5%) were determined to have acne, whereas 121 (44.6%) were determined to not have acne. Of the 145 who had acne, 15 (10.3%) were receiving oral antibiotics, and 130 (89.7%) were not (**Table 1**). Ten of the 15 students receiving oral antibiotics for acne self-reported an episode of pharyngitis in the previous 30 days (66.7%), whereas 47 of the 130 students not receiving oral antibiotics, but who had acne, self-reported an episode of pharyngitis in the prior month (36.2%). Of the 121 students without acne, none reported current use of oral antibiotics, and 35 (28.9%) reported a recent episode of pharyngitis. Combining all 251 students not receiving oral antibiotics, 82 (32.7%) reported an episode of pharyngitis in the prior 30 days.

Several variables were evaluated for their potential to be associated with pharyngitis (Table 1). Of note, 3 of 145 students with acne (2.1%) were found to be colonized with GAS. Three of 266 total students (1.1%) were colonized with GAS. Of these 3, none were receiving oral antibiotics. This did not allow for a prevalence OR to be calculated relating oral antibiotic use and colonization of GAS, since there were no patients with GAS colonization who were receiving oral antibiotics.

The initial, unadjusted OR associating current oral antibiotic use in patients with acne to a self-reported episode of pharyngitis was 3.53 (95% CI, 1.14-10.95) and the adjusted OR was 4.93 (95% CI, 1.41-17.23) (**Table 2**).

FOR THE LONGITUDINAL STUDY

The median age in our study population was 21 years (mean [SD], 21.7 [3.0] years), with a range of 16 to 38 years. There were 358 female and 218 male participants. No students who had enrolled in the cross-sectional study enrolled in the longitudinal study. A total of 579 students participated in the first survey, 359 (62.0%) participated in the second survey, and 312 (53.9%) took part in the third survey. A total of 285 of the students (49.2%) participated in all 3 survey periods, and 193 (33.3%) participated only in the first visit.

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Table 2. Cross-sectional Study: Prevalence Odds Ratios (ORs) and 95% CIs for Developing Pharyngitis With Respect to Several Exposure Variables, Unadjusted and Adjusted for Age, Sex, and Race/Ethnicity

	Prevalence OR (95% CI)			
	Unadjusted		Adjusted	
Type of Antibiotics	Those With Acne	All Patients	Those With Acne	All Patients
Oral	3.53 (1.14-10.90)[a]	4.12 (1.36-12.40)[b]	4.93 (1.41-17.20)[b]	6.52 (1.88-22.60)[b]
Topical	0.74 (0.35-1.56)	1.00 (0.48-1.97)	0.44 (0.17-1.27)	0.78 (0.34-1.80)
Oral and/or topical	1.01 (0.55-2.22)	1.39 (0.74-2.62)	0.45 (0.15-1.38)	0.75 (0.30-1.85)

[a] $P<.05$.
[b] $P<.01$.

Table 3. Longitudinal Cohort Study: Basic Demographic and Exposure Information for All Participants, Those With Acne, and Those Without Acne

	No. (%)		
Demographic and Exposure Information	All Participants (n=579)	Those With Acne (n=306)	Those Without Acne (n=273)
Antibiotics use			
Oral	21 (3.6)	21 (6.9)	0
Topical	74 (12.8)	74 (24.2)	0
Oral and/or topical	86 (14.8)	86 (28.1)	0
Male	218 (37.8)	111 (36.4)	107 (39.5)
White	371 (66.1)	191 (64.1)	180 (68.4)
Age, mean (SD), y	21.6 (3.2)	21.5 (2.9)	21.8 (3.6)
Smoker (any daily cigarette use)	107 (18.6)	55 (18.0)	52 (19.2)
Brushes teeth at least twice daily	538 (93.7)	258 (84.9)	230 (85.2)
Flosses teeth daily	439 (75.8)	80 (26.1)	60 (22.0)
Has any cavities	524 (90.5)	279 (91.2)	245 (89.7)
Washes face daily	138 (23.8)	59 (21.6)	79 (25.8)
Drinks alcohol at least weekly	257 (44.5)	132 (43.3)	125 (46.0)
History of diabetes mellitus	2 (0.4)	1 (0.3)	1 (0.4)

Basic demographic variables and important covariates are listed in **Table 3** for the first survey period. Of the 579 total participants, 358 (61.8%) were determined to have acne at some point during the study. Thirty-six (6.2%) were taking oral antibiotics for acne during the study, and 96 (16.6%) received topical antibiotics for acne. At the time of the first survey, 148 individuals (25.5%) noted a history of pharyngitis within the previous 30 days. During the follow-up period, 210 (36.3%) noted a history of pharyngitis, and 43 (7.4%) noted a history of pharyngitis associated with a health care provider visit (Table 3). Only 8 throat cultures (0.6%) were positive for GAS (6 unique participants), and only 3 of those had a moderate or heavy concentration of the bacteria. *Streptococcus salivarius* was cultured from 1211 of 1228 (98.6%) tongue swabs, and 96.1% had moderate or heavy growth. Of these isolates, 48.1% produced BLIS. Antibiotic sensitivity was analyzed in a convenience sample of 222 *S salivarius* isolates. Of these isolates, 63% were resistant to erythromycin, clindamycin, or tetracycline, and 24% were resistant to all 3 drugs; 58%, 31%, and 32% were resistant to erythromycin, clindamycin, or tetracycline, respectively. The ability for *S salivarius* to produce BLIS did not prevent the new onset of pharyngitis with an OR of 1.07 (95% CI, 0.58-2.00).

We found that the use of oral antibiotics for the treatment of acne was strongly associated with a health care evaluation for pharyngitis in that 11.3% of those receiving oral antibiotic treatment reported pharyngitis, but it was only reported by 3.3% of participants who were not receiving oral antibiotics. Using mixed model logistic regression, the OR associating oral antibiotic use with pharyngitis was 4.34 (95% CI, 1.51-12.47) (**Table 4**). This is an estimated relative risk of 3.91.[24] To provide for a comparison with the cross-sectional study, using any report of pharyngitis as the outcome, an OR of 2.68 (95% CI, 0.98-6.16) was calculated. No association with pharyngitis was noted for those who used a topical antibiotic for acne (OR, 0.63; 95% CI, 0.22-1.81). We evaluated and selected a priori several variables that might be associated with the onset of pharyngitis, and these included age, sex, race/ethnicity, presence and severity of acne, teeth-flossing habits, teeth-brushing habits, face-washing habits, number of cavities, presence of diabetes mellitus, alcohol use, and tobacco use (Table 3 and Table 4). These covariates did not confound our results, and therefore only the unadjusted analyses are reported (Table 4).

COMMENT

Acne is a very common disease. In our cross-sectional and longitudinal studies of college students, respectively, 54.5% and 52.8% of our participants had acne, and

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Table 4. Longitudinal Cohort Study: Adjusted (Age, Sex, Race/Ethnicity) Odds Ratios (ORs) and 95% CIs for Developing Pharyngitis With Respect to Several Exposure Variables

Variable	Adjusted OR (95% CI)
Oral antibiotics	4.34 (1.51-12.47)
Topical antibiotics	0.62 (0.22-1.81)
Has severe acne	1.62 (1.10-2.40)
Age	0.99 (0.90-1.08)
White	2.06 (0.85-5.03)
Female	0.60 (0.30-1.21)
Washes face regularly	1.02 (0.50-2.10)
Chews tobacco	2.23 (0.25-19.65)
Flosses regularly	0.70 (0.33-1.51)
Has >5 cavities	0.64 (0.33-1.51)
Smoker (any daily cigarette use)	1.21 (0.98-1.49)
Alcohol use daily	1.17 (0.91-1.50)
Has acne on chest	1.05 (0.47-2.35)
Has body piercings	3.61 (0.72-17.95)

33.8% and 28.1% of those with acne were using some type of antibiotic for treatment. An oral antibiotic was being used by 10.6% and 6.2%, respectively. As a treatment for acne, antibiotics have been considered extremely safe and effective.[6,25,26] We have previously shown, in retrospective cohort and cross-sectional studies, an association between pharyngitis and the long-term use of antibiotics for acne.[8,9,11,27,28] Our present studies confirm our original hypothesis that antibiotic use in patients with acne is associated with an increase in the risk of self-reported pharyngitis. In our cross-sectional study, a student using oral antibiotics had an almost 3.5-fold (OR, 3.53; 95% CI, 1.14-10.95) increase in the odds of reporting an episode of pharyngitis compared with students not using antibiotics at the time of the survey. Students receiving topical antibiotics showed no such association. In our longitudinal study, we now prospectively demonstrated that there is an association between antibiotic use for acne and, the more conservative outcome definition, having an episode of pharyngitis requiring a health care provider visit (OR, 4.34; 95% CI, 1.51-12.47). An additional feature of the current study was the assessment for GAS and *S salivarius* colonization. However, contrary to our initial hypothesis and a preliminary report, our results did not demonstrate any association between colonization with either of these organisms and the risk of self-reported episodes of pharyngitis.[11]

In our study, pharyngeal colonization with GAS was uncommon. In the cross-sectional study, 3 of 266 participants (1.1%) were colonized by GAS. In the longitudinal study, in total, we noted only 8 cultures out of more than 1200 (0.6%) that revealed GAS from 6 separate participants. Over 98% of cultures revealed *S salivarius*, an organism that can potentially prevent the growth and colonization of GAS. Recovery of this organism was often heavy. The rates of colonization by these 2 organisms did not seem to be associated with antibiotic use.

The association between antibiotic use to treat acne and pharyngitis has been previously reported.[8-11,28] Margolis et al[8] showed by a retrospective cohort study using an electronic health record that a person receiving antibiotics for acne had a more than 2 times increased likelihood of developing an upper respiratory tract infection compared with a person with acne not receiving an oral antibiotic. Our current study showed an even higher strength of association, albeit our rate was within the previously reported 95% CI. The study by Levy et al[10] also showed an increased colonization of GAS in antibiotic users vs nonusers (33% vs 10%). Our current study did not support this result. Our reported rates of GAS pharyngeal colonization are similar to those in historic reports of asymptomatic people aged 15 to 45 years, ranging from 0.8% to 3.2%, whereas the result reported by Levy et al[10] was more of an outlier.[29-31]

A possible mechanism for this effect of antibiotic use could be based on a decrease in normal resident flora in the oropharynx owing to antibiotic exposure, thus causing the overgrowth of more virulent organisms. As an example, *S salivarius* is part of the resident flora of the mouth and throat, it can be sensitive to tetracyclines, and it has been shown to inhibit the overgrowth of GAS via an antibiotic-like substance, BLIS.[32] This mechanism may still be correct, but in our study we did not find alterations in colonization of *S salivarius* or GAS diminution. However, the timing of our swabbing with respect to the onset of pharyngitis may not have been sufficient to reflect colonization status present during the period of pharyngitis.

Like all cohort studies there are several limitations to this study. We were able to evaluate our study participants only at predetermined time points during their school year. Furthermore, the study team was not permitted to treat the students, and, owing to privacy concerns, the student health clinic would not confirm the participants' medical history. We therefore relied solely on the students' self-reports. We do not know for sure if they had pharyngitis, but it is a self-limited condition that usually does not require medical intervention. Finally, unmeasured or not fully measured risk factors could be associated with pharyngitis and antibiotic use for acne (ie, measured or unmeasured confounders). One example could be cigarette use, which we did measure but may not have measured well. Our measurement was based on a survey question querying use based on no use, use up to 1 pack per day, and use more than 1 pack per day. There was a disparity in use in our cross-sectional study between those who had acne and those who did not. This disparity was not noted in our cohort study. While cigarette smoking was associated with pharyngitis in our cross-sectional study (data not shown), it was not in our longitudinal study, and based on our modeling criteria was not part of either final adjusted model. Better measurement might have yielded more consistent results.

We did use 2 different diagnostic algorithms for pharyngitis, and we obtained similar results from similar populations using 2 different study designs. It is also possible, though unlikely, that patients were mistaking pharyngitis for the more severe esophagitis because tetracyclines have been associated with pill-induced esophagitis. It is important to acknowledge, however, that if this was true and pharyngitis is being mistaken for esophagitis, our study would be reporting a serious disease at an unusually high frequency. One other possible shortcoming of this study is due to the nature of it being a prevalence study. This type

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of study, which is based on an assessment at a single point in time, cannot be used to assess causation because the timing of the exposure (eg, oral antibiotics) with respect to the outcome (eg, pharyngitis) is not known.

Finally, with respect to our longitudinal study, we did not have 100% follow-up. It is possible that the loss of these participants influenced our results. It is, however, likely that these individuals were missing at random. The study participants did not know the hypotheses that we were testing. There were no statistical differences between those who participated only in the first survey and those who participated in more than 1 survey with respect to age, sex, presence of acne, the use of antibiotics to treat acne, a history of pharyngitis, and so on.

With respect to our microbial analysis, our goal was to evaluate oropharyngeal colonization. Based on our hypothesis we cultured participants only for GAS and *S salivarius*. Recently, we published a study evaluating the carriage rate of *Staphylococcus aureus*, which conversely seems to be decrease in those using oral antibiotics to treat their acne.[7] Several studies have now shown that there are hundreds of species of bacteria that are part of our normal flora of our skin as well as our oropharynx that are not routinely cultured, and any one of these bacteria could be sensitive to the antibiotics used to treat acne and could have caused the self-reported pharyngitis, not just GAS, which we evaluated.[33] It is also possible that the pharyngitis was caused by viruses. In any event, without further studies, it is impossible to ascertain any relationship between alteration in pharyngeal colonization and pharyngitis.

In conclusion, acne is a very prevalent condition that affects young adults and adolescents. About 2 million US individuals require treatment for acne every year, and 5 to 6 million physician visits occur every year for acne.[5,25,26] Upper respiratory tract infections are also very common and are a major cause of decreased productivity in the United States.[14,15] Pharyngitis is thought to cause over 200 million health care episodes every year, which causes our economy a loss of more than $25 billion in economic revenue per year.[34,35] Our studies show that that the odds of developing self-reported pharyngitis is more than 3 times baseline in patients receiving oral antibiotics for acne vs the odds for those who are not receiving oral antibiotics. The true clinical importance of these findings needs to be evaluated further by prospective studies. However, this observation has now been noted in 3 cross-sectional studies, 2 retrospective cohort studies, and now a prospective longitudinal cohort study.[7-10] While the cause of this phenomenon is not known and should be considered with respect to the risks vs the benefits of using long-term oral antibiotics in acne patients, it is not due to group A streptococcus.

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Author Contributions: All authors had full access to all of the data from the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Margolis, Metlay, Xie, DiRienzo, and Edelstein. *Acquisition of data:* Margolis, Papadopoulos, DiRienzo, and Edelstein. *Analysis and interpretation of data:* Margolis, Fanelli, Kupperman, Metlay, and Xie. *Drafting of the manuscript:* Margolis, Fanelli, Kupperman, and DiRienzo. *Critical revision of the manuscript for important intellectual content:* Margolis, Fanelli, Kupperman, Papadopoulos, Metlay, Xie, DiRienzo, and Edelstein. *Statistical analysis:* Margolis, Kupperman, and Xie. *Obtained funding:* Margolis. *Administrative, technical, and material support:* Margolis, Fanelli, Kupperman, Papadopoulos, DiRienzo, and Edelstein. *Study supervision:* Margolis and DiRienzo.
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Announcement

Dermatologic Photography Tips: Take Great Publishable Images

Tip: When sending a photograph in to a journal, send the original or cropped image file (with .JPG or .TIF extension). ***Do not*** send an image pasted into a Microsoft Word or Microsoft Powerpoint document.[1]

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1. Bhatia AC. The clinical image: archiving clinical processes and an entire specialty. *Arch Dermatol*. 2006;142(1):96-98.

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