Communications to the Editor:

Communications for this section will be published as space and priorities permit. The comments should not exceed 300 words in length, with a maximum of five references; one figure or table can be printed. Exceptions may occur under particular circumstances. Contributions may include comments on articles published in this periodical, or they may be reports of unique educational character. Specific permission to publish should be cited in a covering letter or appended as a postscript.

T-lymphocytosis in Bronchoalveolar Lavage Fluid of Hypersensitivity Pneumonitis

To the Editor:

We agree with Costabel et al (Chest 1984;85:514-18) when they state that "patients with recent hypersensitivity pneumonitis might be differentiated from active pulmonary sarcoidosis by the profile of BAL lymphocyte subsets." In a recent study, not yet published,1 we have done such bronchoalveolar lavages (BAL) in 15 patients with hypersensitivity pneumonitis (HP), ie, 5 farmer's lung and 10 pigeon breeder's lung diseases and in 28 patients with active sarcoidosis (SARC) in whom the activity was assessed by means of clinical criteria.2

Doing lavage with 250 ml of saline solution, analysis of OKT, and OKT, positive T-cells was performed by means of indirect immunofluorescence with fluorescein isothiocyanate conjugated goat-antimouse Ig on a flow cytofluorometer (Ortho - 50 OH). From our results (Table I), we would like to make some comments: with our technic the total number of cells and lymphocytes in BAL fluid was greater in HP than in Costabel's article with highly significant differences when compared to SARC (p<0.00) and p<0.0001, respectively). If we have roughly the same values for the mean proportion of OKT, and OKT, positive T-cells in BAL, however, the total number of OKT, positive T cells per 100 ml of BAL fluid was approximately twofold higher in HP than in SARC, which is in opposition to their results (p<0.02).

Using a flow cytofluorometer, one can work on a larger number of T-cells than with the immunoperoxidase slide assay, and this allows more accurate estimation of the T-cell subpopulations. This can explain variations between results already published. Looking carefully at data expressed in percentages and in total number of cells might be of great interest in separating active SARC and HP and could represent a good biologic test of diagnostic orientation.

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REFERENCES


To the Editor:

We have read with great interest the article by U. Costabel et al. Their study shows that suppressor cells are the predominant cell type in the bronchoalveolar lavage (BAL) fluid of antigen-exposed patients with hypersensitivity pneumonitis, while in patients not exposed for more than 5 days there is a relative increase of helper cells and a fall of suppressor.

By monoclonal antibodies of the OKT series, we studied T-cell subsets in BAL fluid of 13 patients with hypersensitivity pneumonitis and did not note an increase of helper cells in the patients not exposed to antigens for more than seven days. Our results are shown in Table I (top of page 154).

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Table 1—Characteristics of BAL Fluid

<table>
<thead>
<tr>
<th></th>
<th>Total cell count $\times 10^6$</th>
<th>Lymphocytes % of total cells</th>
<th>OKT,$^+$ % of lymphocytes</th>
<th>OKT,$^+$ % of cells per 100 ml $\times 10^6$ of fluid received</th>
<th>OKT,$^+$/OKT,$^-$ Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypersensitivity pneumonitis (n=15)</td>
<td>77±48</td>
<td>69±20</td>
<td>38±17</td>
<td>35±12</td>
<td>18±14</td>
</tr>
<tr>
<td>Active sarcoidosis (n=28)</td>
<td>41±27</td>
<td>43±17</td>
<td>52±18</td>
<td>27±34</td>
<td>10±9</td>
</tr>
<tr>
<td>Difference between groups*</td>
<td>p&lt;0.001</td>
<td>p&lt;0.00001</td>
<td>p&lt;0.002</td>
<td>p&lt;0.0002</td>
<td>p&lt;0.0002</td>
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*All data were expressed as mean value ± standard deviation. Comparison between groups was made with nonparametric Mann-Whitney test.
Table 1—Percentage of T-lymphocyte Subsets in Bronchoalveolar Lavage Fluid

<table>
<thead>
<tr>
<th></th>
<th>Lymphocyte % of Total Cells</th>
<th>OKTII⁺</th>
<th>OKT⁺</th>
<th>OKT⁺⁺</th>
<th>OKT⁺⁺⁺</th>
<th>OKT⁺⁺⁺⁺</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls (n = 6)</td>
<td>3.5 ± 1.4</td>
<td>71.8 ± 16.5</td>
<td>54.3 ± 9.8</td>
<td>36.1 ± 9.8</td>
<td>1.57 ± 0.52</td>
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<tr>
<td>Hypersensitivity Pneumonitis exposed (n = 9)</td>
<td>55.8 ± 20.4</td>
<td>91.5 ± 4.7</td>
<td>31.2 ± 11.2</td>
<td>66.3 ± 11.3</td>
<td>0.47 ± 0.22</td>
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<tr>
<td>Hypersensitivity Pneumonitis not exposed (n = 4)</td>
<td>45.2 ± 24.1</td>
<td>94.0 ± 2.1</td>
<td>33.7 ± 9.0</td>
<td>67.0 ± 8.3</td>
<td>0.47 ± 0.20</td>
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</table>

Significant difference between groups (t-test): A/B A/C A/B A/C A/B A/C

To the Editor:

We used a smaller lavage volume than Delaval et al (a total of 100 ml saline solution instead of 250 ml). This is why the recovery of total numbers of cells was smaller in our study. If we correct the recovery of cells for the instilled volume, the values of both studies are comparable. In our study, the greater number of cells and lymphocytes in hypersensitivity pneumonitis (HP) did not reach statistical significance compared to sarcoidosis (SARC) due to small case numbers and large SD. In the meantime, having enlarged our study population to 9 patients with recent HP and to 17 patients with active SARC, the difference is significant (t-test): total cell count (× 10⁶) in HP 42 ± 10, in SARC 25 ± 18, p < 0.01; lymphocytes (× 10⁶/ml recovery) in HP 519 ± 264, in SARC 207 ± 167, p < 0.01.

We cannot fully explain why we did not see the difference in the amount of OKT⁺⁺ cells between HP and SARC, as Delaval et al did. We think this might be due to different study populations (different criteria for defining active SARC) than due to a more accurate estimation of T-cell subpopulations by the method of Delaval et al. For example, our patients with SARC had a higher percentage of lymphocytes and a higher Tₜ/Tₜ⁺ ratio and thus more Tₜ⁺⁺ cells per ml BAL recovered than the patients of Delaval et al with SARC. The most obvious difference between both diseases, the 6- to 8-fold higher numbers of OKT⁺⁺ cells in BAL of HP compared to SARC was a joint finding in both studies.

Regarding methodology, we think there are clear cut advantages to our method, the immunoperoxidase slide assay, compared to immunofluorescence techniques. These are the use of a light microscope, the durability of the glass slide preparations, simultaneous information about cell morphology, higher sensitivity, and lower amounts of antisera and especially cells needed for this technique. Thus, by our method, we were able to study multiple surface markers in case of low BAL cell numbers and to report recently that normal smokers (who have only 2.5% lymphocytes among BAL cells) had a markedly decreased helper/suppressor cell ratio in BAL, but not in blood.¹

Finally, regarding the fact that there are no standardized protocols for BAL technique so far, we are pleased that our findings were widely confirmed by another independent group using different lavage procedures, a different technique for surface marker analysis, and maybe differently selected patients.

In response to Drs. Pesci, Bertorelli and Marchioni, we wish to point out that we wrote in our article: "In patients with hypersensitivity pneumonitis (HP) not exposed to antigens for more than five days, the OKT⁺⁺⁺/OKT⁺⁺⁺⁺ ratio may be increased." We are well aware that this limit of 5 days defined in our 8 patients is somewhat arbitrary, and that single cases may still have lowered OKT⁺⁺⁺/OKT⁺⁺⁺⁺ ratios also after this limit. On the other hand, one of the purposes of our paper was to show that there are serial changes in lymphocyte subpopulations of bronchoalveolar lavage (BAL) fluid during the course of disease, and that these changes consist of an increase in BAL helper (OKT⁺⁺⁺) and a decrease in suppressor (OKT⁺⁺⁺⁺) cells. That this concept may be true was recently confirmed by a fourth patient whom we were able to re-lavage after 2 years. His data are shown in Table 2. He actually followed the same pattern as the 3 patients who were re-lavaged and reported in our article under debate.

Another aspect is that we are often not completely sure whether patients with HP were really not exposed to antigens any longer. It may be that it also depends on the amount of antigens having entered the lungs as to how fast these changes in lymphocyte subsets will occur after avoidance of further antigen exposure. How long were the 4 patients studied by Pesci et al not exposed to antigens: for days, months, or years? Our patients were not exposed for 5 days (Tₜ/Tₜ⁺ ratio 3.0), for 6 days (Tₜ/Tₜ⁺ 1.3), for 14 days (Tₜ/Tₜ⁺ 1.3), and for 12 months (Tₜ/Tₜ⁺ 5.5), respectively.

Clearly, further studies are needed doing serial lavages in more patients with HP to answer these questions and to fully clarify the role of T cells subsets during the course of disease.

U. Costabel, M.D.; K. J. Bross, M.D.; H. Matthys, M.D., Medizinische Universitätsklinik, Freiburg, FRG

REFERENCE

ACTH Therapy in Status Asthmaticus

To the Editor:

ACTH therapy was effectively used during the past 8 years in treating 15 patients with status asthmaticus who failed to respond to intensive therapy which included IV hydration, O₂, adequate doses of IV aminophylline, massive doses of Solucortef, sympathomimetic drugs, and respiratory physiotherapy.

In case of failure of the patient to respond to an adequate dosage of a corticosteroid drug for at least 48 hours in the absence of acidosis,