Experience with a tuberculosis antigen test in Rhodesia

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Cookson, J. B., Cruickshank, J. G., and Ellis, B. P. B. (1977). Thorax, 32, 616–618. Experience with a tuberculosis antigen test in Rhodesia. Experience with a new serological method for the diagnosis of tuberculosis is reported in a predominantly black population. We have found that in only 69% of 167 patients was there agreement between serology and the presence or absence of tuberculosis. Both false positive and false negative results were common. Of 47 healthy controls, 80% were positive. These results are less satisfactory than previous studies but differences in the reading of the results seems an unlikely explanation. Differences in the populations studied may be an important factor.

Tuberculosis is a common problem in developing countries, entering the differential diagnosis of most chest conditions. Diagnosis may be particularly difficult; Heaf testing is of limited value in populations with a high incidence of primary infection and sputum microscopy and culture requires considerable technical expertise. Thus the findings by Nicholls (Nicholls, 1975; Nicholls and Horsfield, 1976) that a simple serological method appeared to be a useful test for the disease was of great interest to us in Rhodesia. No reports have hitherto been published on the use of this test in a Black population.

In this paper we record our experience with this test on subjects in this country.

Methods

Sera were taken from 167 patients and from 41 healthy controls. Although the patients were largely those in whom tuberculosis was suspected or had been proved, some had a variety of other diseases. All those in whom tuberculosis was suspected were investigated by culture or biopsy of appropriate tissue. The diagnosis of active tuberculosis was considered proven either by positive culture or when a characteristic histological appearance, not necessarily with acid-fast bacilli, was seen in the biopsy specimen. Controls consisted of 10 healthy laboratory staff members who were not investigated further and 31 food handlers at a holiday resort who underwent clinical examination and had chest radiographs performed. All controls were followed up for at least one year. Sera were stored at −20°C without preservative. Antigen was prepared by Dr. A. C. Nicholls, of the Midhurst Medical Research Institute, as previously described (Nicholls, 1975), except that Mycobacterium tuberculosis H37Rv was used rather than the avirulent H37Ra strain. The agglutination tests were performed by the modified Widal technique as used by Nicholls et al. (1975). Titres were recorded as <1/125, 1/125, 1/250, 1/500, and 1/1250. A result equal to or greater than 1/125 was considered positive. Seven sera, of which the titres were at variance with the diagnosis, were sent to Midhurst for confirmation. Serial samples were not obtained.

The results are reported in a similar fashion to those of Nicholls and Horsfield (1976).

Results

In Table 1 subjects have been divided into five groups according to the results obtained. Group 1 are those with both proven tuberculosis and positive serology; group 2, those without proven tuberculosis and with negative serology; group 3, those with proven tuberculosis but negative serology; and group 4, those without proven tuber-
Of the 22 subjects in group 4, 10 were considered to have tuberculosis on clinical grounds and the remainder had a variety of non-tuberculous conditions. All had positive serology (Table 3). Group 5 contained 41 controls. None had developed clinical evidence of tuberculosis after a one-year follow-up period.

Identical titres were obtained in the seven paired sera which were sent to Midhurst for confirmation.

### Discussion

These results do not provide information as clinically useful as those of Nicholls and Horsfield (1976), who found a concordance between serology and culture results in 187 (87%) subjects; only 4 (2%) subjects had positive cultures but negative serology, and 24 (11%) had negative cultures but positive serology. In only 69% of our patients was there agreement between serology and the known presence or absence of active tuberculosis even though histological evidence was accepted as proof of the diagnosis. We did not perform serial estimations and it is possible that some subjects in group 3 (proven tuberculosis but negative serology) might have developed positive titres later. Those of group 4 (no proven tuberculosis but positive serology) who had clinical evidence of tuberculosis did not have higher titres than those who did not. Some may have had tuberculosis in addition to the primary condition, but only necropsy could establish this. The finding of positive titres in 80% of apparently normal controls is further evidence of the unpredictability of the test at least in our hands.

 Nicholls (personal communication) has suggested that the simple designation of a dilution of 1/125 as a positive result is less valuable than a
probability factor assigned to each dilution, this factor being the percentage of subjects with a titre of this magnitude from whom acid-alcohol-fast bacilli have been cultured. In Table 4 we have compared at each dilution the percentage of Nicholls’ subjects who were culture positive with the percentage of our own subjects (excluding the controls) who were either culture or biopsy proven. It will be seen that Nicholls finds that the higher titres are the more significant and that most subjects with low titres had negative cultures. We find some evidence that high titres are more significant than low ones but also find that many subjects with low titres had tuberculosis.

Table 4  Comparison of correlations between presence or absence of tuberculosis and titre levels in Midhurst (Nicholls, personal communication) and Salisbury

<table>
<thead>
<tr>
<th>Titre</th>
<th>Midhurst</th>
<th>Salisbury</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Percentage culture positive</td>
</tr>
<tr>
<td>&gt; 1/1250</td>
<td>55</td>
<td>96</td>
</tr>
<tr>
<td>1/500</td>
<td>119</td>
<td>87</td>
</tr>
<tr>
<td>1/250</td>
<td>797</td>
<td>81</td>
</tr>
<tr>
<td>1/125</td>
<td>1980</td>
<td>56</td>
</tr>
<tr>
<td>&lt; 1/125</td>
<td>5010</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>7961</td>
<td>25</td>
</tr>
</tbody>
</table>

These discrepancies might be accounted for by differences in the reading of results between the two laboratories. Nevertheless there was a good correlation when paired sera were sent to Midhurst for confirmation. Over-reading might explain the results in the control group and in group 4 (positive serology but tuberculosis not proven) but not those in group 3 (negative serology but proven tuberculosis). Under-reading would give the same problem in reverse. An alternative explanation may be the nature of the two populations. All our subjects except for the laboratory staff were Africans. Many, even those without proven tuberculosis, will have had a primary infection. Few will have received BCG. There may be other unknown differences in immunological status.

Most of our patients with proven tuberculosis were receiving treatment but Nicholls and Horsfield (1976) suggest that titre levels remain high, at least during the early months of treatment. In group 1 neither duration of therapy nor time of sputum conversion seemed to influence titre levels, which suggests that the negative titres in group 3 cannot be explained by these factors.

We conclude that in this population the test correlates insufficiently with the clinical state to be useful diagnostically at the present time.

We thank Dr. N. Baker, Mrs. F. E. Brand, and Mrs. J. M. Travers-Drapes for assistance.

References


Requests for reprints to: Dr. J. B. Cookson, Benenden Chest Hospital, Benenden, Cranbrook, Kent, UK.
Experience with a tuberculosis antigen test in Rhodesia.

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Thorax 1977 32: 616-618
doi: 10.1136/thx.32.5.616

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