Lymphocytic Subpopulation Profiles in Bronchoalveolar Lavage Fluid and Peripheral Blood From Tobacco and Marijuana Smokers*

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The effect of heavy, habitual marijuana use compared with tobacco smoking on the composition of bronchoalveolar and peripheral blood lymphocytic phenotypes was examined. Bronchoalveolar lavage (BAL) and peripheral blood (PB) samples were taken from 14 nonsmokers (NS), 14 tobacco smokers (TS), 19 heavy, habitual marijuana smokers (MS), and 9 marijuana and tobacco smokers (MTS). In BAL fluid, marijuana use was associated with significantly higher alveolar macrophage concentrations, whereas tobacco smoking was associated with significantly higher alveolar macrophage, as well as higher bronchoalveolar lymphocyte and neutrophil concentrations. The bronchoalveolar T-lymphocytic phenotypic profiles of marijuana users differed from those of tobacco smokers. Tobacco, not marijuana, was found to have a significant effect toward lower percentages of bronchoalveolar CD4 cells, toward higher concentrations of bronchoalveolar CD8 cells, and toward lower bronchoalveolar CD4:CD8 ratios. Marijuana use had a significant effect toward lower percentages of bronchoalveolar CD8 cells. In peripheral blood, marijuana, but not tobacco, use was associated with significantly higher percentages of CD4 cells, lower percentages of CD8 cells, and higher CD4:CD8 ratios. These findings suggest that tobacco and marijuana have effects on bronchoalveolar and peripheral blood immunoregulatory T-lymphocytic subpopulations that differ in type or magnitude.

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An abundance of epidemiologic and physiologic data have defined the consequences of tobacco smoking on lung health.1 Besides being the major determinant in the development of lung cancer and chronic obstructive pulmonary disease, tobacco use appears to increase the susceptibility to and severity of respiratory tract infections.1,2 Disorders caused by tobacco use may be the result of several mechanisms, including carcinogenic effects, direct irritation and damage within the respiratory tract, and impairment of local and systemic host defense mechanisms.1,3-9

Marijuana smoking continues to be a common practice among American adults and teenagers. Marijuana smoke contains many of the same toxins and irritants as tobacco smoke, as well as chemicals not found in tobacco, such as 9α-tetrahydrocannabinol (THC) and other cannabinoid compounds.10,11 Whether habitual marijuana use can lead to pulmonary disorders similar to those caused by tobacco smoking remains unknown.

Previous studies have demonstrated a variety of alterations that take place at the cellular level in association with smoking. Accumulation of inflammatory cells in the lower respiratory tract has been reported in both tobacco and marijuana smokers.4,6 Other studies have documented local and systemic T-lymphocyte abnormalities in tobacco smokers.4,12-17 Given the similarity of tobacco and marijuana smoke composition, it would be logical to question whether similar immunologic alterations are present in habitual marijuana smokers.

In this study, we compared the composition of bronchoalveolar and peripheral blood lymphocytic phenotypes in heavy, habitual marijuana smokers (MS), tobacco smokers (TS), and smokers of both marijuana and tobacco (MTS). We found distinct differences in the profiles of local and systemic T-lymphocyte populations in marijuana users compared with those of tobacco users.
METHODS

Subjects
Healthy adult volunteers aged 25 to 50 years were recruited by public notices and newspaper advertisements. Eligibility of potential subjects who responded was determined using a standard screening questionnaire. Entry criteria included the following: (1) white; (2) either no marijuana use in the previous 3 years or current heavy, habitual marijuana use (a history of smoking at least 10 joints per week or the equivalent for the past 5 years); (3) no history of illicit drugs injected intravenously or of illicit substances other than cannabis inhaled into the lower respiratory tract; (4) no history of potentially harmful occupational exposure; and (5) no known current cardiorespiratory illness.

Fifty-six subjects fulfilled the entry criteria. Each answered the study questionnaire which elicited a medical history and detailed information regarding past and present marijuana, tobacco, and other substance use. Serum cotinine levels taken previously from a broad sample of subjects responding to this questionnaire were found to have a high degree of correlation with the self-reported smoking status. Based on this information, the subjects were divided into 4 groups: (1) Nonsmokers (NS)—no tobacco or marijuana use in the previous 3 years (n = 14); (2) Tobacco Smokers—current tobacco smokers (at least one cigarette per day on a regular basis for 1 or more years), no marijuana use in the previous 3 years (n = 14); (3) Marijuana Smokers—current heavy, habitual marijuana smokers, no tobacco use in the previous 3 years (n = 19); and (4) Marijuana and Tobacco Smokers—current heavy, habitual marijuana and tobacco smokers (n = 9). Before study participation, written informed consent was given by each subject as approved by the UCLA Human Subject Protection Committee. Within 6 months prior to the day scheduled for bronchoalveolar lavage (BAL), pulmonary function testing, including spirometry, lung volume determination, and diffusing capacity, was performed according to a uniform protocol and with designated equipment.

BAL and Peripheral Blood Samples
Each subject underwent BAL after topical anesthesia with 0.45 percent tetracaine solution containing epinephrine, and, in some cases, intravenous premedication with atropine and diazepam. A total of 300 ml of sterile saline solution in 50-ml aliquots was rapidly infused into a right middle lobe segmental or subsegmental bronchus followed by immediate recovery of each aliquot with gentle manual suction. The first aliquot of recovered lavage fluid was discarded. Subsequent aliquots were pooled after being strained through a gauze sponge into test tubes containing Hanks’ balanced salt solution with 5 percent fetal calf serum and heparin. A peripheral blood (PB) sample was obtained immediately after BAL.

The cells recovered by BAL were washed and resuspended in RPMI-1640 medium (Grand Island Biological Co, Grand Island, NY) containing 5 percent fetal calf serum. An aliquot was taken for the following: (1) a hemocytometer count of the total number of cells recovered; (2) determination of cell viability by trypan blue exclusion; and (3) cytocentrifuge slide preparations stained with Giemsa and counted manually by examination of 200 cells. White blood and differential cell counts were performed on each blood sample by the UCLA Clinical Laboratory in the standard manner.

Identification of PB and BAL lymphocyte phenotypes was performed using the following fluorescein-labeled murine monoclonal agents (Becton-Dickinson, Mountain View, Calif): Leu-4 (CD3 or mature circulating T cells); Leu-3 (CD4 or helper/inducer T cells); Leu-2 (CD8 or suppressor/cytotoxic cells); and Leu-16 (CD20 or mature circulating B cells). The whole blood or BAL cell suspension was diluted with an equal volume of phosphate-buffered saline solution containing 2 percent newborn calf serum and 0.1 percent sodium azide, and incubated with medium containing fluorescein-labeled monoclonal antibody at 4°C for 30 min in the dark. The cells were then washed twice. The PB cells were suspended in ammonium chloride lysing solution, and 5 to 7 min were allowed for erythrocyte lysis. The PB and BAL cell preparations were analyzed in a flow cytometer (Spectrum II, Ortho Diagnostic Systems, Westwood, Mass). Lymphocyte populations were distinguished from monocytes and granulocytes by correlated analysis of forward and wide-angle scatter. On several occasions, a Leu-M3 marker was used to detect monocyte-macrophage lines and to determine the degree of contamination in the window analyzed. Leu-M3 positive cells comprised 0 to 1 percent of cells in these areas. Fluorescence data from 500 to 2,000 lymphocytes were analyzed to determine percentage of positive cells. Blood specimens from normal control subjects were analyzed with each daily run.

Total cell concentrations in the recovered BAL fluid were calculated and expressed as number per milliliter of recovered BAL fluid. Using the cell differential results, absolute concentrations of alveolar macrophages, lymphocytes, and neutrophils in the BAL samples were calculated. Concentrations of CD4-, CD4+, CD8-, and CD20-positive cells were calculated from the percentages determined by the fluorescein-labeled monoclonal assays. Data are expressed as mean value ± SEM.

Data Analysis
Because most of the outcome variables were not normally distributed, the data were log transformed before analysis. Analysis of covariance (ANCOVA) was used to investigate the differences in cell percentages and concentrations among the subject groups, with sex and age as covariates. One-way ANCOVA was used to compare all smoking categories (NS, TS, MS, and MTS). Multiple comparisons were performed by the Tukey-Kramer method. Two-way ANCOVA was used to determine the effects of tobacco and marijuana independently and the interaction between them. Correlation analysis was used to determine the presence of any cell percentage or concentration dose-response relationships with lifetime tobacco and marijuana smoking amounts, using pure tobacco and marijuana smokers, respectively. Correlations were also performed between FEV1/FVC and percent of predicted Dco, and each of the log percentages and concentrations of bronchoalveolar cells. Student’s t test was used to compare smoking amounts between marijuana and tobacco smoking groups and the volume of BAL fluid recovered among the four groups. A p value of less than 0.05 was considered significant for all statistical tests. Analyses were performed using SAS statistical software programs.

RESULTS

Subjects
The age and gender distribution and mean lifetime cigarette and marijuana consumption among the four subject groups are shown in Table 1. The mean ages and male-female ratios were similar among the four groups. The lifetime tobacco consumption was similar between TS and MTS, and both MS and MTS had heavy lifetime marijuana consumption. Although the number of “joint-years” was greater in MS, the amount consumed among individuals varied widely, and there was no statistically significant difference between the MS and
Table 1—Age, Gender, Marijuana Use, and Cigarette Use Among the Four Subject Groups

<table>
<thead>
<tr>
<th></th>
<th>Nonsmokers</th>
<th>Tobacco Smokers</th>
<th>Marijuana Smokers</th>
<th>Marijuana and Tobacco Smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>14</td>
<td>14</td>
<td>19</td>
<td>9</td>
</tr>
<tr>
<td>Mean age,* yr</td>
<td>35.5 ± 1.9</td>
<td>37.5 ± 2.0</td>
<td>35.4 ± 1.6</td>
<td>34.1 ± 2.3</td>
</tr>
<tr>
<td>Male-female ratio</td>
<td>10:4</td>
<td>11.3</td>
<td>13.0</td>
<td>8:1</td>
</tr>
<tr>
<td>Cigarette use, (pack-years)*†</td>
<td>—</td>
<td>22.7 ± 4.2</td>
<td>—</td>
<td>19.8 ± 5.7</td>
</tr>
<tr>
<td>Marijuana use, (joint-years)*†</td>
<td>—</td>
<td>—</td>
<td>85.3 ± 21.1</td>
<td>45.4 ± 9.7</td>
</tr>
</tbody>
</table>

*Data are expressed as mean ± SEM.
†“Pack-years” is the product of packs consumed per day times years of consumption. “Joint-years” is the product of joints consumed per day times years of consumption.

MTS groups.

**Cellular Analysis of BAL Fluid**

Table 2 shows the bronchoalveolar cellular composition in the four study groups. The percentages of alveolar macrophages (AM), lymphocytes, or neutrophils did not differ significantly among the four groups.

The highest mean cell concentrations were observed in the MTS group. Total cell and AM concentrations were significantly higher in TS, MS, and MTS compared with NS, and in TS and MTS compared with MS. Both TS and MTS had significantly higher concentrations of lymphocytes compared with NS. Although TS and MTS had high concentrations of bronchoalveolar neutrophils, only the comparison between TS and MS was significant. There was a significant effect of both tobacco and marijuana use toward higher AM concentrations (two-way ANCOVA). Tobacco use also had a significant effect of increased concentrations of bronchoalveolar lymphocytes and neutrophils.

There were no grossly apparent differences in cellular morphologic features among the four study groups, but AM from TS, MS, and MTS could be easily distinguished by the presence of engulfed particulate material.

Table 3 shows the mean percentages and concentrations of bronchoalveolar lymphocytic phenotypes in each of the four study groups. The percentage of bronchoalveolar CD4 cells was significantly lower in TS compared with NS, MS, and MTS, and in MTS compared with NS. In TS, the percentage of CD3 cells was significantly lower compared with NS, and the percentage of CD8 cells was significantly higher compared with MS. Figure 1 shows that TS had a significantly lower bronchoalveolar CD4:CD8 ratio compared with the other groups. Analysis by two-way ANCOVA confirmed a significant tobacco effect of lower percentages of bronchoalveolar CD3 and CD4 cells, and lower bronchoalveolar CD4:CD8 ratios. There was a significant marijuana effect of lower bronchoalveolar CD8 cell percentages (two-way ANCOVA). A significant interaction was found between tobacco and marijuana on the percentage of bronchoalveolar CD4 cells and the CD4:CD8 ratio. Among marijuana users, the tobacco effect of lower bronchoalveolar CD-4 cell percentages was less pronounced.

The concentrations of bronchoalveolar CD3 and CD8 cells were significantly higher in TS and MTS than in NS. The concentration of bronchoalveolar CD20 cells was greater in MTS compared with NS. Tobacco, but not marijuana use, was found to have

Table 2—Bronchoalveolar Cellular Composition in the Four Subject Groups (Data Expressed as Mean ± SEM)

<table>
<thead>
<tr>
<th></th>
<th>Nonsmokers</th>
<th>Tobacco Smokers</th>
<th>Marijuana Smokers</th>
<th>Marijuana and Tobacco Smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume recovered, ml</td>
<td>241.3 ± 2.6†</td>
<td>191.5 ± 12.2‡</td>
<td>217.7 ± 7.2</td>
<td>212.8 ± 13.9</td>
</tr>
<tr>
<td>Alveolar macrophages, %</td>
<td>89.2 ± 1.5</td>
<td>93.2 ± 0.5</td>
<td>92.6 ± 1.1</td>
<td>93.0 ± 1.4</td>
</tr>
<tr>
<td>Lymphocytes, %</td>
<td>10.0 ± 1.5</td>
<td>5.9 ± 0.2</td>
<td>7.0 ± 1.0</td>
<td>5.9 ± 1.3</td>
</tr>
<tr>
<td>Neutrophils, %</td>
<td>0.5 ± 0.1</td>
<td>0.9 ± 0.2</td>
<td>0.3 ± 0.1</td>
<td>0.8 ± 0.3</td>
</tr>
<tr>
<td>Total cells, × 10⁶/ml</td>
<td>113 ± 10*†‡</td>
<td>601 ± 106†‡</td>
<td>336 ± 54.0*†‡</td>
<td>807 ± 174†‡</td>
</tr>
<tr>
<td>Alveolar macrophages, × 10⁶/ml</td>
<td>99.7 ± 8.2*†‡</td>
<td>561 ± 99.7†‡</td>
<td>312 ± 50.9*†‡</td>
<td>745 ± 156†‡</td>
</tr>
<tr>
<td>Lymphocytes, × 10⁶/ml</td>
<td>12.1 ± 2.4*‡</td>
<td>31.9 ± 5.0‡</td>
<td>22.8 ± 4.2</td>
<td>51.3 ± 18.4</td>
</tr>
<tr>
<td>Neutrophils, × 10⁶/ml</td>
<td>0.6 ± 0.1</td>
<td>7.4 ± 2.7†</td>
<td>0.9 ± 0.3*</td>
<td>6.7 ± 3.4</td>
</tr>
</tbody>
</table>

*Denotes significant difference compared with tobacco smokers.
†Denotes significant difference compared with nonsmokers.
‡Denotes significant difference compared with marijuana smokers.
§Denotes significant difference compared with marijuana and tobacco smokers.
Table 3—Bronchoalveolar Lymphocytic Phenotypes in the Four Subject Groups  
(Data Expressed as Mean ± SEM)

<table>
<thead>
<tr>
<th></th>
<th>Nonsmokers</th>
<th>Tobacco Smokers</th>
<th>Marijuana Smokers</th>
<th>Marijuana and Tobacco Smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD3, %</td>
<td>78.8 ± 2.9*</td>
<td>66.8 ± 3.6†</td>
<td>73.3 ± 2.4</td>
<td>68.5 ± 2.8</td>
</tr>
<tr>
<td>CD4, %</td>
<td>52.2 ± 2.5* §</td>
<td>31.5 ± 3.4‡</td>
<td>47.1 ± 3.5*</td>
<td>41.0 ± 3.6*†</td>
</tr>
<tr>
<td>CD8, %</td>
<td>28.8 ± 2.4</td>
<td>36.7 ± 4.21‡</td>
<td>25.4 ± 2.7*</td>
<td>26.5 ± 3.2</td>
</tr>
<tr>
<td>CD20, %</td>
<td>3.5 ± 0.8</td>
<td>3.0 ± 1.1</td>
<td>4.5 ± 0.8</td>
<td>4.6 ± 1.1</td>
</tr>
<tr>
<td>CD3, × 10³/ml</td>
<td>10.1 ± 2.1* §</td>
<td>19.4 ± 2.5‡</td>
<td>18.1 ± 3.5</td>
<td>29.9 ± 11.7‡</td>
</tr>
<tr>
<td>CD4, × 10³/ml</td>
<td>6.6 ± 1.4</td>
<td>9.6 ± 1.8</td>
<td>12.7 ± 2.9</td>
<td>17.7 ± 7.3</td>
</tr>
<tr>
<td>CD8, × 10³/ml</td>
<td>3.7 ± 0.8* §</td>
<td>10.5 ± 1.5‡</td>
<td>5.1 ± 0.8</td>
<td>11.0 ± 3.8‡</td>
</tr>
<tr>
<td>CD20, × 10³/ml</td>
<td>0.3 ± 0.1‡</td>
<td>0.6 ± 0.2</td>
<td>1.0 ± 0.3</td>
<td>3.2 ± 1.5‡</td>
</tr>
</tbody>
</table>

*Denotes significant difference compared with tobacco smokers.  
†Denotes significant difference compared with nonsmokers.  
§Denotes significant difference compared with marijuana smokers.  
‡Denotes significant difference compared with marijuana and tobacco smokers.

A significant effect of higher bronchoalveolar CD3 and CD8 cell concentrations (two-way ANCOVA). Marijuana use had a significant effect of higher bronchoalveolar CD20 cell concentrations.

Correlation analysis demonstrated no significant relationship between the FEV/FVC ratio or percent of predicted Dco and any of the bronchoalveolar cellular or lymphocytic phenotypic percentages or concentrations.

**Cellular Analysis of PB**

Table 4 displays the mean percentages and concentrations of PB lymphocytic phenotypes in the four study groups. The percentage of PB CD4 cells and the PB CD4:CD8 ratio (Fig 1) were significantly higher in MS and MTS compared with NS and TS. Marijuana, but not tobacco use, had a significant effect in increasing the percentage of PB CD4 cells, decreasing the percentage of CD8 cells, and increasing the PB CD4:CD8 ratio (two-way ANCOVA).

No dose-response relationship of current or accumulated amount of marijuana or tobacco smoked with any of the bronchoalveolar or PB results could be demonstrated.

**DISCUSSION**

In addition to the chemical compounds responsible for its psychoactive effects, marijuana smoke contains many of the same respiratory toxins and irritants as tobacco. Previous studies have suggested that habitual use of marijuana produces many of the same effects as tobacco in causing respiratory symptoms and local inflammatory changes. Thus, the possibility that marijuana use could cause alterations of pulmonary immune and effector cells like those reported in tobacco smokers was a practical concern. This study was designed to compare the effect of heavy, habitual marijuana versus tobacco use on the profile of lymphocytic phenotypes in BAL fluid and PB. We examined four groups of carefully screened volunteers, who were comparable except for the history of habitual marijuana and/or tobacco use. Our findings indicate that tobacco and marijuana have different effects on lower respiratory tract and circulating T-lymphocyte subpopulations.

Analysis of our data confirms previous reports that both tobacco and marijuana use are associated with the accumulation of inflammatory cells in the lower respiratory tract. Increased concentrations of AM, lymphocytes, and neutrophils were observed among TS, and were particularly high in the MTS.
group. Marijuana use was associated with increased concentrations of AM, although the increase was less pronounced than with tobacco smoking. The light microscopic appearance of AM, many being particulate laden, was similar among TS, MS, and MTS.

Among the subjects studied, heavy, habitual exposure to marijuana smoke was not associated with the alterations of bronchoalveolar T-lymphocyte subpopulations observed in TS. Significantly lower bronchoalveolar CD3 and CD4 cell percentages, higher bronchoalveolar CD3 and CD8 cell concentrations, and lower bronchoalveolar CD4:CD8 ratios were associated with tobacco, but not marijuana use. These results confirm a previous report of altered bronchoalveolar T-cell subpopulations among TS. Our findings suggest that the accumulation of lymphocytes in the lower respiratory tract predominantly involves CD8 cells, leading to little increase in concentration of CD4 cells, so that the percentage of CD4 cells and the CD4:CD8 ratio are reduced. Such immunoregulatory abnormalities may contribute to disturbances of pulmonary defense mechanisms manifested by the predisposition to malignancy and infection. Our data suggest that these lymphocytic subpopulation alterations do not occur with marijuana use or are too small to be detected within our sample size.

The information currently available allows only speculative explanations for differences in bronchoalveolar T-lymphocyte subpopulation profiles between MS and TS. Several factors may play a role. First, constituents in tobacco smoke responsible for changes leading to lower BAL CD4 percentages and CD4:CD8 ratios may be absent or present in smaller amounts in marijuana smoke. Second, marijuana smoke may contain substances that counteract some of these local pulmonary effects. Our data would support this possibility in that there was a significant interaction between tobacco and marijuana effects on bronchoalveolar CD4 percentage and the relative proportion of CD4 and CD8 cells in which the tobacco effect was less pronounced in marijuana users. Finally, differences in quantity and pattern of cumulative exposure to tobacco smoke as compared with marijuana smoke may lead to different immunologic effects. The psychoactive effects of marijuana would discourage even heavy habitual users from smoking amounts of marijuana comparable to the quantity to tobacco consumed by the tobacco smokers examined in this study. It is possible that more intense exposure to marijuana smoke would have effects on bronchoalveolar lymphocytic subpopulations similar to those of tobacco.

Both marijuana and tobacco were associated with higher bronchoalveolar B-lymphocytic concentrations, although the increase was statistically significant only among the users of both substances compared with NS. Whether accumulation of B cells in the lower respiratory tract contributes to the local inflammatory changes that occur with marijuana and tobacco use would be of interest.

Our study also found marijuana and tobacco to have different effects on circulating T-lymphocyte subpopulations. Marijuana, but not tobacco use, was associated with increased percentages of CD4 cells, decreased percentages of CD8 cells, and elevated CD4:CD8 ratios in PB. Contrary to this observation, several previous reports have suggested that tobacco smoking is associated with altered circulating T-lymphocytic phenotypic profiles. Heavy TS have been noted to have reduced PB CD4 cell percentages compared with NS. Other studies that have examined large numbers of TS with varying amounts of consumption have reported a small, but statistically significant increase of CD4 cell percentage, and the CD4:CD8 ratio. In this study and another published previously, we also

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Table 4—Peripheral Blood Lymphocytic Phenotypes in the Four Subgroups
(Data Expressed as Mean ± SEM)

<table>
<thead>
<tr>
<th></th>
<th>Nonsmokers</th>
<th>Tobacco Smokers</th>
<th>Marijuana Smokers</th>
<th>Marijuana and Tobacco Smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD3, %</td>
<td>71.4 ± 2.0</td>
<td>76.6 ± 2.0</td>
<td>74.1 ± 2.4</td>
<td>69.7 ± 1.9</td>
</tr>
<tr>
<td>CD4, %</td>
<td>39.5 ± 2.3 +1</td>
<td>39.5 ± 3.4 +1</td>
<td>45.0 ± 2.1</td>
<td>44.6 ± 2.9 +1</td>
</tr>
<tr>
<td>CD8, %</td>
<td>31.6 ± 1.4</td>
<td>35.7 ± 3.6 +1</td>
<td>28.0 ± 1.6</td>
<td>25.2 ± 0.4 +1</td>
</tr>
<tr>
<td>CD20, %</td>
<td>9.1 ± 0.5</td>
<td>8.9 ± 0.5</td>
<td>11.1 ± 2.2</td>
<td>9.7 ± 1.5</td>
</tr>
<tr>
<td>Total lymphocytes × 10³/ml</td>
<td>1.7 ± 0.2</td>
<td>2.1 ± 0.2</td>
<td>1.7 ± 0.1</td>
<td>1.9 ± 0.2</td>
</tr>
<tr>
<td>CD3, × 10³/ml</td>
<td>1.2 ± 0.1</td>
<td>1.6 ± 0.2</td>
<td>1.2 ± 0.1</td>
<td>1.3 ± 0.2</td>
</tr>
<tr>
<td>CD4, × 10³/ml</td>
<td>0.6 ± 0.04</td>
<td>0.9 ± 0.1</td>
<td>0.8 ± 0.1</td>
<td>0.8 ± 0.1</td>
</tr>
<tr>
<td>CD8, × 10³/ml</td>
<td>0.6 ± 0.06</td>
<td>0.7 ± 0.08</td>
<td>0.5 ± 0.04</td>
<td>0.5 ± 0.1</td>
</tr>
<tr>
<td>CD20, × 10³/ml</td>
<td>0.2 ± 0.05</td>
<td>0.2 ± 0.02</td>
<td>0.1 ± 0.02</td>
<td>0.2 ± 0.02</td>
</tr>
</tbody>
</table>

*Denotes significant difference compared with marijuana smokers.
†Denotes significant difference compared with marijuana and tobacco smokers.
‡Denotes significant difference compared to nonsmokers.
§Denotes significant difference compared to tobacco smokers.
measured slightly higher CD4 cell percentages in TS, but the difference was not statistically significant. It is possible that in our smaller sample, we missed a significant difference due to a type II error. Thus, the difference we observed between marijuana and tobacco effects on percentage of PB CD4 cells may have been one of magnitude, rather than mechanism.

The practical significance of a study that examines cellular characteristics is dependent on the associated clinical impact. Immunologic alterations that have been observed in TS are of potential importance because of the correlation with well-documented adverse health effects. The present study suggests that frequent marijuana use may not have the same consequences on lung health as those from tobacco smoking. Understanding the importance of the cellular effects of marijuana will require additional epidemiologic information relating to the incidence of malignancy or infection in habitual marijuana users.

REFERENCES