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# **ORIGINAL ARTICLE**

# Prevalence and risk factors associated with geographic tongue among US adults

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**OBJECTIVE:** To characterize the prevalence of geographic tongue (GT) among US adults.

**DESIGN:** Population-based case-control study.

MAIN OUTCOME MEASURES: The presence or absence of GT.

SUBJECTS AND METHODS: Data from 16 833 adults examined during The Third National Health and Nutrition Examination Survey, 1988–1994 (NHANES III), a study based on multistage probability sampling were analyzed using SAS-callable SUDAAN 9.0.1.

**RESULTS:** Geographic tongue point prevalence was 1.8% (95% CI: 1.4, 2.3). Multivariate logistic regression showed significant effects of race-ethnicity, with Whites (AOR = 1.8; 1.3, 2.5) and Blacks (AOR = 1.6; 1.2, 2.1) having greater odds of GT than Mexican-Americans; current corticosteroid therapy (AOR = 3.7; 1.54, 8.6). Cigarette smokers had lower GT prevalence (AOR = 0.4; 0.3, 0.6). Fissured tongue (FT) was strongly associated with GT among non-smokers: AOR = 17.5 (7.8, 39.5). We did not find significant associations with age, gender, oral contraceptive use, diabetes mellitus, allergy or atopy, psychological or dermatological conditions as previous research has suggested.

CONCLUSIONS: Geographic tongue was more prevalent among Whites and Blacks compared with Mexican-Americans, positively associated with FT, and inversely associated with cigarette smoking.

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**Keywords:** Third National Health and Nutrition Examination Survey; oral epidemiology; geographic tongue; benign migratory glossitis; oral mucosal lesions

#### Introduction

Geographic tongue (GT) was first reported as a 'wandering rash of the tongue' in 1831; however, its etiopathogenesis still remains an enigma (Assimakopoulos et al. 2002). It is a common condition characteristically seen as an asymptomatic presentation of multiple, variably sized, well-demarcated, erythematous areas usually surrounded by a slightly elevated, vellowish-white, circinate linear border, usually occurring on the anterior two-thirds of the dorsal tongue; reminiscent of land masses and oceans on a map. However, the lesions heal and frequently develop quickly in other areas, prompting the name of benign migratory glossitis. The ventral surface and other oral mucosal surfaces may also be uncommonly affected and this has been referred to as geographic stomatitis, pityriasis of the tongue, ringworm of the tongue, psoriasis linguae, and erythema migrans (Hume, 1975). While GT is generally painless, a minority of individuals exhibit discomfort ranging from sensitivity to cigarette smoke, spicy foods, and fruit (Hume, 1975). For others, even painless GT lesions are a source of anxiety (Redman et al, 1965).

Reports of GT prevalence among adults range from 0.28% to 2.4% (Hume, 1975), with most falling between 1.0% and 2.5% (Assimakopoulos et al, 2002). Many risk factors have been proposed for GT: hormonal disturbances and oral contraceptive use (Waltimo, 1991); psychological findings (Redman et al, 1965); diabetes mellitus (Wysocki and Daley, 1987) although Guggenheimer et al (2000) found no difference; allergic conditions such as atopy (Marks and Simons, 1979) hay fever and rhinitis (Marks and Czarny, 1984); dermatological diseases such as pustular psoriasis (Wysocki and Daley, 1987); seborrheic dermatitis (Rahminoff and Muhsam, 1957), pityriasis pilaris (Wysocki and Daley, 1987); and Reiter's Syndrome (O'Keefe et al, 1973; Weathers et al, 1974; Pogrel and Cram, 1988). There is also a reported correlation with Down Syndrome (Ercis et al, 1996) and fissured tongue (FT) (Eidelman et al, 1976). A family history has also been reported to be associated

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with GT (Fenerli *et al*, 1993) which may be genetic and linked to major histocompatibility complexes.

In most previous studies gender differences were either not statistically significant or statistical testing was not performed. In a recent report, Jainkittivong and Langlais, 2005 found that of 188 adults with GT, 114 (61%) were female – a difference that is statistically significant (P < 0.001; *t*-test performed using data from Figure 4 in Jainkittivong and Langlais, 2005). The effect of race is unresolved. Hume (1975) points out that any association between GT and race is of questionable validity if potentially confounding or effect modifying factors (e.g. age and comorbidities) are not adjusted for. GT prevalence appears to decrease with age (Bánóczy *et al*, 1993; Jainkittivong and Langlais, 2005).

Many reports of GT among adults are of uncertain validity. First, with notable exceptions (Axéll, 1976; Bánóczy *et al*, 1993; Reichart, 2000), most were based on convenience samples such as students (Meskin *et al*, 1963), dental outpatients (Darwazeh and Pillai, 1993; Avcu and Kanli, 2003), or specialty clinic referrals (Marks and Czarny, 1984). Secondly, the samples studied had different distributions of gender, raceethnicity, age, and other potential covariates. Finally, while most studies were cross-sectional, reporting point prevalence, others were longitudinal, reporting incidence. This can be problematic as GT is ephemeral and repeated observations on the same individuals may magnify the number seen to have GT (Hume, 1975).

Recently, results from the oral mucosal tissue examination of the Third National Health and Nutrition Examination Survey (NHANES III) were reported (Shulman *et al*, 2004). While the prevalence of GT in individuals 17 years of age and older was given as 1.85% (95% CI: 1.41, 2.29), no further information was provided. This paper presents prevalence data and investigates risk factors associated with GT using NHANES III data.

### Subjects and methods

#### Data

We used available data from the Adult Interview, Laboratory, and Examination files of NHANES III. NHANES III is a periodic survey conducted by the National Center for Health Statistics (NCHS) conducted from 1988 through 1994 based on a complex, multistage sample plan (NCHS, 1996). The Examination file contains the results of general and oral examinations, the Adult Interview file contains socio-demographic data, a thorough health interview to include tobacco and medication use classified as one of 160 drug class codes supplied by United States Food and Drug Administration; and the Laboratory file contains the results of analyses performed from blood and urine collected at the time of examination.

Oral mucosal examination procedures were based on the World Health Organization's Guide to Epidemiology and Diagnosis of Oral Mucosal Diseases and Conditions (Kramer *et al*, 1980). A lesion was classified as GT when: (1) there was localized absence of filiform papillae; (2) the affected area was irregularly shaped; and (3) the area changed location over time. A lesion was classified as FT if (1) there were shallow or deep fissures on the dorsum of the tongue – generally a central fissure from which smaller fissures radiate. As GT and FT have a low prevalence, standardization of the examiners consisted of a presentation of the written criteria along with color photographs to illustrate the characteristic features of GT and FT rather than examining patients with GT and FT as part of a calibration process. Examinations were performed using a standard examination and data recording procedure (Westat Inc, 1994).

#### Covariates

In addition to data from the oral mucosal examination, we used socio-demographic variables: gender, raceethnicity (non-Hispanic White, non-Hispanic Black, Mexican-American), age, and risk factor variables: tobacco and alcohol use, and current antibiotic and steroid use. For analyses using race-ethnicity, we excluded 678 (4.03%) subjects whose race-ethnicity was classified as 'other'.

Income was measured by the poverty income ratio (PIR) that relates family income to the poverty level based on the subject's family size. It is computed by dividing the midpoint of the reported family income category by the Census Bureau's poverty threshold for the calendar year the family was interviewed and the age of the family reference person (NCHS, 1996). Poorer families have low PIR levels. We categorized PIR as low (<1.3), middle (1.3–3.5), and high (>3.5).

Pregnant subjects were identified by response to the question 'Are you now pregnant?' In addition, a urine pregnancy test was conducted on women 20–49 years of age in the mobile examination center. Pregnant subjects were those who responded that they were pregnant and those with positive urine pregnancy tests. Oral contraceptive use was established at interview.

Individuals were classified as having an asthma and hay fever history if they answered 'yes' to the question, 'Has a doctor ever told you that you have asthma (hay fever)?' and they were classified as having asthma (hay fever), if they answered 'ves' to the question 'Do you still have asthma (hay fever)?' Current diabetics were identified as answering 'yes' to the question 'Has a doctor ever told you that you have diabetes other than during pregnancy?' Glycemic control was measured by blood levels of glycosylated hemoglobin A1c. Subjects were asked to show all prescription drugs they were taking. Allergy skin reactivity testing for white oak, cat, mite, alternaria, rye grass, peanut, Russian thistle, German cockroach, Bermuda grass, and ragweed was performed on all examinees 6-19 years of age and on a random half-sample of examinees aged 20-59 years by a trained examiner in the mobile examination center. A test was considered positive if the adjusted mean wheal size on the test site was 3 mm or greater than the control.

Hands and fingers of subjects 5–59 years of age were examined for the presence of redness, inflammation, and vesicles (excluding dry skin and hyperkeratosis) and wrists, elbows and knees were examined for lichenified dermatitis (Westat Inc, 1991). We classified subjects with a finding on any site as having dermatitis. The diagnostic interview schedule (DIS) (Robins *et al*, 1981), a structured psychiatric interview, was administered to individuals 17–39 years of age. The DIS allows diagnoses to be made based on the decision rules in the Diagnostic and Statistical Manual of Mental Disorders, Third Edition (DSM-III) (Onyike *et al*, 2003). Individuals were classified as having a history of major depression if they reported recurrent episodes of depression without bereavement and with no symptoms of mania.

#### Data analysis

As the NHANES III employed a stratified multistage probability design, we used SAS-callable SUDAAN 9.0.1 (Research Triangle Institute, Research Triangle Park, NC, USA) to adjust for the complex sampling used in the study. We screened the covariates using Pearson chi-squared tests for categorical and t-tests for continuous covariates and performed binary logistic regression to explore the relationship between GT and covariates with P < 0.15 on either test as the cutoff for further analysis. Next, we fitted a multivariate logistic regression model using forward selection. Starting with retained covariates with the strongest statistically significant association in the bivariate regressions, we added covariates one at a time, removing those that did not meet our P < 0.05 (Wald F-test) retention criterion. Next, we added first-order interactions and retained those that met our retention criterion. Where relevant, the same process was used for second order interactions. The odds ratio (AOR) for each variable in the multivariate model is adjusted for the effect of the other variables. We used the Hosmer-Lemeshow statistic (Hosmer and Lemeshow, 2000) to test the goodness of fit of the final model.

#### Results

Of the 16 833 adults (18 years of age and older examined) 279 (1.8%) had GT. Table 1 shows that GT has significant bivariate associations with FT, race-ethnicity and cigarette smoking. GT was more Whites prevalent among non-Hispanic (2.0%); OR = 1.7)and non-Hispanic Blacks (1.8%;OR = 1.6) than Mexican-Americans (1.2%). Cigarette (1.2%; OR = 0.4) and cigar smokers (0.7%) had lower GT prevalence than tobacco non-users (2.6%). Individuals taking steroids had higher prevalence and more than three times the odds (5.7%; OR = 3.3) of GT than those not taking steroids (1.8%). Individuals with FT had higher prevalence (15.2%; OR = 10.4) than those without FT (1.7%). The associations between GT and gender, age, PIR, smokeless tobacco use, current asthma and hay fever, positive allergy tests, dermatitis, diabetes mellitus, antifungal medication, estrogen therapy, oral contraceptive use, pregnancy, and major depression were not significant. The number of alcohol-containing drinks per year was not associated with GT (not shown in table).

The final model (Table 2) contained race-ethnicity, FT, cigarette smoking, current steroid use, and an interaction between FT and cigarette smoking. The Hosmer–Lemeshow statistic ( $\chi^2$ : 10.65; 7 d.f.; P = 0.15) indicated that the model is a poor fit to the data. GT was associated with steroid use (AOR = 3.7). Whites (AOR = 1.8) and Blacks (AOR = 1.6) had greater odds of GT than Mexican-Americans. Non-smokers with FT had more than 17 times greater odds of GT than non-smokers without FT (AOR = 17.4) while smokers with no FT had less than half the odds of GT (AOR = 0.4) than non-smokers without FT.

#### Discussion

Whites and Mexican-Americans had higher GT prevalence than Blacks. GT was positively associated with FT and systemic steroid use, and negatively associated with cigarette smoking and taking oral contraceptives. Our finding that systemic steroid use was associated with increased GT prevalence is counterintuitive – perhaps the doses (not reported) were too low or the condition for which the steroids were prescribed was a stronger risk factor that outweighed the presumed mitigating effect of the steroids. As it is possible that some asthmatics and individuals with allergies and hay fever were using steroids, we reanalyzed the data removing the 189 individuals taking steroids. The relationship did not change.

While some studies have reported an association with oral contraceptive use (Waltimo, 1991), psoriasis, asthma, hay fever, and allergy (Barton *et al*, 1982; Daneshpazhooh *et al*, 2004), our data do not support this. We found that Whites and Blacks had greater prevalence of GT than Mexican-Americans. There is no known physiologic basis to believe that race-ethnicity is a risk factor although there may be a hereditary component.

Reports have associated GT with stress (Redman *et al*, 1965). While NHANES III did not have physiologic measures of stress such as serum cortisol levels, or questions directly addressing stress, the DIS provided an opportunity to explore association between GT and depression, arguably a stressful condition. To the extent persistent depression is a valid proxy for stress; our results do not support previous findings. Moreover, the null association between depression and GT may have been biased by those who had their depression treated by medication, thus relieving their feelings of 'stress'. However, we recognize that the DIS yielded a weak proxy for stress and our results here should be interpreted cautiously.

Our findings that GT was associated with FT are consistent with previous studies (Bánóczy *et al*, 1975; Eidelman *et al*, 1976; Yarom *et al*, 2004; Jainkittivong and Langlais, 2005). However we found no difference in GT prevalence among the three age groups as did Jainkittivong and Langlais (2005) and Bánóczy *et al* (1993). We found no significant difference in GT prevalence between males and females, which conflicts with the report of Bánóczy *et al* (1993), Yarom *et al*  Geographic tongue in the US JD Shulman and WM Carpenter

	п	Lesions	Prevalence %	95% CI	OR	95% CI
Race/ethnicity <sup>a</sup>	16 155	273	1.9	1.5, 2.4		
Non-Hispanic White	6796	145	2.0	1.4, 2.5	1.7	1.2, 2.4
Mexican-American	4603	48	1.2	0.9, 1.4	1.6	1.2, 2.0
Non-Hispanic Black	4756	80	1.8	1.4, 2.2	1.0	
Gender	16 833	279	1.8	1.4, 2.3		
Male	7895	117	1.6	1.2, 2.1	0.8	0.6, 1.1
Female	8938	162	2.00	1.4, 2.5	1.0	
Age	16 833	279	1.8	1.4, 2.3		0717
18–39 years	7724	135	2.0	1.3, 2.6	1.1	0.7, 1.7
40–59 years 60+	4212	63 81	1.6	1.0, 2.3	0.9	0.6, 1.6
Poverty income ratio	4897 9060	154	1.8 1.6	1.3, 2.2 1.2, 2.1	1.0	
Low	4267	75	1.0	1.2, 2.1 1.1, 2.7	1.3	0.7, 2.6
Middle	2809	51	1.5	0.8, 2.3	1.5	0.7, 2.0
High	1984	28	1.5	0.8, 2.3	1.0	0.3, 2.1
Cigarette smoking <sup>b</sup>	14 808	252	1.9	1.4, 2.4	1.0	
Yes	6768	72	1.2	0.8, 1.5	0.4	0.3, 0.6
No	8040	180	2.6	1.8, 3.3	1.0	0.5, 0.0
Smokeless tobacco use	11 357	231	2.3	1.7, 2.9	1.0	
Yes	283	5	1.9	-0.1, 3.8	0.7	0.3, 1.7
No	11 074	226	2.3	1.7, 2.9	1.0	0.5, 1.7
Current asthma	16 801	277	1.8	1.4, 2.3	1.0	
Yes	794	19	2.5	1.0, 4.0	1.4	0.7, 2.6
No	16 007	258	1.8	1.4, 2.2	1.4	0.7, 2.0
Current hay fever	16 808	279	1.8	1.4, 2.2	1.0	
Yes	1306	26	1.8	0.8, 2.7	1.0	0.6, 1.7
No	15 502	253	1.8	1.4, 2.3	1.0	0.0, 1.7
Positive allergy test(s)	2455	45	2.3	1.1, 3.4	1.0	
Yes	1287	19	1.9	0.6, 3.2	0.69	0.3, 1.7
No	1168	26	2.6	1.0, 4.2	1.0	0.0, 1.7
Dermatitis on hands/palms	11 237	189	1.9	1.3, 2.4		
Yes	292	8	2.9	-0.3, 6.1	1.6	0.5, 5.3
No	10 945	181	1.8	1.3, 2.4	1.0	,
Diabetes	16 814	279	1.8	1.4, 2.3		
Yes	1332	20	1.7	0.6, 2.9	0.9	0.5, 1.7
No	15 482	259	1.8	1.4, 2.3	1.0	,
Currently taking	16 833	279	1.8	1.4, 2.3		
steroids (systemic)				<i>,</i>		
Yes	189	12	5.7	1.0, 10.3	3.3	1.3, 8.2
No	16 644	267	1.8	1.4, 2.2	1.0	, i i i i i i i i i i i i i i i i i i i
Currently taking	16 833	279	1.8	1.4, 2.3		
steroids (inhalant)						
Yes	139	6	3.9	0.0, 7.8	2.2	0.7, 6.6
No	16 694	273	1.8	1.4, 2.3	1.0	
Currently taking	16 833	279	1.8	1.4, 2.3		
antifungal medications						
Yes	59	2	4.4	-3.0, 11.9	2.5	0.4, 14.8
No	16 774	277	1.8	1.4, 2.2	1.0	
Current estrogen	8938	162	2.00	1.4, 2.5		
replacement therapy						
Yes	499	13	2.6	1.1, 4.1	1.4	0.7, 2.6
No	8439	149	1.9	1.4, 2.5	1.0	
Current oral contraceptive use <sup>c</sup>	8938	162	2.0	1.4, 2.5		
Yes	792	16	0.0	0.0, 0.0	4	
No	8146	146	2.0	1.4, 2.5	1.0	
Currently pregnant	8938	162	2.0	1.4, 2.5		
Yes	316	8	2.3	-0.6, 5.2	1.2	0.3, 4.2
No	8622	154	2.0	1.5, 2.5	1.0	
Recurrent major depression	7144	121	1.9	1.3, 2.6		
Yes	347	7	1.7	0.2, 3.2	0.9	0.3, 2.3
No	6797	114	1.9	1.3, 2.6	1.0	
Fissured tongue <sup>b</sup>	16 833	279	1.8	1.4, 2.3		
Yes	194	28	15.2	4.9, 25.6	10.4	4.6, 23.7
No	16 639	251	1.7	1.3, 2.1	1.0	
HbA1c > $9\%$	16 163	268	1.9	1.4, 2.3		
Yes	430	6	1.3	-0.1, 2.7	1.0	0.3, 3.4
No	15 733	262	1.9	1.4, 2.3	1.0	

**Table 1** Geographic tongue and selected covariates: sample size, number of lesions, point prevalence, 95% confidence intervals bivariate odds ratio, and 95% confidence intervals tervals

HbA1c, hemoglobin A1c. <sup>a</sup>Chi-squared test; P < 0.01. <sup>b</sup>Chi-squared test; P < 0.001. <sup>c</sup>Chi-squared statistic and odds ratio cannot be computed because of zero cell.

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Table 2 Multivariate logistic regressions, adjusted odds ratio	s, 95%
confidence intervals for variables associated with geographic to	ongue

	AOR	95% CI	P-value
Race/ethnicity			
Non-Hispanic White	1.8	1.3, 2.5	0.0003
Non-Hispanic Black	1.6	1.2, 2.1	
Mexican-American	1.0		
Fissured tongue (FT)			
Yes	17.5	7.8, 39.5	< 0.0001
No	1.0	, í	
Current cigarette smoker			
Yes	0.4	0.3, 0.6	< 0.0001
No	1.0		
Currently taking			
steroids (systemic)			
Yes	3.7	1.5, 8.6	0.0004
No	1.0	,	
Cigarette/FT interaction			
Non-smoker, FT	17.5	7.8, 39.5	< 0.0001
Smoker, no FT	0.4	0.3, 0.6	
Smoker, FT	1.8	0.8, 4.2	
Non-smoker, no FT	1.0		

(2004), and Jainkittivong and Langlais (2005). It has been reported that diabetics had higher GT prevalence than non-diabetics (Dawson, 1974); however, neither physician-diagnosed diabetes nor poor glycemic control were significant in our study. Our results are consistent with those of Guggenheimer *et al* (2000).

Cigarette smoking was associated with reduced GT prevalence. A recent study (Rivera-Hidalgo et al, 2004) reported that non-smokers (AOR = 14.96) and smokers of one to nine cigarettes per day (AOR = 9.56) had substantially greater prevalence of recurrent aphthous stomatitis than smokers of 20 or more cigarettes per day. Moreover, nicotine can activate the nicotinic acetylcholine receptors on macrophages reducing the production of tumor necrosis factor  $\alpha$  and interleukins 1 and 6, as well as acting through the central nervous system by activation of the hypothalamus-pituitaryadrenal axis to induce the production of glucocorticoids and activation of the autonomic nervous system to reduce the level of inflammation. However, as steroid therapy was associated with higher GT prevalence, the hypothesized glucocorticoid-releasing effect is unlikely to be relevant to GT etiopathogenesis.

Despite the sophisticated sampling methodology and the use of trained dentist-examiners, the NHANES III dataset has limitations. First, although examiners used a standard definition of GT and FT and were shown slides with their clinical manifestations, there was no calibration as there was for the decayed, missing, and filled surface examination (Westat Inc, 1994). Consequently we cannot say with certainty that the examiners did not consistently understate (fail to identify GT when it was present) or overstate (conflate GT with a normal tongue of another condition). However, we feel that a trained dentist made familiar with the diagnostic criteria should be reasonably consistent in identifying GT and FT. Secondly. NHANES III is cross-sectional and cannot be used to infer causality, merely association. Finally, as GT was present in <2% of the

population, small cell sizes created in the multivariate analysis reduced the statistical power (especially with low prevalence covariates) producing large standard errors and statistical instability as reflected in the Hosmer-Lemeshow statistic. To illustrate this, two of 59 subjects taking antimycotic medication had GT; however, the odds ratio (OR = 2.5) was not significantly different from the null (Table 2). The statistical instability due to the small sizes reduced the power of our model substantially so the possibility that we committed a Type II error cannot be ruled out. Similarly the lack of significance of any type of dermatitis as a risk factor, as suggested in previous reports (Wysocki and Daley, 1987) may be due to a lack of statistical power or failure to establish a definitive diagnosis of pustular psoriasis based on examination of the hands, elbows and knees.

We have presented a population-based multivariate analysis of risk factors associated with GT. While we did not find associations that have been reported in previous studies, it is worth noting that the vast majority of those studies were either based on convenience samples or used only bivariate analysis. Even in this study, a variable that was significant in the bivariate analysis (glycosalated hemoglobin), was not significant in the multivariate model. The results of bivariate analyses should be taken with caution as bivariate associations may not carry over to the multivariate model either because of lack of statistical power, in which case the association is unresolved, or confounding, in which case the association is spurious (Shulman, 2004). However, a multivariate analysis provides a better understanding of the complex factors associated with GT.

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