Original Article

Smoking, Alcohol Consumption, and Leukocyte Counts

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Blood was collected from 684 healthy volunteers and examined for total and differential white blood cell (WBC) counts. A subgroup also was tested for numbers of T cells, B cells, and CD4 and CD8 subsets. Smoking status and alcohol consumption were determined by means of questionnaire, and smoking status was verified with serum cotinine concentration. High smoking rate was associated with increases in all counts. Former smokers abstinent less than 5 years still demonstrated elevated counts, whereas those abstinent more than 5 years had WBC counts comparable to those in persons who were never smokers. Compared with levels in those who had never smoked, total WBC counts were 27% higher in current smokers and 14% higher in former smokers who were abstinent for less than 5 years. Lymphocyte counts were 9% higher in those consuming more than one alcoholic drink per day than in those consuming less alcohol, but drinking was not associated with other cell populations. (Key words: Alcohol; Smoking; WBCs) Am J Clin Pathol 1997;107:64-67.

It has been reported for some time that smoking influences the peripheral blood leukocyte count. Studies in both the United Kingdom[1] and France[2] found that mean total white blood cell (WBC) count was 30% higher in smokers than in nonsmokers. Leukocyte counts in ex-smokers, however, were similar to those in nonsmokers. The French study also found that those who inhaled had higher counts than those who smoked similar amounts without inhaling. Other studies have shown that, although smoking was associated with a higher WBC count, consumption of up to three alcoholic drinks a day was not.[3] Nevertheless, there has been much interest in the effect of alcohol excess on WBC count and function, because alcoholic patients are prone to serious bacterial infections.[4] Impaired WBC function has been recorded in alcoholic patients[5]; however, data on WBC count in persons who regularly consume modest amounts of alcohol are few. Furthermore, recent evidence indicates that for nonsmokers (but not smokers), temperate drinking is associated with increased resistance to experimentally induced upper respiratory tract infections.[6] We studied the peripheral WBC count in 684 healthy volunteers and related it to the amount they smoked and drank. We confirmed earlier findings, and extend this work by providing data on how long smoking-associated elevation in cell count persists after persons stop smoking. We also provide data on the potential role of social drinking on WBC count, differential counts, and lymphocyte subsets.

MATERIALS AND METHODS

Subjects

Two hundred eighty-three men and 401 women volunteered to take part in studies at the Common Cold Unit, Salisbury, England. They were screened by means of medical history, routine clinical examination, and laboratory tests as part of the regular admission procedures of the Unit.[7] Pregnant women were excluded from the study. Mean age of the study subjects was 33 years (±10.4 SD). All studies were approved by the Harrow District Ethical Committee

Hematologic Studies

Blood was collected on arrival at the Unit. In most cases, blood was collected in the morning, within a few hours of the volunteers' usual breakfast. Volunteers were seated for up to half an hour, after which blood was drawn while they were recumbent or, occasionally, sitting. Full blood cell counts were performed using an ELT-800 blood counter (Becton-Dickinson, Mountain View, Calif). Differential WBC counts were performed on May-Grunwald– or Giemsa-stained smears using 200 cell counts. Differential counts were available for all 684 subjects, and lymphocyte subsets were determined on a subsample of 163 of these. Smears were examined with the alkaline phosphatase–antialkaline phosphatase labeling technique[8] for the presence of HLA class II– and CD3-positive cells because these are characteristic of B cells and T cells, respectively. They were also stained for the presence of CD4- and CD8-positive cells using reagents (Ortho Diagnostics, Westwood, Mass). All hematologic studies were performed by technicians blinded to smoking and drinking status of the volunteers.

Smoking status

Cotinine, a metabolite of nicotine, provided a biochemical measure of smoking status.[9,10] The mean of the log of two cotinine assays (one using blood from the same blood draw described above and the other using blood drawn 28 days later) was used as a measure of smoking rate. Among smokers, it correlated reasonably well with self-reported number of cigarettes smoked each day ($r=.63$). Nonsmokers were those who had never smoked, and ex-smokers were subdivided into those who had stopped smoking within the last 5 years and those who had stopped earlier. Nonsmokers and ex-smokers all had cotinine levels <15 ng/mL, biochemically verifying they were not smokers at the time of the study. The median cotinine value among current smokers was 238 ng/mL (approximately equivalent to 15 cigarettes per day) and was used to classify them as light or heavy smokers.

Drinking status

Alcohol consumption was assessed by means of a questionnaire. The average number of drinks consumed on weekdays was multiplied by the number of weekdays on which individuals drank; similarly, the number of drinks consumed on weekend days was multiplied by the number of weekend days on which they drank. From these was calculated the average number of drinks consumed per day. Subjects were then classified as those who (1) never drink, (2) do not drink every week but do drink occasionally, (3) drink 0.1 to 1 drink per day, (4) drink 1.1 to 2 drinks per day, or (5) drink more than 2 drinks per day. For this analysis, 1 drink was a unit of 8 to 10 g of alcohol (ie, half pint of beer, glass of wine, shot of liquor).

Statistical analysis

Analyses of covariance were used to detect significant differences in the number of WBCs in persons in the various smoking and drinking categories. These analyses adjust for possible effects of covariate (control) variables and are the source of the probability values quoted. Analyses of variance, without controls, also were performed, and the probabilities obtained were almost identical. The covariates included gender, age, education, allergic status, ponderal index (weight/height^3), and number of hours of daylight on the first day of the study (highly correlated with average external air temperature on that day [$r=.80$]). All of the outcome variables were log^{-10} transformed to normalize their distributions.

RESULTS

The Table presents the mean of the observed (not logged) numbers of peripheral WBC populations by smoking status. Note the substantial and consistent relationship between smoking status and cell counts. There is, for example, a gradient in the total WBC count, rising from a mean of 5.56×10^6 for nonsmokers to 7.67×10^6 for heavy smokers. Within this gradient, those who stopped smoking in the past 5 years had significantly more leukocytes than those who never smoked, and there is a substantial difference in values between heavy and light smokers. A similar gradient exists when the neutrophils, lymphocytes, and monocytes are considered separately, indicating that the effect is on all major WBC populations in circulation and that differential counts are associated with smoking status. Furthermore, there are similar gradients in B-cell, total T-cell, and CD4 and CD8 cell counts. The results for the lymphocyte subsets are statistically significant even though the sample examined was substantially smaller than that for the other cells.

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MEAN NUMBERS OF PERIPHERAL WHITE BLOOD CELL POPULATIONS BY SMOKING STATUS

	Non-smokers	Smoking Status				P
		Ex-smokers		Current Smokers		
		>5 Years	≤5 Years	Light	Heavy	
Total white blood cells	5 56*†‡	5 74‡	6 32‡§	6 46‡§	7 67*†§‖	≤ 001
	(1 34)	(1 24)	(1 87)	(1 83)	(2 19)	
Monocytes	0 45*†‡	0 48‡	0 51	0 54§	0 60§‖	≤ 001
	(0 15)	(0 27)	(0 19)	(0 22)	(0 22)	
Neutrophils	3 20*†‡	3 32‡	3 80‡	3 72‡§	4 62*†§‖	≤ 001
	(1 05)	(0 99)	(1 57)	(1 41)	(1 81)	
Lymphocytes	1 90*†‡	1 94‡	2 01‡	2 20‡§	2 46*†§‖	≤ 001
	(0 53)	(0 47)	(0 62)	(0 60)	(0 73)	
T cells	1 40‡	1 36‡	1 74	1 60	2 00§‖	≤ 001
	(0 46)	(0 31)	(0 71)	(0 47)	(0 86)	
B cells	0 30	0 27	0 35	0 35	0 39	≤ 034
	(0 12)	(0 12)	(0 24)	(0 18)	(0 15)	
Helper cells (CD4)	0 67‡	0 68	0 84	0 76	1 05§	≤ 004
	(0 29)	(0 20)	(0 55)	(0 31)	(0 59)	
Suppressor cells (CD8)	0 31‡	0 27‡	0 34	0 33	0 46§‖	≤ 010
	(0 16)	(0 08)	(0 17)	(0 14)	(0 34)	

All values given as 10^9/mL. Numbers in parentheses represent standard deviation. Means are actual (observed) means of the untransformed variables. P values are from analyses of covariance of log transformed variables that controlled for sex, age, education, weight, allergic status, and number of hours of daylight on the first day of the study. Cell sizes for WBCs, monocytes, neutrophils, and lymphocytes are 346 for nonsmokers, 74 for ex-smokers >5 years, 54 for ex-smokers ≤5 years, 105 for current light smokers, and 105 for current heavy smokers. Cell sizes for T, B, helper, and suppressor cells for each of the smoking status groups are 85, 21, 16, 22, and 19 respectively.

* Mean differs significantly from the mean for ex-smokers ≤5 years (P< 05)
† Mean differs significantly from the mean for current light smokers (P< 05)
‡ Mean differs significantly from the mean for current heavy smokers (P< 05)
§ Mean differs significantly from the mean for nonsmokers (P< 05)
‖ Mean differs significantly from the mean for ex-smokers >5 years (P< 05)

In all but one case, the relationship between smoking status and cell counts was the same for men and women In the case of B cells, the gradient in cell numbers across smoking status categories held true for women but not for men: male smokers who quit within the previous 5 years had lower cell counts than did men who had never smoked.

Data on alcohol consumption were analyzed similarly Only the number of circulating lymphocytes was related to drinking rate Persons who consumed on average more than one drink per day had higher numbers of lymphocytes than those who drank less (P< 025).

DISCUSSION

As in earlier studies, we found similar smoking-related increases in all populations of peripheral WBCs. Most WBC counts were within normal limits Indeed, any person with unexplained leukocytosis would have been excluded from the study. The reason for smoking-associated increases in WBCs in peripheral blood is not clear. It is possible this is a manifestation of a cell trafficking phenomenon, with cells moving from other lymphoid organs to peripheral blood. or that smoking decreases the ability of these cells to adhere to endothelial cells lining blood vessels, resulting in high blood cell counts.

It is of particular interest that we found smoking-associated elevation in leukocyte counts as long as 5 years after cessation of smoking. Moreover, because we biochemically verified smoking status in this study, we can be confident that this group indeed is not currently smoking Thus, whatever the mechanism responsible for these changes, it persists long after smoke exposure is terminated

Consistent with earlier work, we found little relation between modest alcohol intake and WBC counts Only the number of lymphocytes was elevated in persons who drank on average more than one drink per day. The mechanism responsible for this effect is unknown It is possible, however, that alcohol triggers

the release of hormones that alter lymphocyte adherence to endothelial cells lining blood vessels. Overall, the evidence relating alcohol to susceptibility to bacterial infection is limited to studies in heavy drinkers. Our own work with this sample suggests that modest drinking is protective against upper respiratory tract viral infections.[6] The lack of association between alcohol consumption and number of leukocytes suggests that WBC counts do not provide a possible explanation for this lessened susceptibility.

A major implication of this work is that the means and distributions of WBC counts may vary among subgroups with somewhat different characteristics. Our results show that smokers, ex-smokers, and non-smokers compose such subgroups and that this information could be used to refine analysis for clinical or research purposes. If critical use is to be made of WBC counts, it is important to recognize that both current and past smoking behavior alter expected counts. Finally, it is interesting that, although the evidence for smoking-induced leukocytosis first was reported in the mid-1970s, many standard texts do not refer to it and many physicians practicing laboratory medicine are unaware of it.

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