# Smoking and Use of Hair Treatments in Relation to Risk of Developing Systemic Lupus Erythematosus

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*ABSTRACT.* ***Objective.*** To examine the association between smoking and hair treatments (dyes, permanents) and risk of developing systemic lupus erythematosus (SLE).

***Methods.*** Patients (n = 265) diagnosed between January 1, 1995, and July 31, 1999, were recruited through 4 university based and 30 community based rheumatology practices in eastern North Carolina and South Carolina. Controls (n = 355) were identified through driver's license records and were frequency matched to patients by age, sex, and state. Data collection included a 60 min in-person interview. Analyses were limited to experiences that occurred before age at diagnosis (patients) or reference age (controls). Because the prevalence of use of hair treatments among men was very low, the analyses of those exposures were limited to women.

***Results.*** There was no association with smoking history and risk of developing SLE when analyzed as status (current, former, or never-smoker) or measures of dose (duration or pack-years). Use of permanent hair dyes in women was associated with a small increased risk of developing SLE (OR 1.5, 95% CI 1.0, 2.2). This association increased with longer duration of use (compared with non-users, OR 1.7, 95% CI 1.0, 2.7 for 6 or more years). There was little evidence of an association between SLE and use of temporary dyes or of permanents and straighteners.

***Conclusion.*** These results suggest at most a weak association between SLE risk and permanent hair dyes or smoking. Genetic variability in the metabolism of these products may be important to assess in future studies. (J Rheumatol 2001;28:2653–6)

*Key Indexing Terms:*
SYSTEMIC LUPUS ERYTHEMATOSUS
AUTOIMMUNE DISEASE
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Studies in humans and in murine models suggest that multiple genetic polymorphisms affect an individual's susceptibility to the development or progression of systemic lupus erythematosus (SLE)[1,2]. Environmental exposures may also be involved in the etiology of this disease, and tobacco smoke and some hair treatment products (i.e., hair dyes and permanents) have been postulated to be risk factors for the development of SLE[3-5]. Several recent studies reported an association between the risk of developing SLE and smoking, with odds ratios (OR) around 2.0[6-8], although no association was seen in the Nurses Health Study[9]. A strong association (OR 7.2) between use of hair dyes and connective tissue disease (SLE, scleroderma, polymyositis, or undifferentiated connective tissue disease) was reported in a study by Freni-Titulaer, *et al*[5], but this association was not observed in subsequent studies[4,9-11]. We analyzed smoking and hair treatments as risk factors for the development of SLE in a large, population based case control study in the southeastern United States.

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## MATERIALS AND METHODS

The Carolina Lupus Study is based in 60 contiguous counties in eastern and central North Carolina and South Carolina. Cases were primarily identified through 30 community based rheumatologists and 4 university based rheumatology practices in the study area. Eligibility was based on fulfillment of the 1997 revised American College of Rheumatology classification criteria for SLE[12,13], diagnosis between January 1, 1995, and July 31, 1999, and age 18 years or older at study enrollment. We received 285 referrals of patients who were eligible for the study based on diagnostic criteria, and 265 of these patients participated in the study. The median time from diagnosis to study interview was 13 months and 75% of patients were interviewed within 1.7 years of diagnosis.

Population based controls were identified through driver's license records and were frequency matched to cases by age (5 year age groups),

sex, and state. Eligibility criteria were the same as the nonmedical criteria used for cases, with the additional criterion of never having been diagnosed with any kind of lupus. We included 355 controls (75% of those who were screened and eligible) in the study. Controls were randomly assigned a reference month and year to correspond to the frequency distribution of the diagnosis month and year of cases.

Data collection included a structured 60 min in-person interview that included information on smoking and use of hair treatments. A positive smoking history was defined as at least one cigarette a day for 3 or more months. Current, former, and never-smoking status was recorded as of diagnosis age (cases) or reference age (controls). We also obtained information on age started smoking, average amount smoked (cigarettes per day), and for former smokers, age stopped smoking. "Pack-years" was calculated as the product of the number of cigarettes per day and the number of years smoked. Information about hair treatments was divided into 3 categories: permanents to curl or straighten hair, permanent hair dyes in which liquids are mixed together, and temporary dyes (hair rinse, color or frosting that washes out after a few shampoos). A positive history was defined as lifetime use of 5 or more times. We asked about age first used, age last used, and total number of years used. This information was used to eliminate the period of use at or after diagnosis age (cases) or reference age (controls). For dyes, we asked what color(s) were used most often. Black and dark browns were classified as "dark colors" with the remaining classified as "other colors."

Logistic regression was used to examine the association between smoking and risk of developing SLE. The associations were estimated as the OR and 95% confidence interval (CI), and were adjusted for age, state, race (2 groups: whites, and African-Americans and other minorities), and education (did not complete high school, high school degree, some college or technical school, and college graduate). We also ran separate models for men and women. Associations with smoking were similar, and the results from the combined sample are presented. A similar strategy was used for the analysis of hair treatments. However, the use of these products was very low among men (e.g., < 5% use of permanent or temporary dyes among males vs > 25% use among females). This low prevalence, combined with the small number of men in the study (10% of cases and controls), resulted in highly imprecise effect estimates in men. We limited the analyses of hair treatments to the 240 female cases and 321 female controls in the study.

Since controls were selected from the state driver's license registries, we also repeated the analyses excluding 27 (10%) cases who reported they did not have a state issued driver's license. This exclusion had little effect on any of the measures examined. We present the results from the full sample.

## RESULTS

Ninety percent of the SLE cases in the Carolina Lupus Study are female and 60% are African-American. The mean age at diagnosis was 39 years. Because of the age- and sex-matching procedure we used, these characteristics are similar in the controls. We did not match by race, so our sample of controls is representative of the population in the study area: 28% African-American, 65% white, and 7% other ethnicities.

There was no association with smoking history and risk of developing SLE when analyzed as status (current, former, or never-smoker) or measures of dose (duration or pack-years) (Table 1). The prevalence of smoking and amount smoked was higher among whites compared with African-Americans, but no association with disease risk was seen in separate analyses within each of these groups.

Among women, use of permanent hair dyes was associated with a small increased risk of developing SLE (OR 1.5, 95% CI 1.0, 2.2) (Table 2). This association was somewhat higher with longer duration of use (OR 1.7, 95% CI 1.0, 2.7 for 6 or more years' use). Similar patterns were seen in African-Americans and whites, with a somewhat stronger association with duration of use seen among African-Americans. There was little evidence of an association between SLE and use of temporary dyes or of permanents and straighteners. Including permanent dyes and temporary dyes in the same model did not appreciably change either estimated association, nor were the associations with smoking status or permanent dyes altered when both these variables were included (data not shown).

## DISCUSSION

The Carolina Lupus Study is a large, population based case control study of recently diagnosed SLE that we used to assess environmental risk factors for lupus. We observed no association between risk of developing SLE and smoking history (OR 1.1 for current smoking, OR 0.6 for former smoking). Our results are similar to those reported in the Nurses' Health Study cohort (relative risk 1.1, 95% CI 0.7, 1.8 for current smoking, relative risk 0.9, 95% CI 0.5, 1.6 for former smoking)[9]. In contrast, 2 previous population based case control studies from Japan and the United Kingdom reported statistically significant increased risks of SLE among current smokers, with OR of 2.3 (95% CI 1.3, 4.0)[6] and 2.0 (95% CI 1.1, 3.3)[7]. A smaller study (56 patients) by Benoni, *et al*[8] reported an association that was not statistically significant (OR 1.8, 95% CI 0.8, 4.0), and one other case control study reported no association (OR 0.9, 95% CI 0.6, 1.5)[4]. Thus the data on smoking and risk of SLE are inconsistent but suggestive of, at most, a weak association.

We observed a small increased risk (OR 1.5) with use of permanent hair dyes that was somewhat stronger with higher duration of use and when limited to dark-colored dyes. The chemical content of dyes varies by many factors including color, manufacturer, and production year[14]. A more detailed analysis of the specific products or chemicals used by participants was not possible given limitations in recall accuracy inherent in a retrospective study. A strong association (OR 7.2, 95% CI 1.9, 26.9) between use of hair dyes and connective tissue disease was reported in a study by Freni-Titulaer, *et al*[5]. However, no associations were seen in subsequent studies that used friends or relatives as controls[4,10] or in a recent population based case control study[11] (OR 1.2, 95% CI 0.8, 2.0 for use of permanent dyes, and OR 1.3, 95% CI 0.8, 2.1 for temporary dyes). No association was seen between hair dyes and SLE in the Nurses' Health Study cohort[9]. The results of our study, in conjunction with these previous studies, are more consistent with a weak association between SLE risk and permanent hair dyes than with the strong association initially reported by Freni-Titulaer, *et al*[5].

*Table 1.* Smoking and risk of developing SLE, by race.

| | Total Sample* | | | African-Americans* | | | Whites* | | |
|---|---|---|---|---|---|---|---|---|---|
| | Cases n (%) | Controls n (%) | Adjusted OR (95% CI)† | Cases n (%) | Controls n (%) | Adjusted OR (95% CI)† | Cases n (%) | Controls n (%) | Adjusted OR (95% CI)† |
| Status | | | | | | | | | |
| Never | 163 (62) | 184 (52) | 1.0 (referent) | 111 (69) | 65 (66) | 1.0 (referent) | 43 (48) | 102 (44) | 1.0 (referent) |
| Former | 38 (14) | 89 (25) | 0.6 (0.4, 1.0) | 17 (11) | 20 (20) | 0.5 (0.2, 1.0) | 20 (22) | 64 (28) | 0.7 (0.4,1.3) |
| Current | 64 (24) | 82 (23) | 1.1 (0.7, 1.7) | 32 (20) | 14 (14) | 1.3 (0.6, 2.8) | 26 (29) | 64 (28) | 1.0 (0.5, 1.8) |
| Duration, yrs | | | | | | | | | |
| 1–5 | 13 (5) | 41 (12) | 0.5 (0.2, 1.0) | 6 (4) | 4 (4) | 0.8 (0.2, 3.2) | 7 (8) | 34 (15) | 0.4 (0.2,1.1) |
| 6 –14 | 29 (11) | 49 (14) | 0.8 (0.5, 1.4) | 15 (9) | 13 (13) | 0.8 (0.3, 1.8) | 11 (12) | 33 (14) | 0.7 (0.3, 1.6) |
| 15–24 | 19 (7) | 38 (11) | 0.7 (0.4, 1.4) | 7 (4) | 8 (8) | 0.5 (0.2, 1.5) | 9 (10) | 28 (12) | 0.8 (0.3, 1.8) |
| ≥ 25 | 41 (15) | 43 (12) | 1.5 (0.8, 2.6) | 21 (13) | 9 (9) | 1.2 (0.5, 3.1) | 19 (21) | 33 (14) | 1.5 (0.7, 3.3) |
| Pack–years | | | | | | | | | |
| <10 | 40 (15) | 83 (23) | 0.7 (0.4, 1.1) | 23 (14) | 18 (18) | 0.8 (0.4, 1.6) | 14 (16) | 60 (26) | 0.6 (0.3,1.1) |
| 10–19.9 | 30 (11) | 35 (10) | 1.1 (0.6, 2.0) | 14 (9) | 11 (11) | 0.7 (0.3, 1.7) | 13 (15) | 22 (10) | 1.5 (0.7, 3.3) |
| ≥ 20 | 32 (12) | 53 (15) | 1.0 (0.6,1.8) | 12 (8) | 5 (5) | 1.3 (0.4, 4.2) | 19 (21) | 46 (20) | 0.9 (0.5, 1.8) |

* Total sample: 265 cases, 355 controls. African-Americans: 160 cases, 99 controls. Whites: 89 cases, 230 controls. † Logistic regression adjusted for age (continuous), sex, state, and education (did not complete high school, high school degree, some college or technical school, and college graduate). Analysis of total sample also adjusts for race (2 groups: whites, African-Americans and other minorities).

*Table 2.* Use of hair treatments and risk of developing SLE among women, by race.

| | All Women* | | | African -American Women* | | | White Women* | | |
|---|---|---|---|---|---|---|---|---|---|
| | Cases n (%) | Controls n (%) | Adjusted OR (95% CI)† | Cases n (%) | Controls n (%) | Adjusted OR (95% CI)† | Cases n (%) | Controls n (%) | Adjusted OR (95 % CI)† |
| Permanent dyes | | | | | | | | | |
| No use | 155 (65) | 214 (67) | 1.0 (referent) | 106 (71) | 71(80) | 1.0 (referent) | 40 (53) | 126 (61) | 1.0 (referent) |
| Any use | 85 (35) | 107 (33) | 1.5 (1.0, 2.2) | 44 (29) | 18 (20) | 1.7 (0.9, 3.2) | 35 (47) | 80 (39) | 1.4 (0.8, 2.5) |
| Years of use | | | | | | | | | |
| 1-5 | 33 (14) | 40 (12) | 1.2 (0.7, 2.1) | 22 (15) | 11 (12) | 1.4 (0.6, 3.2) | 8 (11) | 25 (12) | 1.0 (0.4, 2.5) |
| ≤ 6 | 52 (22) | 67 (21) | 1.7 (1.0, 2.7) | 22 (15) | 7 (8) | 2.1 (0.8, 5.3) | 27 (36) | 55 (27) | 1.7 (0.9,3.0) |
| Coloring | | | | | | | | | |
| Dark | 25 (10) | 15 (5) | 1.8 (0.9, 3. 8) | 19 (13) | 6 (7) | 1.9 (0.7, 5.2) | 4 (5) | 6 (3) | 2.3 (0.6, 9.0) |
| Other | 60 (25) | 92 (29) | 1.4 (0.9, 2.1) | 25 (17) | 12 (13) | 1.5 (0.7. 3.3) | 31 (41) | 74 (36) | 1.4 (0.8, 2.4) |
| Temporary dyes | | | | | | | | | |
| No use | 195 (81) | 245 (76) | 1.0 (referent) | 122 (81) | 74 (83) | 1.0 (referent) | 60 (80) | 152 (74) | 1.0 (referent) |
| Any use | 45 (19) | 76 (24) | 0.9 (0.5, 1.3) | 28 (19) | 15 (17) | 1.3 (0.7, 2.8) | 15 (20) | 54 (26) | 0.7 (0.3, 1.3) |
| Years of use | | | | | | | | | |
| 1–5 | 25 (10) | 47 (15) | 0.7 (0.4, 1.2) | 19 (13) | 11 (12) | 1.3 (0.6, 2.9) | 6 (8) | 31 (15) | 0.4 (0.2, 1.2) |
| ≥ 6 | 20 (8) | 29 (9) | 1.1 (0.6, 2.2) | 9 (6) | 4 (5) | 1.5 (0.4, 5.4) | 9 (12) | 23 (11) | 1.0 (0.4, 2.4) |
| Permanents and straighteners | | | | | | | | | |
| No use | 51 (21) | 86 (27) | 1.0 (referent) | 17 (11) | 8 (9) | 1.0 (referent) | 26 (35) | 66 (32) | 1.0 (referent) |
| Any use | 189 (79) | 235 (73) | 1.0 (0.6, 1.5) | 133 (89) | 81 (91) | 0.8 (0.3, 2.1) | 49 (65) | 140 (68) | 0.8 (0.5, 1.5) |
| Years of use | | | | | | | | | |
| 1 – 10 | 70 (29) | 116 (36) | 0.8 (0.5, 1.3) | 43 (29) | 33 (37) | 0.6 (0.2, 1.6) | 24 (32) | 74 (36) | 0.8 (0.4, 1.5) |
| ≥ 11 | 119 (50) | 119 (37) | 1.2 (0.7, 2.0) | 90 (60) | 48 (54) | 1.0 (0.4. 2.4) | 25 (33) | 66 (32) | 0.9 (0.5, 1.8) |

* Total sample: 240 cases, 321 controls. African-Americans: 150 cases, 89 controls. Whites: 75 cases, 206 controls.
†Logistic regression adjusted for age (continuous), state and education (did not complete high school, high school degree, some college or technical school, and college graduate). Analysis of total sample also adjusts for race (2 groups: whites, African-Americans and other minorities).

The onset of SLE can be difficult to pinpoint, and symptoms may occur over a period of years before the diagnosis is made. In our study, most cases (60%) reported it had been less than one year between the occurrence of the first symptom and diagnosis, 13% reported it had been 1–2 years, 6% reported 3–4 years, and 20% reported 5 or more years. However, we did not obtain additional information that would have allowed us to differentiate between a slow

onset disease (one that developed over the course of many years) and a fully expressed but undiagnosed disease. A misclassification bias would have occurred if some of the exposures (i.e., smoking, hair treatments) had actually occurred after the disease was fully developed but before it was diagnosed. Exposures that occurred after the first symptom, but before full expression of the disease, would not necessarily introduce a bias to the study if the effect of these exposures is to accelerate or "promote" the onset of the disease. To examine the potential influence of the longer onset cases on our results, we repeated the hair dye analysis excluding cases who reported 5 or more years between their initial symptom and diagnosis and whose first use of these products occurred after the reported age at first symptom. The estimated association with permanent hair dyes was somewhat reduced (OR 1.3, 95% CI 0.9, 2.4). This suggests that the effect of this exposure is stronger among those with a longer onset of disease, which would be more consistent with the effect of a "promotor" than that of an "initiator" of disease. Given the limited data we had on timing of exposure and disease expression, however, this idea should be viewed as speculation that would require additional research for confirmation.

The Carolina Lupus Study is a large, population based case control study. It was limited to patients with recently diagnosed SLE and includes relatively detailed information about specific environmental exposures that have been postulated to affect disease risk. Our results are consistent with only weak associations between SLE risk and permanent hair dyes or smoking. Genetic variability in the metabolism of these products (e.g., polymorphisms in N-acetyl transferase, glutathione-S-transferase, and the cytochrome P-450 oxidative enzyme system) may be important to assess in future studies, to clarify whether a small overall association reflects a larger association in specific subgroups of the population[15].


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