The Open-Negative Tuberculous Patient

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Prior to the chemotherapeutic era, the presence of a persistent open tuberculous cavity required a guarded prognosis. Relapse rates of about 75 per cent were expected. It has been said that the majority of patients with persistent cavitation died within five years. However, the advent of isoniazid has resulted in modification of this concept.

The enthusiasm for resectional surgery, especially noted in the period between 1952 and 1955, provided an opportunity to compare patients whose lesions were resected with those who refused surgery. It was soon apparent that patients treated medically did as well as those treated surgically. The Veterans Administration-Armed Forces Tuberculosis Chemotherapy Cooperative Study 6—"Randomized Resection of Closed, Necrotic Lesions," was designed to answer this question for solid lesions, and at the February, 1957 Chemotherapy Conference, Raleigh reported—"There has been no significant difference in the incidence of relapse thus far between resected and nonresected patients in Pilot Study 6."

The same sequence of events occurred with patients having persistent cavities on chest x-ray film despite sputum bacteriologically negative for tuberculosis. Patients who refused resectional surgery did as well as those undergoing resection. Clinicians became reluctant to advise what appeared to be unnecessary resections. The present follow-up study of open-negative tuberculous patients was undertaken to learn how these patients fared subsequent to their discharge from the hospital.

A. Present Study

Sixty patients are the basis of this report. They satisfied the following criteria: (1) definite diagnosis of active tuberculosis with positive sputum and cavity on chest roentgenogram originally; (2) bacteriologic negativity for tubercle bacilli for at least six months prior to discharge (at least two sputum or gastric cultures were done each month); and (3) residual cavitation on chest x-ray film or planigram after six months of sputum negativity for tuberculosis. All patients received isoniazid, usually with para-aminosalicylic acid (PAS), and most continued on prolonged isoniazid (300 mg. daily) alone after sputum conversion. Twenty-five per cent of the patients have been followed for six years or more, either in the hospital chest clinic or at nearby health departments.

All but one of the patients were older than 30 years, and 78 per cent were older than 40 years (Table 1). Since most of the patients at this hospital are white men, this group was naturally the largest. There were 52 men and eight women. Fifty-four patients were white, five were Negro, and one was of Japanese descent.

Sixty-eight per cent of the 60 patients with "open-negative" tuberculosis were started on isoniazid therapy within six months of the diagnosis of tuberculosis, usually within one month (Table 2). Many patients in this group had extensive pulmonary disease as revealed by chest roentgenograms (Figures 1, 2 and 3).

Eighty-three per cent converted their sputum to negative within six months of


TABLE 2—MONTHS FROM DIAGNOSIS OF TUBERCULOSIS TO BEGINNING OF INH THERAPY

<table>
<thead>
<tr>
<th>Duration</th>
<th>Patients</th>
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<tbody>
<tr>
<td>1 month or less</td>
<td>33</td>
</tr>
<tr>
<td>2 months</td>
<td>4</td>
</tr>
<tr>
<td>3–6 months</td>
<td>4</td>
</tr>
<tr>
<td>More than 6 months</td>
<td>17</td>
</tr>
<tr>
<td>Unknown</td>
<td>2</td>
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institution of isoniazid. The median time for conversion was two months, with a range of less than one month to 30 months.

One patient suffered a relapse. He was 52 years old and his tuberculosis was first diagnosed in early 1959. At that time he was hospitalized for acute alcoholism, cough, fever and chest pain, and the chest film revealed extensive, bilateral infiltration with bilateral cavitation. Sputum con-

FIGURE 1

FIGURE 2

FIGURES 1 AND 2: Far advanced pulmonary tuberculosis with cavitation. Sputum and gastric cultures have remained negative for tubercle bacilli in these illustrative patients.
centrates and cultures were heavily positive for tubercle bacilli. He received isoniazid 300 mg. and PAS 12 gm. daily starting May 1, 1959. After positive sputum culture of November 19, 1959, there were 12 successive negative concentrates and cultures for tubercle bacilli from December 19, 1959 through May 5, 1960. Since he had had six consecutive months of negative cultures and his cavities persisted, he was classified as having open-negative tuberculosis and was subsequently discharged on June 27, 1960, to continue the isoniazid under the care of the local health department. Three weeks later, he was readmitted to the hospital with a diagnosis of aspiration pneumonia, secondary to acute alcoholism. He was acutely ill, very toxic, and expired within 20 hours. A sputum specimen secured prior to death was heavily positive for acid-fast bacilli on concentrate.

Three patients (two men and one woman) each had a single one-colony positive sputum or gastric culture for tubercle bacilli, followed by many negative cultures. All three patients have had no further difficulty with pulmonary tuberculosis. The two men are working and the woman is an active housewife.

Two patients expired. One was a woman 47 years of age whose sputum and gastric washings had been consistently negative for seven years prior to death, and the other was a man 40 years of age whose sputum had been negative for five years prior to death. Both expired with advanced pulmonary emphysema and cor pulmonale.

B. Discussion

Several reports have appeared in the literature recently with results substantially similar to the present series. Of 170 patients from five different series (Table 3), only one suffered a relapse, a rate of less than 0.6 per cent. Six of these 170 patients have died from cardiac disease without evidence of active pulmonary tuberculosis at necropsy. More recently, Pfuetze et al. have reported a different experience with 50 open-negative patients. Nineteen had one or two positive cultures after hospital discharge without any chest roentgenographic change. Four (8 per cent of their original group) had more than two posthospital positive cultures for tubercle bacilli and must be considered as relapses. All but two of these positive cultures were five colonies or less. Of the 40 patients reported by Wilson et al., 92 per cent became sputum negative after six months of chemotherapy, and 100 per cent were negative after 15 months of therapy. There were no relapses.

Table 3—Collected Data

<table>
<thead>
<tr>
<th>Patients</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>Wilson et al.³</td>
</tr>
<tr>
<td>23</td>
<td>Ryder⁴</td>
</tr>
<tr>
<td>32</td>
<td>Worobec⁵</td>
</tr>
<tr>
<td>15</td>
<td>Bosworth⁶</td>
</tr>
<tr>
<td>60</td>
<td>Present series</td>
</tr>
<tr>
<td>170</td>
<td>Total</td>
</tr>
</tbody>
</table>

FIGURE 3: Same as Figs. 1 and 2.
OPEN-NEGATIVE TUBERCULOUS PATIENT

SUMMARY
Evidence indicates that the open-negative tuberculous patient usually can be treated medically with prolonged administration of isoniazid, and without resection. Clinical results have been excellent and the relapse rate is amazingly low (only one patient in this group of 60 patients).

RESUMEN
La evidencia indica que el enfermo negativo abierto con tuberculosis puede generalmente ser tratado medicamente con isoniazida prolongada y sin reseccion.

La experiencia clinica ha sido excelente y la proporcion de recadas es notablemente baja (solo un enfermo en este grupo de 60).

RESUME
Il parait evident que les cas de tuberculose pulmonaire "ouverte-negative" peuvent etre traites par un traitement medical prolonge d'isoniazide et sans resection chirurgicale. L'experience clinique est excellente et les rechutes sont etonnant rares (une seulement pour un groupe de 60 malades).

ZUSAMMENFASSUNG
Es finden sich Anhaltspunkte dafur, daβ der offen-negative tuberkulose Patient gewohnlich konservativ behandelt werden kann mit lange gegebenem INH und ohne Resektion. Die klinischen Erfahrungen waren ausgezeichnet, und die Haufigkeit von Riickfallen ist verbluffend niedrig (nur 1 Fall in dieser Gruppe von 60 Patienten).

REFERENCES

PRECORDIAL CONTINUOUS MURMURS

Seven unusual experiences with continuous murmurs are recounted. Two patients had peripheral pulmonary stenosis, one had patent ductus arteriosus with intermittent disappearance of the murmur, one had an apparent venous hum, one tetralogy of Fallot with left pulmonary artery atresia and an anomalous branch of the innominate artery supplying the left lung, one a partial blockade to the left subclavian artery with a continuous murmur after exercise and one had aortic insufficiency and no adequate explanation for the murmur after extensive diagnostic work-up.

The cases described illustrate that, when a continuous murmur is found, evaluation of the general clinical status and location and timing of maximum intensity of the murmur may aid in differentiating the actual lesion present from patent ductus arteriosus. Continuous murmurs associated with severe pulmonary hypertension or cyanosis are not likely to be due to a ductus arteriosus; for when a ductus is the underlying basis of such signs, "atypical" auscultatory findings are generally present (systolic, diastolic or no murmur).

Continuous murmurs may be intermittent in an otherwise "typical" patent ductus arteriosus. They may also occur only when exercise produces inadequacy of the collateral circulation about a peripheral site of partial obstruction.