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Puffing Topography as a Determinant of Smoke Exposure

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BRIDGES, R. B., J. G. COMBS, J. W. HUMBLE, J. A. TURBEK, S. R. REHM AND N. J. HALEY. *Puffing topography as a determinant of smoke exposure.* PHARMACOL BIOCHEM BEHAV **37**(1) 29–39, 1990.—Puffing topography variables were measured in a well-characterized, male population smoking their own brand of cigarette. Of the puffing topography variables, interpuff interval appeared to be the primary determinant of blood concentrations of smoke constituents; however, preliminary data in a homogeneous population according to the nicotine yield of their cigarette suggest that total puff volume per cigarette may also be a significant determinant of blood levels of smoke constituents. Smokers of low nicotine yield cigarettes partially compensated for these lower yields by increasing the total volume puffed per cigarette. Observed differences in puffing topography associated with increased daily cigarette consumption and cumulative smoking history were consistent with a higher smoke exposure per cigarette. Further, although both alcohol and coffee consumption are associated with present and cumulative smoking history, coffee consumption is uniquely associated with differences in puffing topography consistent with a higher smoke exposure per cigarette. However, by multiple regression analyses, neither coffee nor alcohol consumption histories added significantly to the prediction of blood concentrations of smoke constituents over that obtained by smoking history and puffing topography.

Thiocyanate Carboxyhemoglobin Plasma nicotine Plasma cotinine Cigarette yield Puffing topography Smoking history Coffee Alcohol

THE "standard" tar and nicotine deliveries of commercial cigarettes have been reduced by increasing the efficiency of the filters, by changing the tobacco blend, and by smoke dilution (12). The yields were reduced on the assumption that decreased yields would lessen the health risks for those who smoke (44). However, because nicotine is probably the primary reinforcer controlling smoking behavior (37), smokers of low yield cigarettes modify their smoking behavior in order to derive a greater nicotine yield than that obtained under standardized smoking conditions.

Although some studies suggest that smokers compensate for lower yield cigarettes by increasing the number of cigarettes smoked per day (41,43), more recent studies using larger populations were unable to demonstrate this relationship (4, 16, 38, 40). Compensation by changes in puffing topography [number of puffs (2, 11, 20, 21, 24), interpuff intervals (3, 15, 24, 39), and puff duration (2, 11, 20, 21)] have also been reported. Although these changes in puffing characteristics are consistent with increased total volume puffed per cigarette, volume compensation has been reported by some investigators (2, 11, 35) but not by others (3, 13, 15, 20). Many of these previous studies utilized relatively small

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populations of smokers who switched from their own cigarette to another cigarette of either higher or lower yield. Using a relatively large population of smokers (67 males and 43 females) smoking their own brand of cigarette, a relatively recent study reported volume compensation in those smoking cigarettes ≤0.8 mg nicotine/cigarette (4).

In a previous study of 170 male cigarette smokers (7), we found that decreased plasma cotinine concentrations were significantly associated with decreased nicotine yield of the cigarette. However, the decrease in plasma cotinine was not comparable to the decrease in yield, suggesting that while smokers compensate for yield, this compensation is inadequate to attain the same smoke exposure. Daily cigarette consumption was unrelated to cigarette yield, suggesting that differences in puffing topography or inhalation behavior might account for this compensation. The purpose of the present study was to determine if differences in puffing topography were associated with cigarette yield in the same population as previously described (7). Further, we sought to determine the relationships of puffing topography with population or smoking history characteristics and smoke exposure or absorption (i.e., blood concentrations of thiocyanate, carboxyhemoglobin, nicotine or cotinine).

METHOD

The population for this study consisted of 170 male smokers who gave written informed consent. This study was approved by the Human Investigations and Study Committee of the University. Each subject completed an extensive questionnaire concerning health, smoking and drug usage histories and alcohol and coffee consumption. Methods utilized for the recruitment and characterization of this smoking population have been previously described (7).

Subjects for this study smoked their own brand of cigarette ad lib and reported to the laboratory at 8 a.m. At this time, the subjects were requested to smoke one of their own cigarettes five minutes prior to venipuncture, using a cigarette holder-pneumotachograph. The signal from the differential pressure transducer was fed directly into a microcomputer (Apple IIE) which was programmed to calculate the number of puffs per cigarette, intervals between puffs (interpuff interval), duration and volume of each puff, mean volume and duration per puff, and total puff volume and duration per cigarette. The pneumotachograph was calibrated by drawing puffs of standard volume from the subject's unlit cigarette into the cigarette holder. Puff volumes were not corrected for temperature, since temperature changes do not significantly affect volume measurements unless the cigarette rod is smoked within 8 mm of the filter (1).

Serum thiocyanate and blood carboxyhemoglobin concentrations were determined spectrophotometrically, while plasma nicotine and cotinine concentrations were determined by radioimmunoassay as previously described (7). Subjects who consumed tobacco in a form other than cigarette smoking were excluded from the analyses.

Results are expressed as means ± standard deviations or standard errors; significant differences between groups were determined by analysis of variance (ANOVA) taking into account differences in population sizes. Univariate and multivariate linear regression analyses were also performed to determine relationships among puffing topography variables, population characteristics, smoking history, and blood concentrations of smoke constituents, using appropriate SAS (Statistical Analysis System, SAS Institute, Inc., Cary, NC) programs and an IBM 3083 Computer.

TABLE 1

PUFFING TOPOGRAPHY VARIABLES IN TOTAL SMOKING POPULATION*

	Mean ± S.D.	Range
Total Smoking Time/Cigarette (sec)	285.9 ± 67.6	75–472
Puffs/Cigarette	11.0 ± 4.1	4–29
Interpuff Interval (sec)	26.5 ± 12.8	7.9–74.8
Duration/Puff (sec)	2.03 ± 0.72	0.51–5.26
Volume/Puff (ml)	56.4 ± 20.2	17.6–159.1
Total Duration/Cigarette (sec)	21.8 ± 9.3	5.9–53.8
Total Volume/Cigarette (ml)	601.3 ± 268.9	137–2014
Volume/Duration (ml/sec)	28.3 ± 6.3	14.2–53.8

*Results are expressed as means (±S.D.) for 161 smokers. Of the original 170 smokers, nine reported to the laboratory without bringing a cigarette of their own brand, and therefore puffing topography was not measured.

RESULTS

Population Characteristics

The characteristics of the 170 male smokers used in this study have previously been described (7). Briefly, the smoking population was relatively young (mean age 37.8 years) and asymptomatic. These subjects had smoked a mean of 20.3 years with a mean normal daily cigarette consumption of 31.8 cigarettes/day giving a mean cumulative smoking history of 24.6 pack-years. They had smoked a mean of 24.8 cigarettes in the 24 hours preceding participation in these studies. The nicotine yield of cigarette brands smoked ranged from 0.28 to 1.56 mg nicotine/cigarette (mean 0.98) as calculated from values determined by the Federal Trade Commission utilizing standardized smoking conditions (14). Mean blood levels of smoke constituents (or their metabolites) were serum thiocyanate, 161.2 μmoles/l; carboxyhemoglobin, 7.4%; plasma nicotine, 31.3 ng/ml; and plasma cotinine, 384 ng/ml.

Puffing Topography

The puffing topography variables for the overall population are given in Table 1. Considerable variability existed for each of these parameters in the total smoking population, some of which was attributable to a few extremely low or high values. For example, only 4 smokers had a mean volume/puff of greater than 100 ml, while only 2 smokers had a mean volume/puff of less than 30 ml. Similarly, only 3 smokers had a total puff volume per cigarette greater than 1250 ml with 1 smoker having a total puff volume less than 250 ml. Thus, although the highest total puff volume per cigarette was 14.7-fold higher than the lowest value, the majority of smokers varied over only a 5-fold range.

The relationships among the puffing topography variables are given in Table 2. An increase in the number of puffs per cigarette correlated significantly with a decrease in the mean interval between puffs (interpuff interval). Although an increase in the number of puffs per cigarette correlated with a decrease in the mean duration and volume of individual puffs, it also correlated with an increase in both the total puff duration and total puff volume per cigarette. Significant, negative correlations were observed between interpuff interval and the total duration or volume per cigarette (i.e., as the interval between puffs decreases, the total duration or volume per cigarette increases). Highly

TABLE 2

RELATIONSHIPS AMONG PUFFING TOPOGRAPHY VARIABLES*

	Interpuff Interval	Duration/ Puff	Volume/ Puff	Duration/ Cigarette	Volume/ Cigarette
Puffs/Cigarette	−.642§	−.230†	−.260‡	.546§	.535§
Interpuff Interval		−.032	.010	−.518§	−.488§
Duration/Puff			.823§	.631§	.466§
Volume/Puff				.464§	.612§
Duration/Cigarette					.845§

*Pearson's correlates for 161 smokers.
†$p \leq 0.05$; ‡$p \leq 0.01$; §$p \leq 0.0001$.

significant positive correlations were observed between mean duration per puff and mean volume per puff and between mean duration per cigarette and mean total puff volume per cigarette.

Relationships Between Puffing Topography and Smoking History

As has previously been described (7), the smokers were arbitrarily divided into six groups according to the nicotine yield of their cigarette (Table 3). Groups 5 and 6 differed significantly in mean age, years smoked and pack-years smoking history from Groups 1 through 4, and Group 6 also had a significantly higher mean coffee and alcohol consumption (7). However, Groups 1 through 4 were similar in age, daily cigarette consumption, years smoked, pack-years smoking history, and coffee and alcohol consumption. These differences in population and smoking history characteristics necessitated the exclusion of Groups 5 and 6 to examine the relationships of population or smoking history characteristics with puffing topography.

Smokers smoking the lowest yield cigarettes (Group 1) had significantly higher total puff volume per cigarette than did the other groups, and significantly higher mean puff volume and flow rate (volume divided by duration) than Groups 3 and 4. Smokers of lower yield cigarettes also tended to have higher numbers of puffs per cigarette, decreased interpuff interval, increased duration per puff, and increased duration per cigarette, but these differences did not reach statistical significance. These results are consistent with changes in puffing topography to compensate for lower yield cigarettes.

Relationships Between Puffing Topography Variables and Population Characteristics or Smoking History

The linear correlations between puffing topography variables and population characteristics or smoking history are given in Table 4. Both increased age and increased years smoked were significantly associated with increased total puff duration per cigarette and decreased flow rate (volume divided by duration); however, neither age nor years smoked were significantly and linearly related to total puff volume per cigarette. The relationships of age to these puffing topography variables were likely due to the significant relationship between age and years smoked ($r = .929$, $p = 0.0001$).

Although no significant linear relationship was observed between alcohol consumption (either present or cumulative) and the puffing topography variables, increased coffee consumption was associated with decreased interpuff interval, increased mean puff volume and duration, and increased total puff duration and volume per cigarette.

Daily cigarette consumption, as measured by either normal daily cigarette consumption or cigarettes past 24 hours, was

TABLE 3

PUFFING TOPOGRAPHY VARIABLES IN GROUPS OF SMOKERS ACCORDING TO THE NICOTINE YIELD OF THEIR CIGARETTE*

Group	1	2	3	4	5†	6†
Nicotine Yield	0.28–0.43	0.50–0.70	0.71–0.90	1.05–1.10	1.11–1.20	1.40–1.60
n	5	16	22	65	17	14
Puffs/Cigarette	13.2 ± 2.8	11.4 ± 1.4	11.1 ± 0.9	10.6 ± 0.5	11.4 ± 0.8	10.2 ± 1.2
Interpuff Interval (sec)	23.9 ± 7.9	26.5 ± 2.9	26.8 ± 2.5	25.8 ± 1.4	26.7 ± 3.2	33.0 ± 5.3
Duration/Puff (sec)	2.48 ± 0.45	2.31 ± 0.30	1.94 ± 0.09	1.93 ± 0.07	2.05 ± 0.15	2.22 ± 0.28
Volume/Puff (ml)	85.4 ± 10.6‡	63.7 ± 8.0	54.1 ± 2.6	52.2 ± 1.8	62.4 ± 5.5	64.7 ± 6.8
Duration/Cigarette (sec)	31.9 ± 7.0	25.2 ± 3.7	21.0 ± 1.7	19.8 ± 0.9	22.6 ± 1.8	21.8 ± 3.3
Volume/Cigarette (ml)	1141.6 ± 281.4§	686.4 ± 89.7	577.9 ± 40.8	528.7 ± 20.3	692.6 ± 71.4	601.1 ± 64.1
Volume/Duration (ml/sec)	35.6 ± 2.1‡	28.5 ± 1.3	28.2 ± 1.1	28.3 ± 0.8	29.6 ± 1.2	30.7 ± 2.9

*Puffing behavior variables are expressed as means (±S.E.M.) for indicated number of subjects in each group. These groupings included 139 smokers of the original 170 smokers studied, since 9 smokers did not bring a cigarette of their own brand on the morning of participation in this study (puffing topography not measured) and 22 smokers consumed generic cigarettes for which the cigarette yield was unavailable.
†Groups 5 and 6 differed significantly ($p \leq 0.05$) from the other 4 groups in mean age, years smoked, and pack-years history as previously described (7). Group 6 also had a higher coffee and alcohol consumption than did the remaining 5 groups.
‡Significantly ($p \leq 0.05$) higher than for Groups 3 and 4.
§Significantly ($p \leq 0.05$) higher than for remaining 5 groups.

TABLE 4

RELATIONSHIPS BETWEEN PUFFING TOPOGRAPHY AND POPULATION CHARACTERISTICS OR SMOKING HISTORY*

	Age	Alcohol Consumption		Coffee Consumption	Normal Daily Cigarette Consumption	Cigarettes Past 24 Hours	Years Smoked	Pack-Years Smoking History	Nicotine Yield
		Present	Cumulative						
Puffs/Cigarette	.086	.102	.053	.085	.352§	.253‡	.114	.273‡	−.163
Interpuff Interval	−.044	.001	−.048	−.196†	−.318§	−.242†	−.121	−.299§	.012
Duration/Puff	.144	−.137	.098	.237†	−.034	−.019	.156	.164	−.160
Volume/Puff	−.004	−.091	−.018	.188†	−.081	−.033	−.029	.027	−.294‡
Duration/Cigarette	.206†	−.054	.096	.263‡	.174	.069	.218†	.288‡	−.282‡
Volume/Cigarette	.069	.000	.004	.239‡	.154	.034	.052	.190†	−.407¶
Volume/Duration	−.232†	.099	−.156	−.064	−.007	.036	−.262‡	−.154	−.200†

*Pearson's correlates for 108 smokers (Groups 1–4 according to nicotine yield).
†$p \leq 0.05$; ‡$p \leq 0.01$; §$p \leq 0.001$; ¶$p \leq 0.0001$.

significantly associated with increased number of puffs per cigarette and decreased intervals between puffs. Increased cumulative smoking history as measured by pack-years was also significantly associated with increased number of puffs per cigarette, decreased interpuff interval, and increased total puff duration and volume per cigarette. The significant linear relationships between pack-years smoking history and number of puffs per cigarette, total puff duration per cigarette or total puff volume per cigarette are shown in Fig. 1. The relationships between pack-years and number of puffs per cigarette or interpuff interval were possibly due in part to the relationships between pack-years smoking history and normal daily cigarette consumption ($r = .702$, $p = 0.0001$) or cigarettes past 24 hours ($r = .498$, $p = 0.0001$) observed in this population, whereas the relationships between pack-years smoking history and total puff duration and volume per cigarette were probably due to the relationships of pack-years smoking history with both daily cigarette consumption and cumulative smoking history (years smoked; $r = .594$, $p \leq 0.0001$).

Linear correlations between puffing topography variables and nicotine yield are given in Table 4. Significant, negative correlations were observed between nicotine yield of the cigarette and mean puff volume, total duration and volume per cigarette and flow rate. Marginally significant decreases in the number of puffs per cigarette ($p = 0.09$) and decreases in mean puff duration ($p = 0.10$) were also observed with increasing nicotine yield. The linear relationships between nicotine yield and number of puffs per cigarette, total puff duration per cigarette and total puff volume per cigarette are shown in Fig. 2.

Relationships of Puffing Topography With Blood Concentrations of Smoke Constituents

The linear correlations of the puffing topography variables with blood concentrations of thiocyanate, carboxyhemoglobin, nicotine, and cotinine are given in Table 5. Clearly the blood concentrations of smoke constituents do not correlate well with puffing topography parameters. Serum thiocyanate concentration was negatively correlated with both mean puff volume or total puff volume per cigarette while plasma nicotine concentration was negatively correlated with interpuff interval. Since it appeared likely that these relationships might be confounded by the nicotine yield of the cigarette smoked, a similar analysis was done in the largest available subset of the population smoking the same cigarette brand (Table 6). In this subset, plasma nicotine concentrations were significantly associated with the interpuff interval and the total puff duration and volume per cigarette, while only marginally associated with the number of puffs per cigarette (Fig. 3). Plasma cotinine concentrations, on the other hand, were significantly and negatively correlated with the interpuff interval and marginally ($p \leq 0.10$) and positively correlated with both the total duration and volume per cigarette.

Predictors of Number of Puffs, Interpuff Interval and Total Puff Volume Per Cigarette

Stepwise multiple linear regression analyses were done to determine the significant predictors of puffing topography variables and blood levels of smoke constituents. Two sets of regression models were investigated: noninteractive or first order models and interactive models. In the noninteractive models, the pool of possible predictor variables are limited to the set of independent variables, while in the interactive models this pool is expanded to include all possible pairwise products of the independent variables. Interactive models are useful in determining the robustness of noninteractive models by identifying those pairs of variables that have a joint relationship with the dependent variable that is not simply additive and those pairs of variables that because of colinearity (e.g., nicotine yield and total puff volume/cigarette) would not allow both variables to be entered simultaneously into a first order model.

The regression models presented include only those independent variables which were significant or marginally significant predictors; dashed lines in the tables indicate that the particular independent variable, while entered as a potential independent variable, did not add significantly to the prediction of the dependent variable. Regression models were determined with and without considering all possible two-term interactions of the independent variables, with those including interaction terms always providing the better total prediction.

In the noninteractive regression model, daily cigarette consumption and nicotine yield were significant predictors of number of puffs per cigarette (Table 7). In this model, increased number of puffs per cigarette was significantly associated with increased daily cigarette consumption and decreased nicotine yield, with these independent variables accounting for 8.25% of the variation in the number of puffs per cigarette. In the interactive regression model (data not shown), increased years smoked and decreased body weight (either as independent variables or their interactions) were, in addition, significant predictors of increased number of puffs per cigarette giving a total prediction of 18.53%.

In the noninteractive regression model, only increased coffee consumption history was significantly ($p \leq 0.05$) associated with a

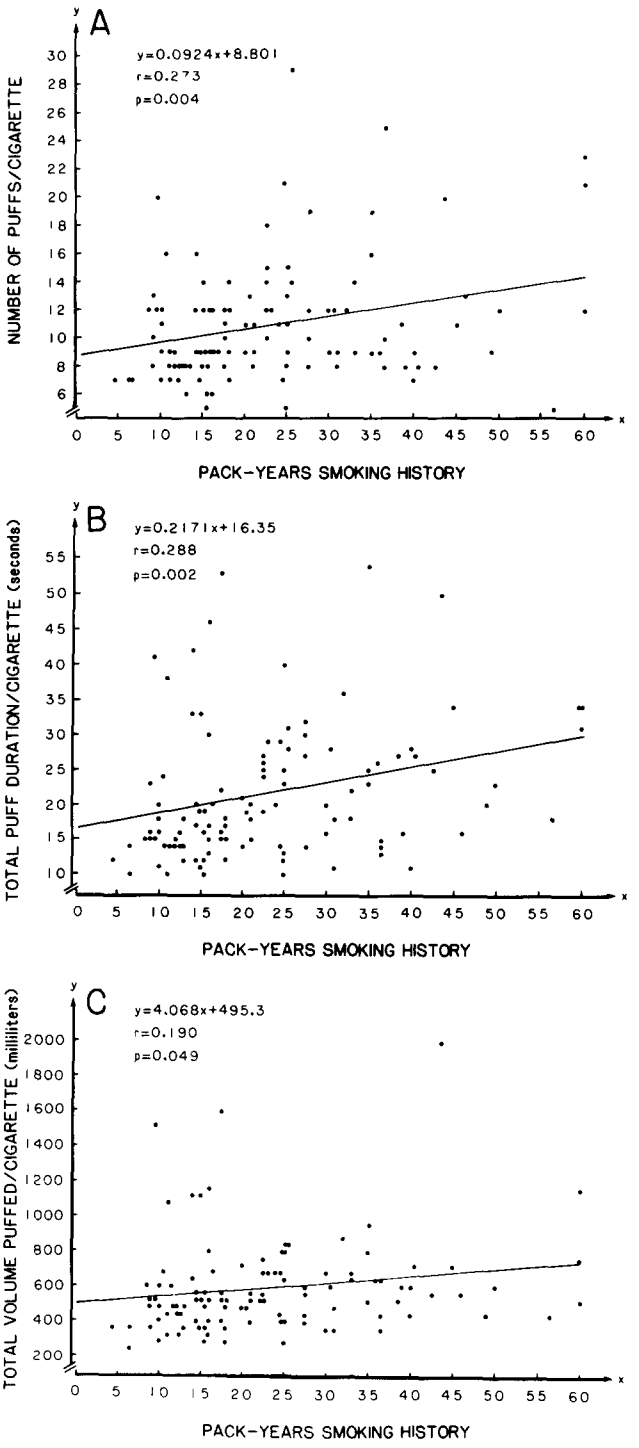

FIG. 1. Linear relationships between pack-years smoking history and puffing topography measures. (A) Number of puffs per cigarette; (B) Total puff duration per cigarette; and (C) Total volume puffed per cigarette. The graphical representation for each of these relationships includes the equation for the inserted least-squares best fit line; the correlation coefficient (r); and the level of significance for the correlation. The data are for Groups 1–4, n = 108.

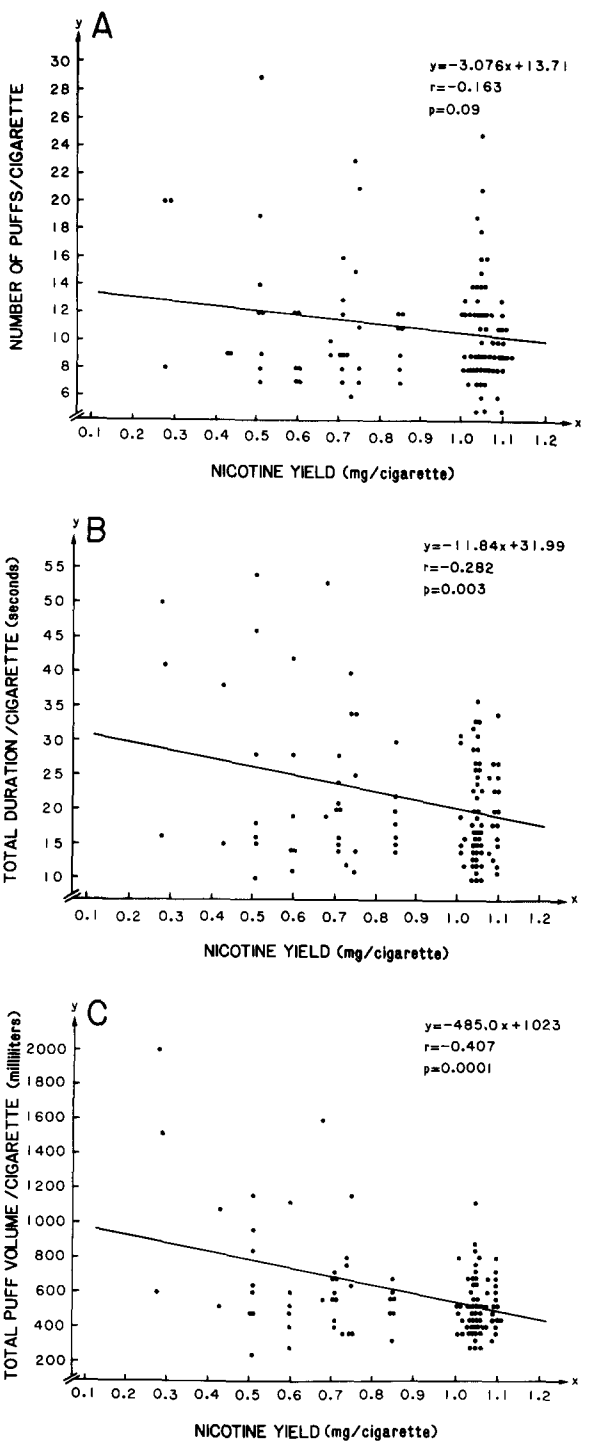

FIG. 2. Linear relationships between nicotine yield and puffing topography measures. (A) Number of puffs per cigarette; (B) Total puff duration per cigarette; and (C) Total volume puffed per cigarette. The graphical representation for each of these relationships includes the equation for the inserted least-squares best fit line; the correlation coefficient (r); and the level of significance for the correlation. The data are for Groups 1–4, n = 108.

TABLE 5

RELATIONSHIPS OF PUFFING TOPOGRAPHY WITH BLOOD CONCENTRATIONS OF SMOKE CONSTITUENTS*

	Serum Thiocyanate	Carboxy-hemoglobin	Plasma Nicotine	Plasma Cotinine
Puffs/Cigarette	−.088	.046	.123	.015
Interpuff Interval	.047	−.093	−.296‡	−.118
Duration/Puff	−.079	−.091	.003	−.116
Volume/Puff	−.190†	−.070	−.022	−.112
Duration/Cigarette	−.122	−.069	.095	−.094
Volume/Cigarette	−.222†	−.054	.068	−.098
Volume/Duration	−.164	.100	.008	.050

*Pearson's correlates are given for 108 smokers (Groups 1–4 according to nicotine yield).
†$p \leq 0.05$; ‡$p \leq 0.01$.

decrease in interpuff interval accounting for 3.40% of its variation (Table 7). In contrast, the interactive model demonstrated that only increased daily cigarette consumption was a significant ($p = 0.05$) predictor of decreased interpuff interval with marginally significant ($p \leq 0.10$) predictors of decreased interpuff interval being increased years smoked, increased coffee consumption history and decreased weight. The prediction of interpuff interval by these independent variables (and their interactions), although significant ($p \leq 0.04$), was still relatively poor, accounting for only 9.12% of the variability in interpuff interval.

Finally, multiple regression analysis (without interactions) demonstrated that increased total puff volume per cigarette was significantly ($p \leq 0.001$) associated with decreased nicotine yield and increased coffee consumption history, with these two independent variables accounting for 27.09% of the variation in total puff volume (Table 7). In the interactive model (data not shown), increased total puff volume per cigarette was shown to be significantly associated with not only increased coffee consumption history and decreased nicotine yield, but also increased daily cigarette consumption. These independent variables (and their interactions) accounted for 33.93% of the variability in the total puff volume per cigarette.

Predictors of Serum Thiocyanate, Blood Carboxyhemoglobin, and Plasma Nicotine and Cotinine Concentrations

The results of multiple regression analyses (excluding interaction terms) with serum thiocyanate, blood carboxyhemoglobin, and plasma nicotine and cotinine concentrations expressed as their logarithmic transformation as the dependent variables are given in Table 8. These regression models revealed that daily cigarette consumption was always significantly and positively associated with the blood concentrations of each of these smoke constituents. On the other hand, body weight was negatively associated with carboxyhemoglobin ($p \leq 0.01$), nicotine ($p \leq 0.005$) and cotinine ($p \leq 0.07$) concentrations, but not thiocyanate concentrations. Although total puff volume per cigarette was a significant predictor of serum thiocyanate concentration (but not carboxyhemoglobin, nicotine or cotinine), increased total puff volume per cigarette was associated with decreased serum thiocyanate as was obtained in the univariate regression analysis. Unlike the blood concentrations of the other smoke constituents or their metabolites, decreased interpuff interval and increased years smoked were also significantly associated with increased plasma nicotine levels.

TABLE 6

RELATIONSHIPS OF PUFFING TOPOGRAPHY WITH BLOOD CONCENTRATIONS OF SMOKE CONSTITUENTS*

	Serum Thiocyanate	Carboxy-hemoglobin	Plasma Nicotine	Plasma Cotinine
Puffs/Cigarette	.218	.084	.306†	.187
Interpuff Interval	−.213	−.124	−.438‡	−.398‡
Duration/Puff	−.110	.254	.185	.128
Volume/Puff	−.151	.087	.161	.093
Duration/Cigarette	−.007	.248	.400‡	.320†
Volume/Cigarette	−.009	.163	.424‡	.316†

*Pearson's correlates are given for 31 smokers smoking the same brand of cigarette (nicotine yield = 1.05 mg/cigarette).
†$p \leq 0.10$; ‡$p \leq 0.05$.

Multiple regression analyses with blood levels of smoke constituents as the dependent variable and including the total population (Groups 1–6) gave essentially the same result as that for Groups 1–4 given above. Only plasma nicotine differed in that significant predictors included not only cigarettes past 24 hours, years smoked, body weight and interpuff interval but also cumulative alcohol consumption and puffs/cigarette. However, this multiple regression model did not increase the total prediction (27.95%) of the variation of plasma nicotine concentration over that obtained for Groups 1–4.

Multiple regression analyses with two-variable interaction terms always increased the prediction of blood concentrations of smoke constituents or their metabolites (serum thiocyanate from 11.47% to 22.29%; blood carboxyhemoglobin from 17.70% to 30.71%; plasma nicotine from 28.98% to 38.47%; and plasma cotinine from 27.60% to 43.62%). These interactive models were complex, with some interaction terms consisting of two independent variables which were significantly and linearly correlated with one another by univariate regression analysis. In all cases, individual independent variables which were significant predictors in the noninteractive models were also significant predictors in the interactive model, but were frequently present as interaction terms with one or more of the other independent variables.

Despite the complexities of these interactive models, they provided preliminary evidence to suggest that increased years smoked was significantly associated with increased blood carboxyhemoglobin and plasma cotinine, as well as plasma nicotine; increased nicotine yield was significantly associated with increased plasma nicotine and cotinine; and decreased interpuff interval was significantly associated with increased plasma cotinine as well as nicotine. Although total puff volume per cigarette entered as a significant predictor (within interaction terms) of both carboxyhemoglobin and cotinine, increased total puff volume per cigarette was associated with decreased blood concentrations of these smoke constituents. Coffee consumption history also entered within interaction terms as a predictor of both carboxyhemoglobin and plasma cotinine concentrations; increased coffee consumption was associated with increased carboxyhemoglobin levels, and decreased plasma cotinine concentrations.

DISCUSSION

In this study, puffing topography was measured in a well-characterized male population smoking their own brand of cigarette (7). Although high test-retest reliability correlations have previously been observed for the puffing topography measures (4, 31, 45), these measures are likely affected by the cigarette holder pneumotachograph (33,42) and the particular smoking setting

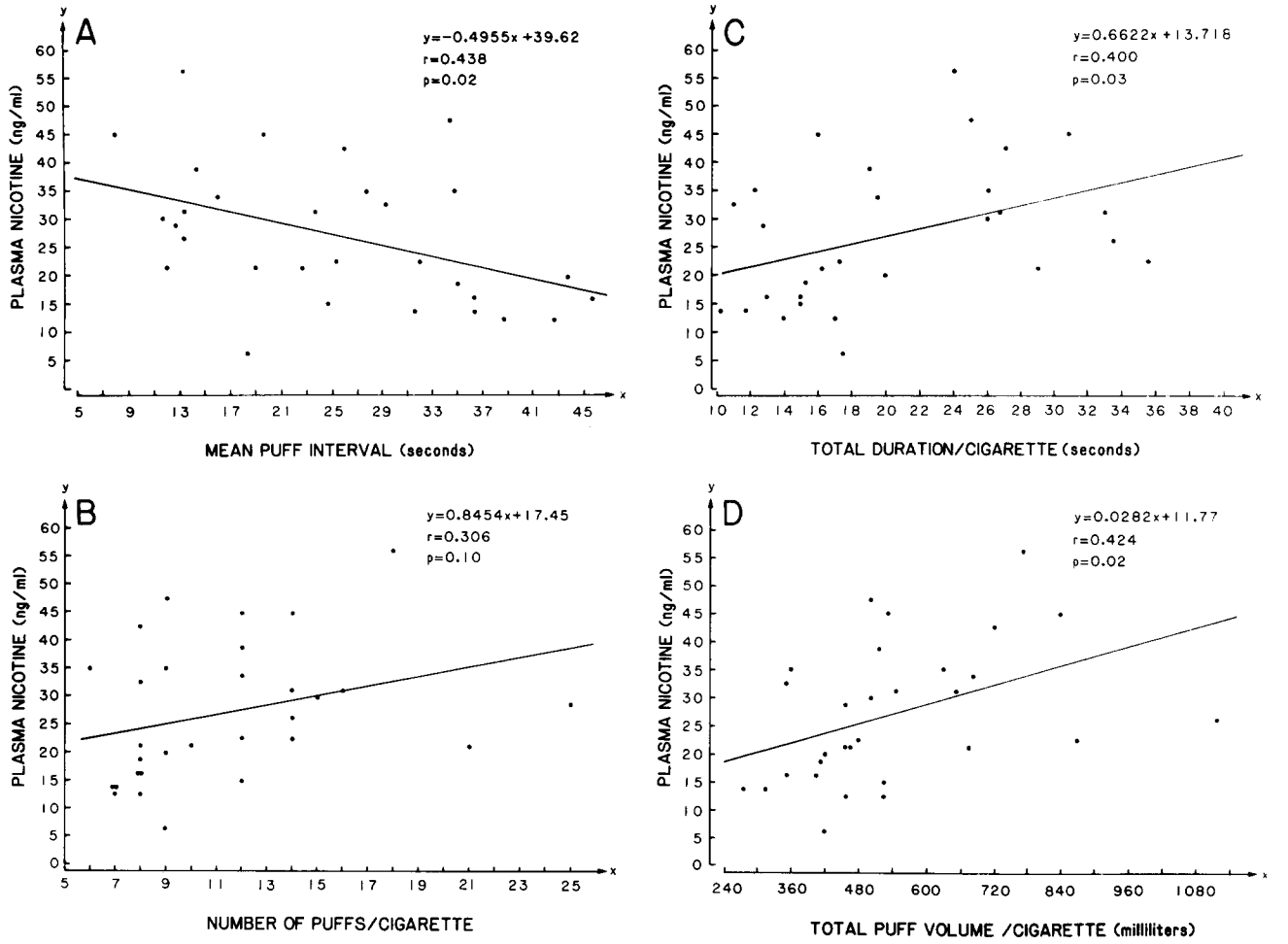

FIG. 3. Linear relationships between plasma nicotine concentration and puffing topography measures. (A) Mean puff interval; (B) Total puff duration per cigarette; (C) Number of puffs per cigarette; and (D) Total puff volume per cigarette. The graphical representation for each of these relationships includes the equation for the inserted least-squares best fit line; the correlation coefficient (r); and the level of significance for the correlation. The data are for 31 subjects smoking the same brand of cigarette (nicotine yield = 1.05 mg per cigarette).

(9,33). Puffing topography measures are also affected by the timing since the last cigarette (8,18). Since the 'normal' smoking topography was sought in this study, the subjects were allowed to smoke ad lib on the morning before participation. Thus, the measured blood levels of smoke constituents reflected not only that obtained by the cigarette smoked with measurements of puffing topography but also the baseline, blood levels of these smoke constituents which would be dependent upon the number of prior cigarettes smoked, their timing, and the half-life of these smoke constituents in peripheral blood.

Although considerable intersubject variability in the puffing topography measures were observed in this study, the values obtained were similar to those previously described (1, 4, 9, 25, 27, 36). This is the first study which has attempted to relate puffing topography measures to smoking history, cigarette yield, histories of alcohol and coffee consumption, and blood levels of smoke constituents in a relatively large, well-characterized population.

Univariate linear regression analysis among the puffing topography variables revealed that the total puff volume per cigarette was significantly and positively correlated with both the number of puffs and the mean volume per puff. However, an increase in number of puffs per cigarette was correlated with both a decrease in mean volume per puff and an increased total puff volume per cigarette, suggesting that the increase in number of puffs more than compensates for the decrease in mean volume per puff. The highly significant, positive correlations between duration per puff and volume per puff and between total puff duration per cigarette and total volume per cigarette suggests that duration explains approximately 70% of the variation in volume. On the other hand, flow rate correlated less significantly with total puff volume per cigarette ($r = .249$, $p \leq 0.002$) suggesting that variation in flow rate accounts for a relatively smaller percentage of the variation in total puff volume per cigarette.

Previous investigators (1) suggested that marked intersubject variation in puffing topography measures may partially account for the variability in blood concentrations of smoke constituents. However, significant relationships between puffing topography measures and blood levels of smoke contituents have not generally been observed (1), unless differences in inhalation were taken into account (25). Since we are attributing compensatory mechanisms in smokers of low yield cigarettes to differences in puffing

TABLE 7

PREDICTORS OF PUFFS PER CIGARETTE, INTERPUFF INTERVAL AND VOLUME PER CIGARETTE BY MULTIPLE REGRESSION ANALYSES*

	Puffs Per Cigarette†			Interpuff Interval‡			Volume Per Cigarette§		
	Coefficient	Standard Error	*p*	Coefficient	Standard Error	*p*	Coefficient	Standard Error	*p*
Intercept	9.42082			27.57903			1014.5063		
Independent Variables:									
Cigarettes Past 24 Hours	1.61855	0.67434	0.02	—			—		
Years Smoked	—			—			—		
Nicotine Yield	−3.59955	1.73813	0.04	—			−555.1600	99.7552	0.0001
Coffee Consumption	—			−.62445	0.32028	0.05	23.2605	6.9002	0.001
Alcohol—Present	—			—			—		
—Cumulative	—			—			—		
Body Weight	—			—			—		

*Multiple regression analysis performed on the homogeneous smoking population with nicotine yield of 0.28 to 1.10 mg/cigarette (Groups 1–4, n = 108). Cigarettes past 24 hours and total volume per cigarette were entered as their logarithmic transformation.

†Total R^2 for puffs per cigarette was .0825 ($p \leq 0.01$) for the two-variable model.

‡Total R^2 for interpuff interval was .0340 ($p \leq 0.05$) for the one-variable model.

§Total R^2 for total volume per cigarette was .2709 ($p \leq 0.0001$) for the two-variable model.

topography, it seemed imperative to be able to demonstrate a relationship of puffing topography to blood concentrations of smoke constituents or their metabolites.

Few significant linear relationships were observed in the total smoking population between the puffing topography variables and blood levels of smoke constituents by either univariate or multiple regression analyses in the total population. Significant decreases in serum thiocyanate concentration were associated with increased total puff volume per cigarette; the rationale for this correlation is not apparent. Also, increased plasma nicotine concentration was significantly associated with decreased interpuff interval. Further, in multiple regression models with interaction terms (but not in models without interaction terms), decreased interpuff interval was similarly associated with increased blood carboxyhemoglobin and plasma cotinine concentrations. However, no significant positive correlations were observed by univariate regression analysis between total puff volume per cigarette and any of the blood levels of smoke constituents in the total population consuming cigarettes with various nicotine yields.

When nicotine yield was eliminated as a confounding variable, increased plasma nicotine concentrations were significantly associated with decreased interpuff interval and increased total puff volume (and duration) per cigarette, while only marginally associated with increased number of puffs per cigarette. Further, although plasma cotinine concentration is considered the best measure of 24-hour cigarette consumption (6), and although the smokers in this group varied considerably in daily cigarette consumption (i.e., 6 to 60), increased plasma cotinine concentrations were also significiantly associated with decreased mean interpuff interval and marginally associated with increased total puff volume (and duration) per cigarette.

The above data suggest that of the puffing topography variables, interpuff interval is the single most important determinant of blood levels of smoke constituents, especially nicotine. The significant association of decreased interpuff interval with increased plasma nicotine may result, in part, from differences in smoke deliveries associated with smoking patterns (10). In this prior study, decreased interpuff interval was associated with decreased filtration efficiency and greater delivery of total particulate matter, although the effect on delivery of total nicotine alkaloids was more variable (10). It is also conceivable that the correlation of decreased interpuff interval with increased plasma nicotine is in part due to the highly significant correlation of decreased interpuff interval with increased total puff volume per cigarette observed in this study. Although total puff volume per cigarette, itself, was not demonstrated to be an important predictor of plasma nicotine and cotinine concentrations in populations smoking cigarettes with different yields, univariate analyses of a population smoking the same yield cigarette suggest that it may, nevertheless, be a potentially important determinant of smoke exposure. Other factors which likely account for the relatively poor prediction of the blood levels of smoke constituents by the puffing topography variables include: differences in baseline blood levels of these smoke constituents due to prior cigarette smoke exposure; differences in inhalation behavior; and potential differences in rates of metabolism or excretion.

In this population, body weight was previously shown to be inversely correlated with blood concentrations of smoke constituents (7). This inverse relationship was suggested to be due to the relationship between body weight and the volume of distribution. In the present study, although body weight did not correlate significantly with puffing topography measures by univariate regression analysis or multiple regression analysis without interaction terms, inclusion of interaction terms in multiple regression models revealed that increased body weight was a significant predictor of decreased number of puffs per cigarette and a marginally significant predictor of increased interpuff interval, both being associated with a lower smoke exposure. Although less than definitive, these data support the hypothesis that lower blood levels of smoke constituents associated with higher body weight may not only be due to a greater volume of distribution, but a lower smoke dose due to less intense puffing behavior.

The co-occurrence of tobacco, coffee and alcohol consumption habits is well established (26). However, the relationships, if any, of coffee or alcohol consumption with puffing topography or cigarette smoke exposure are yet to be clearly described. Acute consumption of caffeinated or decaffeinated coffee has been shown to be associated with increased puff rate and number of cigarettes (28) which was apparently not due to changes in urinary pH associated with coffee consumption (29). In contrast, acute

TABLE 8

PREDICTORS OF SERUM THIOCYANATE, BLOOD CARBOXYHEMOGLOBIN AND PLASMA NICOTINE AND COTININE IN SMOKERS BY MULTIPLE REGRESSION ANALYSES*

	Thiocyanate†			Carboxyhemoglobin‡		
	Coefficient	Standard Error	p	Coefficient	Standard Error	p
Intercept	3.24381			1.83018		
Independent Variables:						
Cigarettes Past 24 Hours	.13800	0.0461	0.003	.20648	0.05437	0.0002
Years Smoked	—			—		
Nicotine Yield	—			—		
Coffee Consumption	—			—		
Alcohol—Present	—			—		
—Cumulative	—			—		
Body Weight	—			−.00623	0.00249	0.01
Puffs/cigarette	—			—		
Interpuff Interval	—			—		
Volume/cigarette	−.17771	0.07087	0.01	—		
	Nicotine§			Cotinine¶		
	Coefficient	Standard Error	p	Coefficient	Standard Error	p
Intercept	3.26094			4.70735		
Independent Variables:						
Cigarettes Past 24 Hours	.28315	0.07372	0.0002	.58804	0.09900	0.0001
Years Smoked	.01101	0.00414	0.009	—		
Nicotine Yield	—			—		
Coffee Consumption	—			—		
Alcohol—Present	—			—		
—Cumulative	—			—		
Body Weight	−.01025	0.00355	0.005	−.00876	0.00482	0.07
Puffs/cigarette	—			—		
Interpuff Interval	−.00808	0.00390	0.04	—		
Volume/cigarette	—			—		

*Multiple regression analysis performed on the homogeneous smoking population with nicotine yield of 0.28 to 1.10 mg/cigarette (Groups 1–4, n = 108). Serum thiocyanate, blood carboxyhemoglobin, plasma nicotine, plasma cotinine, cigarettes past 24 hours, and total puff volume per cigarette were entered as their logarithmic transformations.

†Total R^2 for thiocyanate was .1147 ($p = 0.008$) for the two-variable model.

‡Total R^2 for carboxyhemoglobin was .1770 ($p \leq 0.0001$) for the two-variable model.

§Total R^2 for plasma nicotine was .2898 ($p \leq 0.0001$) for the four-variable model.

¶Total R^2 for plasma cotinine was .2760 ($p \leq 0.0001$) for the two-variable model.

caffeine administration (either alone or in combination with ethanol consumption) has been shown in females not to consistently affect puffing behavior (30). While acute ethanol ingestion has been associated with an increased number of puffs and number of cigarettes in alcoholics, the effects of ethanol ingestion with smoking patterns in nonalcoholics is variable (17, 22, 23). Yet others have demonstrated that acute ethanol ingestion in females was associated with an increased mean puff volume and total puff volume per cigarette (30).

This study differs from previous studies in that the association of coffee or alcohol consumption histories with puffing behavior were sought, rather than studying the acute effects of coffee (or caffeine) or alcohol ingestion. Increased history of coffee consumption was significantly associated with decreased interpuff interval and increased total puff volume per cigarette. Although the relationships of coffee consumption with daily cigarette consumption ($r = .190$, $p = 0.05$), years smoked ($r = .257$, $p = 0.008$) and pack-years smoking history ($r = .283$, $p = 0.003$) might partially account for these univariate correlations between puffing topography and coffee consumption, these associated variables do not explain the fact that coffee consumption history is a significant predictor of puffing topography by multiple regression analyses. In contrast, although cumulative alcohol consumption was also significantly associated with daily cigarette consumption ($r = .375$, $p = 0.0001$), years smoked ($r = .289$, $p = 0.002$) and pack-years smoking history ($r = .452$, $p = 0.0001$), no significant relationships were observed between any of the puffing topography variables and cumulative (or present) alcohol consumption history. The mechanism whereby coffee (or caffeine) consumption influences puffing topography is uncertain, but these observed differences in puffing topography are clearly consistent with a higher smoke exposure per cigarette in individuals who have a greater

coffee consumption history.

The relationships between coffee or alcohol consumption histories and blood levels of smoke constituents were also complicated by the fact that in this population both coffee and alcohol consumption histories were both significantly correlated with daily and cumulative smoking histories and each of these sets of variables are significantly correlated with smoke dose (especially plasma nicotine) by univariant regression analysis (7). History of coffee or alcohol consumption was not a significant predictor of the blood levels of smoke constituents by multiple regression analyses including the puffing topography variables as independent variables, but without interaction terms. Results of multiple regression analyses including interaction terms were complex, and they frequently (but inconsistently) implicated coffee and alcohol consumption histories as determinants of blood concentrations of smoke constituents. Thus, we conclude that coffee and alcohol consumption histories appear to add little to the prediction of blood levels of smoke constituents over that obtained by present and cumulative smoking histories and puffing topography. Thus, the fact that coffee and alcohol consumption histories are significantly correlated with blood concentrations of smoke constituents by univariate (but not multivariate) regression analyses suggests that these beverage consumption histories may primarily affect smoke dose through their effects on (or their association with) smoking history or puffing topography.

However, coffee or alcohol consumption may mediate blood levels of smoke constituents by a variety of distinct (and, in some cases, possibly opposing) physiologic and pharmacologic actions, separate from their association with smoking history or puffing topography. Although increased caffeine body clearance has been demonstrated in smokers (34), to our knowledge the effect of caffeine on nicotine metabolism or body clearance has not yet been studied. For example, caffeine could potentially increase nicotine body clearance as a result of its metabolic or diuretic actions. Thus, the net effect of coffee consumption might be to increase the intake of smoke constituents as a result of more intense puffing without a concomitant increase in blood concentrations of smoke constituents due to increased excretion. Similarly, acute ethanol ingestion increases renal clearance of nicotine (5), yet (unlike alcohol consumption history) may be associated with more intense puffing behavior (17, 22, 23, 30). Thus, it remains to be determined if coffee and alcohol consumption histories affect smoke dose through their association with smoking history or puffing topography or their metabolic, pharmacologic or physiologic effects. It is additionally conceivable that these histories are coincident with other personality characteristics which are related to smoking (and puffing) behavior.

As expected, the daily cigarette consumption was previously shown to be significantly and linearly related to all of the blood concentrations of smoke constituents in this population (7). By multiple regression analyses with number of puffs, interpuff interval, and total puff volume per cigarette as the dependent variables, we have shown that the interpuff interval is shorter among heavy smokers, confirming a previous report (19); increased daily cigarette consumption is also associated with an increased total puff volume per cigarette; and increased years smoked is associated with an increased number of puffs per cigarette and a decreased interpuff interval. These differences in puffing topography are consistent with a greater smoke exposure per cigarette. They may partially explain the significant, linear relationships of pack-years smoking history with blood levels of smoke constituents (7) and the puffing topography measures obtained by univariate regression analysis, since pack-years smoking history is significantly and linearly related to both daily cigarette consumption ($r = .499$, $p \leq 0.0001$) and years smoked ($r = .594$, $p \leq 0.0001$).

In this population, nicotine yield was previously shown to be a significant predictor of plasma nicotine and a marginally significant predictor of plasma cotinine (7). Also, decreased plasma cotinine concentrations were significantly associated with lower nicotine yield of the cigarette smoked; however, the decrease in plasma cotinine was not comparable to the decrease in nicotine yield suggesting partial compensation by smokers of low yield cigarettes. Since we did not find that compensation occurred as a result of increased cigarette consumption, compensatory differences in puffing topography seemed likely.

The association of nicotine yield with the puffing topography measures was determined in groups of smokers according to nicotine yield and by seeking linear correlations between nicotine yield and puffing topography measures by both univariate and multivariate regression analyses. Groups smoking low yield cigarettes had significantly higher mean total puff volumes per cigarette as well as higher mean puff volume and flow rates with a trend toward higher number of puffs per cigarette. Results obtained by univariate and multivariate analyses were consistent with this group analysis. By univariate analyses, a decrease in nicotine yield was significantly correlated with increases in total puff volume per cigarette, mean puff volumes, and flow rate. Multiple regression analysis revealed that nicotine yield (or its interactions) were significant predictors of number of puffs per cigarette and total puff volume per cigarette. Thus, our data are consistent with some investigators (2, 11, 35), but not others (3, 13, 15, 20), that compensation for low yield cigarettes occurs by increased total puff volume per cigarette. This increased total puff volume per cigarette observed in the present study was apparently achieved by both increased mean puff volumes and number of puffs with presumably minimal contributions by increased flow rate. Unlike other investigators (3, 15, 24, 39), we found no evidence to implicate interpuff interval as a part of this compensatory mechanism to low yield cigarettes, and in fact nicotine yield (either itself or its interaction) did not enter as a significant predictor of interpuff interval.

The multiplicity of factors influencing smoking behavior in heterogeneous populations of human smokers makes difficult the identification of specific factors which are significant determinants of smoke exposure. There is evidence to suggest that smoking behavior may differ according to sex (4), alcohol intake (23), degree of nicotine 'dependency' (32), smoking history (19) nicotine yield of the cigarette smoked (2, 3, 11, 13, 15, 20, 21, 24, 39), and timing since the last cigarette (8,18). Data in this study suggest that daily exposure to cigarette smoke must not only take into account the number of cigarettes smoked per day and cigarette yield, but differences in puffing topography associated with daily cigarette consumption, cigarette yield, cumulative smoking history, coffee consumption history and body weight. An understanding of the interrelationships of these factors (as well as smoking history and alcohol and coffee consumption) is essential for studies of inhalation toxicology, the potential mechanisms of disease induction in smokers, and intervention strategies for successful smoking cessation.

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