Antinuclear Antibodies Associated with Pulmonary Involvement in Systemic Sclerosis

To the Editor:

Previous studies on antinuclear antibodies in systemic sclerosis (SSc) have described a high frequency of anti-Scl-70 antibodies in patients with diffuse cutaneous subset of the disease.1-4 Further, some authors have recorded that serologic abnormalities (such as circulating immune complexes, rheumatoid factor, anti-Scl-70 and antineuclear antibodies) may be associated with severe visceral involvement of SSc, including restrictive lung disease.5-11

In this study we report the association between serum autoantibodies with pulmonary abnormalities in SSc. We included 41 diffuse SSc patients (ARA criteria).1-4 Respiratory function tests and serologic studies were performed as previously described.12-16 Values of FVC and TLC less than 80 percent of predicted, FEV1/FVC less than 70 percent and MEF25 less than 60 percent of predicted were considered abnormal and indicative of obstructive, restrictive-ventilatory defects and disease of the small airways, respectively. Antinuclear antibodies were carried out by the standard indirect immunofluorescent test using mouse kidney monolayers, Hep-2 and Crithidia luciliae targets. Antibodies to Csl-70, nRNP, Sm, SSA(Ro) and SSB(La) nuclear antigens were determined by the Ouchterlony test using rabbit thymus and human spleen preparations.12

A summary of the results is shown in Table 1. The relation between the abnormal restrictive pulmonary function tests with positive fluorescent antinuclear antibodies, as well as the anti-Scl-70 antibodies reached significant values (p<0.001 and p<0.005 by x² analysis). In contrast, no association with anti-ssDNA or anti-nRNP antibodies was noted. Antibodies to dsDNA, Sm, SSA(Ro) and SSB(La) antigens and anticientromere antibodies were negative. Secondary Sjögren syndrome and pulmonary alterations were more frequent in the SSc group with a positive rheumatoid factor test,10 although the differences were not statistically significant. There was no relation with other SSc manifestations.

Antibodies to topoisomerase I (Scl-70) have been reported to be present in over 30 percent of SSc patients, and recently this figure appears to be more frequent in cases with severe disease, including a subgroup of limited scleroderma patients with prominent visceral manifestations.10-19

We have previously described that positive anti-Scl-70 antibodies occurred more frequently in SSc patients with slow progressive skin stiffness proximal to MCP joints sparing the trunk and in those cases with extensive skin changes all over the body.12-15 Also known as diffuse cutaneous SSc.14-15 Such analysis, like other reports,14 have focused primarily on the extent of cutaneous abnormalities as the major criterion of the disease severity. However, the search for factors that may lead to recognition of the population at risk of developing visceral manifestations in SSc is relevant, and some authors have emphasized that chromosomal instability, nail fold capillaroscopy changes,14-16 as well as serologic alterations including elevated levels of circulating immune complexes and rheumatoid factor are related to internal organ involvement.5,10

We report the association of anti-Scl-70 antibodies with restrictive lung disease, an organ involvement that may lower the survival rate and contribute to a poorer quality of life in SSc.5,14,15

Our findings showed a correlation between abnormal respiratory function and positive antinuclear antibodies similar to those reported previously.14 Further, SSc patients who had positive antinuclear anti-U3-RNP antibodies have also been related to more lung and heart involvement.11 Like these authors, we were unable to support a direct role of the autoantibodies in pathogenesis of pulmonary disease. However, experimental studies in SSc avian models may give an insight about the value of antinuclear or antineuclear antibodies in visceral damage. These studies have revealed that fluorescent antibodies' pattern changes from a cytoplasmic spider web or nuclear staining to diffuse and finely-speckled, as well as to peripheral and homogeneous nuclear staining with sera from avians, in which the disease turns to chronic multi-organ involvement.17 Autoantibodies production may also be increased by the high production of interleukin-2 that has been

Table 1—Association of Autoantibodies with Pulmonary Functional Abnormalities in Systemic Sclerosis

<table>
<thead>
<tr>
<th>Functional abnormality</th>
<th>Antinuclear antibodies (IF test)</th>
<th>Anti-Scl-70 antibody (Ouchterlony)</th>
<th>Anti-nRNP antibody (Ouchterlony)</th>
<th>Anti-ssDNA antibody (Hemagglutination)</th>
<th>Rheumatoid factor (Latex test)</th>
<th>% positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLC (&lt; 80% of predicted)*</td>
<td>69.2†</td>
<td>75†</td>
<td>33.3</td>
<td>37.5</td>
<td>55.5</td>
<td></td>
</tr>
<tr>
<td>FVC (&lt; 80% of predicted)*</td>
<td>76.9†</td>
<td>83.3†</td>
<td>33.3</td>
<td>25†</td>
<td>44.4</td>
<td></td>
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<tr>
<td>FEV1/FVC (&lt; 70% of predicted)</td>
<td>7.6</td>
<td>8.3</td>
<td>0</td>
<td>12.5</td>
<td>11.1</td>
<td></td>
</tr>
<tr>
<td>MEF25 (&lt; 60% of predicted)</td>
<td>15.3</td>
<td>16.6</td>
<td>8.3</td>
<td>12.5</td>
<td>11.1</td>
<td></td>
</tr>
<tr>
<td>SSc cases with and without functional abnormalities (n = 41)</td>
<td>31.7</td>
<td>29.3</td>
<td>29.3</td>
<td>19.5</td>
<td>21.9</td>
<td></td>
</tr>
</tbody>
</table>

IF = indirect immunofluorescent test
*All patients but one have both low FVC and TLC values
†p<0.001 and p<0.005 by x² test

To the Editor:

In response to Dr. Homasson, my comments are as follows:
1) My paper is about a personal experience with laser bronchoscopy only.
2) In the introduction, I mentioned a statement by Dr. Shapshay drawn from reference 1 of my paper.
3) I have no personal experience with that technique and therefore I am unable to judge Dr. Homasson's letter. I think Dr. Shapshay or Dr. Sanderson, who initiated cryotherapy, would be more competent in answering properly.

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described in SSc patients with pulmonary fibrosis or by spontaneous release of interleukin-1 since these alterations may enhance T helper cell function in antibody synthesis. This report emphasizes that antinuclear anti-Scl-70 antibodies may distinguish not only the diffuse cutaneous subset of SSc, but also patients at risk of developing severe lung disease.

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REFERENCES

Tuberculosis Screening In 1,161 Elderly Patients

To the editor:

The prevalence rates of positive purified protein derivative (PPD) skin tests in nursing home patients range from 10 to 41 percent. Anergy is responsible for very few nonreactors. Two-step PPD skin tests and chest X-ray examinations were performed in 1,161 elderly patients in two long-term healthcare facilities located in New York City. All tuberculin skin tests were given intradermally by a staff physician using PPD 5 units in 0.1 mL and read at 48 to 72 hours. If the induration was less than 10 mm at its greatest diameter, the test was repeated within 2 to 4 weeks. The PPD skin test was considered positive if induration ≥10 mm was measured on either of the two tests. Table 1 shows the prevalence of positive PPD skin tests in elderly patients at both facilities, separately and combined. Clinical tuberculosis was present in none of the 1,161 patients based on chest X-ray films taken at the Hebrew Home for the Aged, Riverdale and based on chest X-ray and sputum cultures for acid fast bacilli (when clinically indicated) at the Hebrew Hospital for Chronic Sick.

Two-step PPD skin testing minimizes confusing a subsequent true positive PPD skin test from a positive PPD skin test due to the booster phenomenon. Patients who convert to a positive PPD skin test with subsequent testing can be assumed to be newly infected. Since elderly patients in nursing homes have an increased risk of developing clinical tuberculosis, two-step PPD skin tests should be performed in all nursing home residents at admission and subsequently when clinically indicated.

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Table 1—Prevalence of Positive PPD Skin Tests in Elderly Patients in Two New York City Long-term Health Care Facilities

<table>
<thead>
<tr>
<th>Facility</th>
<th>No. of positive tests (total)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hebrew Hospital for Chronic Sick</td>
<td>34/321</td>
<td>7</td>
</tr>
<tr>
<td>Hebrew Home for the Aged at Riverdale</td>
<td>73/640</td>
<td>11</td>
</tr>
<tr>
<td>Both facilities</td>
<td>107/1161</td>
<td>9</td>
</tr>
</tbody>
</table>

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REFERENCES

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