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Racial and Ethnic Differences in Serum Cotinine Levels of Cigarette Smokers


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Context.—Cotinine, a metabolite of nicotine, is a marker of exposure to tobacco smoke. Previous studies suggest that non-Hispanic blacks have higher levels of serum cotinine than non-Hispanic whites who report similar levels of cigarette smoking.

Objective.—To investigate differences in levels of serum cotinine in black, white, and Mexican American cigarette smokers in the US adult population.


Participants.—A nationally representative sample of persons aged 17 years or older who participated in the survey.

Outcome Measures.—Serum cotinine levels by reported number of cigarettes smoked per day and by race and ethnicity.

Results.—A total of 7182 subjects were involved in the study; 2136 subjects reported smoking at least 1 cigarette in the last 5 days. Black smokers had cotinine concentrations substantially higher at all levels of cigarette smoking than did white or Mexican American smokers (P<.001). Serum cotinine levels for blacks were 125 nmol/L (22 ng/mL) (95% confidence interval [CI], 79-176 nmol/L [14-31 ng/mL]) to 539 nmol/L (95% CI, 289-630 nmol/L [51-111 ng/mL]) higher than for whites and 136 nmol/L (24 ng/mL) (95% CI, 85-182 nmol/L [15-32 ng/mL]) to 641 nmol/L (113 ng/mL) (95% CI, 386-897 nmol/L [68-158 ng/mL]) higher than for Mexican Americans. These differences do not appear to be attributable to differences in environmental tobacco smoke exposure or in number of cigarettes smoked.

Conclusions.—To our knowledge, this study provides the first evidence from a national study that serum cotinine levels are higher among black smokers than among white or Mexican American smokers. If higher cotinine levels among blacks indicate higher nicotine intake or differential pharmacokinetics and possibly serve as a marker of higher exposure to cigarette carcinogenic components, they may help explain why blacks find it harder to quit and are more likely to experience higher rates of lung cancer than white smokers.

See also pp 152 and 179.

Cotinine is widely applied as a marker of both tobacco use and exposure to environmental tobacco smoke (ETS) because it has a longer half-life (average, 18 to 20 hours) than nicotine does (average, 2 to 3 hours). On average, a cigarette smoker absorbs about 1 mg of nicotine per cigarette smoked. The increment in blood nicotine concentration after smoking a single cigarette ranges from 0.031 to 0.185 µmol/L (5-30 ng/mL), depending on how the cigarette is smoked. An average of 70% to 80% of the nicotine absorbed is metabolized to cotinine.

THE BIOCHEMICAL measurement of serum cotinine, the primary metabolite of nicotine, is widely applied as a marker of both tobacco use and exposure to environmental tobacco smoke (ETS). Previous studies have suggested that non-Hispanic blacks have higher levels of serum cotinine than do non-Hispanic whites who report similar levels of cigarette smoking. The interpretation of the results in these studies has been subject to debate, however. Some researchers have suggested that differences between levels of serum cotinine in non-Hispanic black smokers and non-Hispanic white smokers are attributable, at least in part, to racial differences in nicotine metabolism or elimination. Others believe that such differences are attributable to other variables, including differences in the type of cigarette smoked, length of cigarette, menthol or nonmenthol, filter or nonfilter, and nicotine yield and differences in how the cigarettes are smoked (blocking ventilation holes by fingers or lips, frequency and depth of inhalation, retention time of smoke in the lungs, and percentage of available tobacco smoked). Serum cotinine differences by race have also been attributed to differences in the accuracy of cigarette smoking self-reports and to differences in exposure to ETS.
efficient of variation of the correction factor is 22%, however, and does not take into account possible racial or ethnic differences in the conversion of nicotine to cotinine.

Scientists at the National Center for Environmental Health of the Centers for Disease Control and Prevention recently developed a new, highly sensitive biochemical measurement method for detecting levels of serum cotinine as low as 0.3 mmol/L (0.05 ng/mL). Using the new method, we investigated racial and ethnic differences in serum cotinine levels. We obtained data on serum cotinine levels from a representative sample of adult smokers and non-smokers of the third National Health and Nutrition Examination Survey (NHANES III), a nationwide household collection of health and nutritional information from a representative sample of the US civilian, noninstitutionalized population aged 2 months or older.

METHODS

The NHANES III, conducted from 1988 to 1994, consisted of a number of questionnaires administered in the household followed by standardized physical examinations and additional tobacco use questions administered in specially equipped mobile examination centers (MECs). We used NHANES III phase 1 data collected between October 25, 1988, and October 21, 1991, because the data for some of the key variables for the analyses were available for only this 3-year period. The nationally representative sample of the eligible population surveyed during phase 1 permitted calculation of national estimates.

Subjects and Demographics

Our study sample was limited to participants aged 17 years or older who described themselves as non-Hispanic blacks, non-Hispanic whites, or Mexican Americans, who had a serum cotinine measurement and provided tobacco use information in the MEC, and who did not use any other significant sources of nicotine in the previous 5 days. Of the 12391 persons selected, 2271 refused the interview; 1315 were interviewed at home and did not visit the MECs; 281 did not answer the MEC tobacco questionnaire; 682 had no cotinine measurement; 434 reported using other significant sources of nicotine in the previous 5 days; and 226 were other than non-Hispanic white, non-Hispanic black, and Mexican American. Data from 2136 subjects who reported smoking 1 cigarette or more in the past 5 days were included in the analyses. One of the analyses had data from both smokers and non-smokers (n = 7182).

Race and ethnicity based on self-report were categorized as non-Hispanic black, non-Hispanic white (henceforth referred to as blacks and whites), and Mexican American. Age at interview was categorized as 17 to 24, 25 to 44, 45 to 64, or 65 or more years. Educational level was categorized as 0 to 8, 9 to 11, 12, or 13 or more completed years of schooling. Poverty status was based on a measure developed by the US Bureau of the Census. Members of families whose incomes were equal to or greater than poverty thresholds were categorized as “at poverty level” or “above poverty level”; those with family incomes below the poverty threshold, as “below poverty level.” Each subject’s weight in kilograms, measured using a digital scale, was categorized as less than 60, 60 to 69.99, 70 to 79.99, and 80 kg or more.

Reported exposure to ETS at home was based on the following questions posed to 1 member of the household (usually the head of the family or spouse of the head): “Does anyone who lives here smoke cigarettes in the home?” When the answer was yes, the interviewee was then asked: “Who?” When any household member smoked, each member of that household was classified as being exposed to ETS at home. The number of household members who smoked was categorized as 0, 1, or 2 or more. In addition, one of the family members was asked how many rooms were in the home, excluding bathroom. The number of rooms in the home was categorized as 1 to 4 or 5 or more. Persons aged 17 years or older who reported having a job or business were also asked how many hours per day they were close enough to tobacco smoke at work that they could smell the smoke. The number of hours exposed to ETS at work was categorized as 0, 1 to 3, or 4 or more. Data were also categorized by region as Northeast, North Central, South, or West, according to standard US Bureau of the Census definitions.

The MEC tobacco questionnaire asked participants: “How many cigarettes have you smoked in the past 5 days?” A smoker was defined as a person who reported smoking 1 cigarette or more during the previous 5 days. The average number of cigarettes smoked per day was calculated and used for the analyses.

Serum Cotinine Measurement

Biochemical determination of tobacco exposure was performed by measuring serum cotinine levels in blood specimens obtained by venipuncture in the MEC. The cotinine assay involved isotope dilution, liquid chromatography, and tandem mass spectrometry. As in the study by Pirkle and colleagues, we used cutoff points of higher than 85 nmol/L (15 ng/mL) and 85 nmol/L (15 ng/mL) or less of cotinine in serum to designate active tobacco users and nontobacco users, respectively.

Cotinine data were originally reported in nanograms per milliliter. A conversion factor of 5.67 was used to convert cotinine levels in nanograms per milliliter to cotinine levels in nanomoles per liter, based on a molecular weight for cotinine of 176.22. A conversion factor of 0.006 was used to convert nicotine levels previously reported in nanograms per milliliter to nicotine levels in micro-moles/liter, based on a molecular weight for nicotine of 162.23.

Statistical Analysis

Determination of serum cotinine levels by race and ethnicity involved fitting a series of nonlinear exponential regression models of the form: ln(cotinine) = b0 + b1exp(−b2O) + error, where ln(cotinine) is the natural logarithm of serum cotinine; O is the number of self-reported cigarettes smoked per day; b0, b1, and b2 are parameters that describe the exponential relationship; and error is the residual error left unexplained by the model. This exponential model facilitated modeling serum cotinine as a monotonically increasing function of the number of cigarettes smoked, with cotinine increasing at a decreasing rate toward an upper asymptote. The variable b0 represents the upper bound (maximum achievable level) of ln(cotinine) at the highest levels of daily smoking, and b2 represents the rate at which cotinine increases with consumption. The quantity (b2−b1) represents the expected ln(cotinine) at a consumption level of 0 cigarettes per day.

Prior to model fitting, we divided the self-reported number of cigarettes smoked in the last 5 days by 5 and rounded to the nearest integer. Therefore, in the model, less than 1 represents a response of 1 to 4 cigarettes smoked in the last 5 days.

We fit 3 exponential models, one for each racial or ethnic group, and used weights supplied with the NHANES III data set to make the results more applicable to the US population. After fitting the simple exponential model, a series of covariate adjusted models were fit to the data from each racial and ethnic group. These models investigated the relationship between serum cotinine and cigarettes smoked per day after adjustment for each of the following covariates: sex, number of smokers in the household, hours of exposure to ETS at work, age, and weight.

The more complicated models were fit by adding covariates one at a time to the base model in an ordered sequence determined by the results of an F test of significance for each variable when added individually to the base model. We assessed the adequacy of the fit of the exponential regression models by using plots of the studentized residuals vs the predicted values. The assumption of
RESULTS

Study Population

Proportionately more black smokers than white smokers were poor and weighed 80 kg or more (Table 1). In terms of sociodemographic characteristics, Mexican American smokers differed from other racial and ethnic groups of smokers more than either their white or black counterparts.

Among self-reported smokers, both blacks and whites had serum cotinine levels consistent with their reported smoking levels (Table 2). Therefore, among blacks and whites, the ability of the biochemical measurement to detect smokers and nonsmokers was similar. Self-reported Mexican American smokers were less likely than blacks or whites to have serum cotinine levels consistent with their reported smoking levels. Self-reported nonsmokers (97.9% of blacks, 98.5% of whites, and 99.4% of Mexican Americans) had biochemically assessed cotinine threshold levels consistent with their reported smoking levels.

Self-reported and biochemically assessed smoking prevalences among blacks (34.9% and 34.7%, respectively) were similar to those for whites (33.1%, 32.1%) and higher than Mexican Americans (27.0%, 20.1%) (results not shown). Although blacks were as likely to have smoked in the past 5 days as whites, they reported smoking fewer cigarettes per day than whites (Table 3). Mexican Americans smoked fewer cigarettes per day than did either blacks or whites.

Statistics and Modeling

Fitting a nonlinear exponential unadjusted regression model (Figure) to determine the relationship between serum cotinine levels and self-reported cigarette smoking showed that cotinine concentrations were substantially higher among black smokers than among white or Mexican American smokers at all levels of cigarette smoking. Whites and Mexican Americans had similar serum cotinine levels when they smoked up to 5 cigarettes per day, but serum cotinine levels increased significantly more for whites than for Mexican Americans with each additional cigarette smoked. Serum cotinine levels for blacks were 125 nmol/L (22 ng/mL) (95% confidence interval [CI], 79-176 nmol/L [14-31 ng/mL]) to 539 nmol/L (95 ng/mL) (95% CI, 289-630 nmol/L [51-111 ng/mL]) higher than for whites and 136 nmol/L (24 ng/mL) (95% CI, 85-182 nmol/L [15-32 ng/mL]) to 641 nmol/L (113 ng/mL) (95% CI, 386-897 nmol/L [68-158 ng/mL]) higher than for Mexican Americans. Verification of the results of this analysis by unweighted analysis yielded similar results. Previous analyses had revealed that variables such as education, poverty status, time of day the blood was drawn, number of rooms in the house, and geographic region were not significantly associated with serum cotinine (data not shown). These variables were excluded from the final model in this study.

An F test comparing a full model (adjusting the relationship for the effects of race and ethnicity, age, sex, body weight, and other factors) to a reduced model (adjusting only for the effects of race and ethnicity) yielded similar results. Previous analyses had revealed that variables such as education, poverty status, time of day the blood was drawn, number of rooms in the house, and geographic region were not significantly associated with serum cotinine (data not shown). These variables were excluded from the final model in this study.
Table 3.—Percentage of 2136 Self-reported Smokers Aged 17 Years or Older, by Number of Cigarettes Smoked per Day in the Past 5 Days and by Race/Ethnicity, NHANES III, United States, 1988-1991*  

<table>
<thead>
<tr>
<th>Cigarettes per Day</th>
<th>Non-Hispanic Blacks, No. (% ± 95% CI)</th>
<th>Non-Hispanic Whites, No. (% ± 95% CI)</th>
<th>Mexican Americans, No. (% ± 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1</td>
<td>41 (6.2 ± 2.3)</td>
<td>45 (6.5 ± 1.7)</td>
<td>127 (24.3 ± 6.1)</td>
</tr>
<tr>
<td>1-7</td>
<td>200 (30.1 ± 3.7)</td>
<td>120 (12.6 ± 2.1)</td>
<td>240 (41.7 ± 3.9)</td>
</tr>
<tr>
<td>8-14</td>
<td>193 (29.3 ± 2.8)</td>
<td>152 (17.7 ± 3.0)</td>
<td>111 (17.9 ± 3.5)</td>
</tr>
<tr>
<td>15-24</td>
<td>186 (27.8 ± 3.8)</td>
<td>315 (36.5 ± 3.5)</td>
<td>80 (13.4 ± 2.8)</td>
</tr>
<tr>
<td>≥25</td>
<td>45 (6.6 ± 1.7)</td>
<td>266 (27.7 ± 4.5)</td>
<td>13 (2.7 ± 1.5)</td>
</tr>
<tr>
<td>Total</td>
<td>665 (100.0)</td>
<td>900 (100.0)</td>
<td>571 (100.0)</td>
</tr>
</tbody>
</table>

*NHANES III indicates third National Health and Nutrition Examination Survey; CI, confidence interval.

Table 4.—Sequential F Tests and Associated P Values for Each Covariate When Added to the Previous Weighted Nonlinear Exponential Regression Model for 2127 Smokers Aged 17 Years or Older, by Race/Ethnicity, NHANES III, United States, 1988-1991*  

<table>
<thead>
<tr>
<th>Result</th>
<th>Base Model</th>
<th>No. of Smokers in Home</th>
<th>Body Weight Category</th>
<th>Age Category</th>
<th>Hours of Work Exposure to Smoke</th>
<th>Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blacks, Covariates Added</td>
<td>F 1258</td>
<td>4.65</td>
<td>3.75</td>
<td>2.36</td>
<td>1.16</td>
<td>0.59</td>
</tr>
<tr>
<td>P 0.001</td>
<td>0.001</td>
<td>0.01</td>
<td>0.33</td>
<td>0.62</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. 662</td>
<td>656</td>
<td>647</td>
<td>638</td>
<td>632</td>
<td>629</td>
<td></td>
</tr>
<tr>
<td>Whites, Covariates Added</td>
<td>F 116</td>
<td>7.97</td>
<td>5.84</td>
<td>3.62</td>
<td>3.26</td>
<td>2.28</td>
</tr>
<tr>
<td>P 0.001</td>
<td>0.001</td>
<td>0.001</td>
<td>0.004</td>
<td>0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. 897</td>
<td>891</td>
<td>888</td>
<td>879</td>
<td>873</td>
<td>864</td>
<td></td>
</tr>
<tr>
<td>Mexican Americans, Covariates Added</td>
<td>F 3.3</td>
<td>4.26</td>
<td>6.64</td>
<td>3.38</td>
<td>1.72</td>
<td>1.64</td>
</tr>
<tr>
<td>P 0.001</td>
<td>0.001</td>
<td>0.003</td>
<td>0.08</td>
<td>0.10</td>
<td>0.72</td>
<td></td>
</tr>
<tr>
<td>No. 568</td>
<td>562</td>
<td>556</td>
<td>547</td>
<td>538</td>
<td>535</td>
<td></td>
</tr>
</tbody>
</table>

*NHANES III indicates third National Health and Nutrition Examination Survey.

Correlation between serum cotinine levels and number of cigarettes smoked per day, as predicted by preliminary regression models.

<table>
<thead>
<tr>
<th>Serum Cotinine Level, nmol/L (ng/mL)</th>
<th>No. of Cigarettes Smoked per Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Hispanic Blacks</td>
<td>Mexican Americans</td>
</tr>
<tr>
<td>&lt;1 500</td>
<td>56 (10)</td>
</tr>
<tr>
<td>500-1000</td>
<td>2840 (500)</td>
</tr>
<tr>
<td>1000-1500</td>
<td>57 (10)</td>
</tr>
<tr>
<td>1500-2000</td>
<td>6 (1)</td>
</tr>
</tbody>
</table>

Serum cotinine differences between black smokers and white smokers have also been suggested to be attributable to differential reports of the number of cigarettes smoked. Although we did not measure the validity of the study participants’ self-reports, we found no differences in the reliability of self-reports among blacks, whites, and Mexican Americans. Clark and colleagues designed a study to determine differences in self-reports of cigarettes smoked per day. They collected information about the nicotine content of the cigarette, inhalation frequency, how far smokers let their cigarette burn when they smoked, and weekly exposure to sidestream smoke from the burning end of a cigarette. The serum level of thiocyanate, a metabolite of cyanide that reflects exposure to tobacco smoke, was similar for the groups when the results were adjusted for the number of cigarettes smoked per day. This finding suggests that the higher cotinine levels found among blacks were not the result of inhaling more smoke than whites do.

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COMMENT

This study provides the first evidence from a national study that black smokers have higher serum cotinine levels than do white or Mexican American smokers, after adjustment for the number of cigarettes smoked per day, age, sex, body weight, number of smokers living in the home, and ETS exposure at home and at work. The results for nicotine content of the cigarette, inhalation frequency, how far smokers let their cigarette burn when they smoked, and weekly exposure to sidestream smoke from the burning end of a cigarette suggest that Mexican Americans derive more cotinine per cigarette than whites do.

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rum cotinine levels in blacks than in whites. They concluded that the disproportionately high cotinine levels observed in their study among black, blac


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