Serum Mucoproteins in Pulmonary Tuberculosis and in Bronchopulmonary Cancer*

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Serum globulins are bound to carbohydrates in varied proportions. Thus, while alpha globulin is bound to half the total of carbohydrates, beta and gamma globulins are bound in smaller amounts. After Meyer, those serum proteins conjugated to carbohydrates which contain more than 4 per cent hexosamine are called mucoproteins, while the name of glycoproteins was the designation for those which contain less than 4 per cent hexosamine.

Important studies carried by Winzler and associates have shown that mucoproteins are polypeptides of a high molecular weight which contain: 15 per cent hexoses, 12 per cent hexosamines, 13 per cent lipids, 58 per cent proteins (0.50 per cent cystine, 2.10 per cent methionine, 1.8 per cent tryptophane, 4.2 per cent tyrosine). They are soluble in perchloric acid and precipitate with phosphotungstic acid. In paper electrophoresis, there is a coincidence in the mobility of mucoproteins and of alpha 2 globulin.

The serum contents in mucoproteins may be determined by their behavior in the presence of various reagents. One of the most frequently used procedures is that of Winzler and co-workers, in which the serum proteins are precipitated by means of perchloric acid; then the amount of tyrosine present is determined by means of Folin's reagent. Mucoprotein values may be expressed in mg. of tyrosine or by total values. If we remember that mucoproteins contain 4.2 per cent of tyrosine, we may multiply the conversion factor 23.8 by the tyrosine value in order to know total values.

In normal subjects, Winzler and Smyth found average values of 2.7 mg. of tyrosine. Greenspan and Dryling studied 185 normal subjects and found mucoprotein values which ranged from 39 to 80 mg. per ml. in men, and from 36 to 75 mg. per ml. in women (total values). Musajo and Mariotti found in 60 normal subjects average values of 70, 76 and 81.5 mg. (the older the subject, the higher the values). Marenzi et al. found average tyrosine values of 3.70±0.93 mg. (Table 1).

Material and Methods

We have determined mucoprotein values in healthy individuals, in patients who suffered from pulmonary tuberculosis and lung cancer. The tuberculous patients (all of them women, hospitalized in the Koch ward) had the diagnosis confirmed by bacteriologic findings; ten showed a deplorable general condition due to the extensive character of their lesions, while the remaining 117 had moderately advanced

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### Table 1—Average Values of Mucoproteins, as Expressed in Tyrosine According to Different Authors

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of Cases</th>
<th>Mg of Tyrosine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Winzler and Smyth (1948)</td>
<td>337</td>
<td>2.7</td>
</tr>
<tr>
<td>Jager, Brown and Nickerson (1951)</td>
<td>30</td>
<td>3.39</td>
</tr>
<tr>
<td>Berkman, Rifkin and Ross (1953)</td>
<td>15</td>
<td>3.7</td>
</tr>
<tr>
<td>Mancini and Garberi (1953)</td>
<td>26</td>
<td>4.06</td>
</tr>
<tr>
<td>Gomez (1954)</td>
<td>20</td>
<td>3.7</td>
</tr>
<tr>
<td>Marenzi, Gomez and Braegger (1955)</td>
<td>40</td>
<td>3.7</td>
</tr>
<tr>
<td>Pilheu, Iannello and Willson (1962)</td>
<td>37</td>
<td>3.025</td>
</tr>
</tbody>
</table>
clinical forms of tuberculosis. In all of the 114 lung cancer patients, diagnosis was confirmed by biopsy during bronchoscopy, during surgical operation or by necropsy.

The technique proposed by Winzler was followed, that is, values expressed in mg. of tyrosine per ml. of serum. Total mucoprotein values are obtained multiplying tyrosine values by the conversion factor 23.8.

**Results**

*Normal Subjects.* In 37 normal young adults, the mucoprotein values were relatively variable (Table 2). The values ranged from 1.88 to 4.58 mg., with an average of 3.025±0.658 mg. per 100 ml., as expressed in tyrosine. Total average mucoprotein value would be 71.89 mg. per 100 ml. serum.

*Moderately Advanced Pulmonary Tuberculosis.* One hundred seventeen patients were studied. Their average value is 2.99 ±1.23 mg. of tyrosine which corresponds to a total value of 71.16 mg. of mucoproteins per 100 ml. of serum. Extreme values were 1.02 and 10.26 mg., but 64 per cent of the total ranged between 1.98 and 3.90 of tyrosine.

*Severe Tuberculosis.* Only ten cases were studied. The values were above normal, with an average value of 4.74±1.525 mg. of tyrosine which are equal to a total of 112.81 mg. of mucoprotein. In some patients, several determinations were carried out, and it was observed that high values became lower as the condition improved.

*Bronchopulmonary Cancer.* One hundred fourteen patients were studied, in all of whom there existed histologic confirmation of the malignancy. Most values were found to be high; the average value was 5.69±1.39 mg. of tyrosine equal to 137.80 mg. of mucoprotein. The extreme values were 2.08 and 10.48 mg. of tyrosine while 69 per cent showed values which ranged from 4.60 to 7.96 mg. In some patients, we actually could carry out several determinations which showed the invariability of said levels.

**Discussion**

The mucoprotein values found by us in healthy subjects are very similar to those found by other authors in our country, as well as abroad. Nevertheless, there are differences which may be ascribed to method.

In *pulmonary tuberculosis*, significant variations may be found. When the disease is severe and there are extensive and highly destructive lesions, mucoprotein values rise and sometimes reach considerably high levels. In the ten cases of severe tuberculosis studied by us, the mucoprotein average value was much higher than in normal subjects; then as the condition subsides and stabilization sets in, mucoprotein levels slowly return to normal values. In the group formed by 117 patients under specific chemotherapy who were more or less stabilized, the serum mucoprotein average value was found to be similar to that of normal subjects. A similar disturbance is observed in serum proteins of patients with pulmonary tuberculosis; there are quantitative and qualitative modifications directly related to severity of the condition with normalization as the disease subsides. Thus, serum mucoprotein determination is a valuable method in assaying pulmonary tuberculosis, in assessing its activity, as well as establishing the prognosis. In cases of severe tuberculosis with higher than normal mucoprotein values, its improvement is
parallel to a decrease in the serum mucoprotein value. Several other authors have reported similar conclusions.6,11,13,14

Serum mucoproteins have also been studied in patients with diversely located cancer. High levels were found frequently. In 1948, Winzler and Smyth1 had already noted high levels of serum mucoproteins in a limited group of cancer patients. Seibert and colleagues10 also stressed this fact, as well as the modification in proteins in this category of patient. Musajo and Mariotti,4 in their study of 210 cancer cases which included the gastrointestinal tract, prostate, breast, etc. found high levels in almost all of them, specially when there were metastases. Cancer of the breast did not raise these values. When it is possible to remove the malignancy through surgery, values return to normal levels.

We have not found reports with special reference to bronchopulmonary cancer in the bibliography we consulted, and since we have the opportunity to examine many patients of this type, we undertook this study. We were not able to determine which patients had metastases and which had not at the time when the blood samples were drawn. The serum levels recorded were undoubtedly high when compared to those of normal subjects, and these high levels were persistently sustained, as shown by repeated determinations.

Based on our findings, we conclude that mucoprotein values are markedly high in severe pulmonary tuberculosis, as well as in bronchopulmonary cancer. Thus, it is only logical to agree with those observers who assert that extensive tissue destruction raises blood mucoprotein levels. This increased value persists in spite of its being present in such dissimilar diseases. The clinical and radiologic picture of severe tuberculosis and that of cancer are so different that the fact of having high mucoprotein levels in common almost never is a factor for confusion.

**Summary**

Serum mucoprotein levels were determined in healthy individuals, tuberculous patients and bronchopulmonary cancer cases by means of Winzler's technique.

In 37 healthy subjects, the average was 3.025±0.658 mg. of tyrosine per 100 ml. of serum.

In ten patients with severe tuberculosis the average was 4.74±1.525 mg. In 117 stabilized pulmonary tuberculosis patients, the average was 2.99±1.23 mg. of tyrosine.

In 114 cases of bronchopulmonary cancer the average was 5.79±1.39 mg. of tyrosine per ml. of serum.

The value of the determination of mucoprotein in evaluating the prognosis of these patients is considered.

**Resumen**

Por medio de la técnica de Winzler se determinaron las concentraciones séricas de las mucoproteínas en personas sanas y en enfermos de tuberculosis y cáncer broncopulmonar.

En 37 personas el término medio fue de 3.025 ±0.658 mg. tirosina por 100 ml. de suero.

En 10 enfermos con tuberculosis grave la media fue 4.74±1.525 mg. En enfermos de tuberculosis ya estabilizados (117 de ellos) fue de 2.99±1.23 mg. de tirosina. En 114 casos de cáncer broncopulmonar la media fue de 5.79±1.39 mg. de tirosina. El valor de la determinación de la mucoproteína para estimar el pronóstico de estos enfermos es motivo de consideración.

**Resumé**

Les taux de mucoprotéines du sér um furent déterminés pour des individus sains, des malades tuberculeux et des patients atteints de cancer broncho-pulmonaire au moyen de la technique de Winzler. Chez 37 sujets sains, la moyenne fut 3,025±0,658 mg. de tyrosine pour 100 ml. de sér um.

Chez 10 malades atteints de tuberculose grave, la moyenne fut de 4,74±1,525 mg. Chez 117 malades atteints de tuberculose pulmonaire stabilisée, la moyenne fut de 2,99±1,23 mg. de tyrosine. Dans 114 cas de cancer broncho-pulmonaire, la moyenne fut de 5,79±1,39 mg de tyrosine.

L'auteur envisage la valeur du taux de mucoprotéine pour établir de pronostic de ces malades.

**Zusammenfassung**

Es wurden Serum-Mucoprotein-Spiegel-Bestimmungen bei gesunden, tuberkulösen Patienten und Fällen mit bronchopulmonalem Krebs vorgenommen mit der Methode von Winzler. Bei 37 gesunden Personen lag der Durchschnittswert bei 3,025±0,658 mg Tyrosin auf 10 ml Serum.
Bei 10 Patienten mit schwerer Tuberkulose betrug der Durchschnittswert 4,74±1,525 mg. Bei 117 Patienten mit stabilisierter Lungentuberkulose lag der Durchschnitt bei 2,99±1,23 mg Thiazide. In 114 Fällen mit bronchopulmonalem Krebs betrug der Durchschnittswert 5,79±1,39 mg Thiosil. Die Bedeutung der Bestimmung des Mucoprotein-3 zum Erkennen solcher Patientengruppen wird diskutiert.

REFERENCES

For reprints, please write Dr. Pilheu, Juncal 3715, Buenos Aires.

MEDIASTINAL TERATOMA WITH LUNG ABSCESS

The patient was a 38-year-old man and had a ten-year history of cough and foul sputum. He had trichomycosis about ten years ago. His chest x-ray film revealed a sharply defined round shadow of about 13 cm. in the left lower field. Bronchogram, chest roentgenogram and bronchoscopy suggested that this shadow may represent an infected teratoma in the mediastinum communicating with the lower lobe of the lung. The mediastinal tumor and the lower lobe of the lung were resected under hypothermic anesthesia. The tumor measured 13x9x8 cm. and contained hair and a large quantity of pus. Clinical diagnosis was confirmed by the histologic examinations of the resected materials. Yamamoto, T. et al.: "A Case of Mediastinal Teratoma with Lung Abscess," Japanese J. Thor. Surg., 16:334, 1965.

ANTIHYPERTENSIVE DRUGS

The average blood pressure reading was significantly reduced by polythiazide (−21 mm. Hg) and by chlorothiazide (−16 mm. Hg) as compared to placebo values. Significant decreases unattended by symptoms occurred in concentrations of serum potassium and of plasma chlorides and in body weight, while statistically significant, but slight decreases occurred in pulse rate, serum uric acid, urea, and carbon dioxide levels during treatment with polythiazide. Polythiazide caused a greater mean increase in pulse rate and serum uric acid level, a larger decrease in level of serum chloride, and a slightly less loss of weight than did chlorothiazide, but these differences were not significant. The mean decreases in serum potassium were ident- 

cial (0.4 mEq per L) during treatment with polythiazide and chlorothiazide. No change occurred in levels of serum sodium and no consistent changes were noted in blood sugar levels. Only temporary reduction in dosage was required to reverse infrequent side effects of dizziness in the more responsive patients. Polythiazide appears to be a safe and effective addition to the increasing number of benzothiadiazide drugs. It does not possess any readily apparent advantages over other drugs of this group in the treatment of nonedefataneous hypertensive patients. Speckerman, R. E., Achon, R. W. F., Berge, K. G. and McGuickin, W. F.: "Antihypertensive Properties of Polythiazide and Chlorothiazide," JAMA, 184:125, 1963.