Nobody would now question the dramatic impact of chemotherapy on the overall picture of tuberculosis. This applies particularly to the fortunate countries where the balance between the disease and the public health services favors the side of the treasury. In areas where the disease is still very prevalent but where resources are minimal, progress is much less spectacular.

Early diagnosis followed by appropriate specific drug therapy for about two years is usually all that is required to achieve lasting results. The more scrupulously this chemotherapy program is carried out, the less need will there be for resorting to ancillary drug regimens or to surgery.

Tuberculosis remains a major public health problem in Hong Kong. In spite of the very remarkable decline that has taken place over the last decade, the death-rate still remains in the region of 40 per 100,000. Ambulatory chemotherapy constitutes the main line of management and the limited hospital facilities are reserved largely for patients who have failed on the standard drugs, who are potential candidates for surgery, or who have some other complication, medical or social, which renders them unsuitable for treatment on an ambulatory basis.

During the period 1961-1964, over 400 patients with pulmonary tuberculosis were treated surgically at the Ruttonjee Sanatorium. This paper refers to 208 of them. These were all failures on standard chemotherapy (streptomycin, para-aminosalicylic acid and isoniazid) and were sputum positive. They were chosen for analysis because they had, in addition, one common factor—they all received the same second-line drug regimen—a combination of pyrazinamide and ethionamide in preparation for surgery.

Most of the patients admitted to the Ruttonjee Sanatorium are candidates for second-line chemotherapy. If the diseased area appears resectable, especially if it contains obvious cavitation, the advisability of surgery is discussed. The majority of the patients do not have surgical treatment, however. In many of them the disease is far too widespread or the presence of emphysema etc. outrules the possibility of surgery. Others, whose disease is much less advanced, produce a satisfactory response to chemotherapy alone.

**Materials and Methods**

There were 208 patients in this series. All had active long-standing pulmonary tuberculosis and had failed on standard chemotherapy. About 80 per cent of them were between the ages of 20-40 years (Table 1); there were only two patients over age 50 years. Men accounted for 70 per cent of the group. They were all sputum-positive before surgery.

The indications for surgery (Table 2) were the commonly accepted ones, i.e., destroyed lobe or lung, persistent cavitation, unpredictable lesions and in a few patients, the predominant reason was recurrent hemoptysis. An additional indication common to the whole group was the fact that they had all failed to respond to standard drug therapy. It was the considered opinion that in all of these patients, surgery in conjunction with second-line chemotherapy would give better results than just second-line drugs alone.

The vast majority (131) of the patients had received standard chemotherapy for at least two years, but the disease process was not controlled and the sputum remained positive. Only 28 had received the drugs for less than one year, but because of persistent cavitation, it was thought advisable to submit them to resection. All the patients...
in the series were bacteriologically or clinically resistant to the standard drugs.

Before submitting these patients to surgery, it was the practice to prescribe a combination of pyrazinamide, 0.5 gm. three times a day and ethionamide 250 mg. twice a day for two or three months. An attempt was thus made to get the disease more under control and if possible to convert the sputum before operating. The sputum usually converted after about six weeks, but 63 patients were operated on a few weeks after starting the chemotherapy and so did not really get an opportunity to convert on the drugs alone. There were 45 who had the second-line drugs for as long as six months before surgery, but showed no tendency to sputum conversion. These were considered second-line drug failures.

Because of the more chronic nature of the disease in patients with drug resistant infections, lung function tests were carried out routinely before surgery. Those with a maximum breathing capacity lower than 30 liters per minute were excluded from this form of treatment. Those whose residual lung function was suspect, were also checked by bronchospirometry. All were bronchoscoped before surgery.

In 140 patients, lobectomy was performed. This included one who had lobectomy on the opposite lung some months later as she had bilateral cavitation. Pneumonectomy was performed on 38 patients and segmentectomy on 30.

Results

In 170 patients, the outcome of surgery was uneventful and the progress was satisfactory. We refer here to the remaining 38 patients who required further special attention. Postoperative complication necessitating a second thoracotomy occurred in 29 (14 per cent). In 12 of them, bronchopleural fistulas had developed and four of these had, in addition, an infected space.

<table>
<thead>
<tr>
<th>Table 1—Age Group</th>
<th>Grand Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Under 20  20-29 30-39 40-49 50-59 Total</td>
</tr>
<tr>
<td>Total</td>
<td>4 89 78 35 1 208</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2—Indications for Surgery</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Destroyed lobe or lung</td>
<td>50</td>
</tr>
<tr>
<td>Cavitated lesion</td>
<td>137</td>
</tr>
<tr>
<td>Non-cavitated unstable lesion</td>
<td>17</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>4</td>
</tr>
<tr>
<td>Grand Total</td>
<td>208</td>
</tr>
</tbody>
</table>

In four other cases, the persistence of a leak brought them back to the operating room. In all 16 patients, the defects were successfully repaired and there was no further untoward event. Eleven had a second thoracotomy because of postoperative hemorrhage. The scarcity of blood for transfusion was often the decisive factor in submitting patients to a second operation. The further course of these 11 patients was smooth. One whose right upper and middle lobes had been resected failed to get expansion of his lower lobe. This remaining lobe was therefore removed a couple of weeks after his first operation. One, who developed empyema, had thoracoplasty performed after drainage of the empyema. His further progress was satisfactory.

Mild jaundice, which was attributed to pyrazinamide, occurred in one after four months’ treatment. He recovered spontaneously on withdrawal of the pyrazinamide. His surgery was uneventful, but he was not given any more pyrazinamide.

In seven patients, there was failure to convert the sputum by surgery. Three of these, however, later converted on further chemotherapy (in two cases) or further surgery (in one case). The remaining four remain sputum positive to date and as they are already a couple of years after surgery, they are counted as treatment failures.

There was no operative or postoperative death in this series attributed to the surgery or to the disease, but one died three months after surgery from carcinoma of the liver. Its presence had not been detected before surgery. Repeated liver function tests, which were routine for patients on pyrazinamide, revealed no abnormality. He had not shown a favorable response to the
chemotherapy and his sputum converted only after surgery.

After discharge from hospital, usually about three months after surgery, patients continue their chemotherapy and attend the Follow-Up Clinic for routine check-up examinations. At the time of writing all patients are known to be making satisfactory progress except the four who remain sputum positive and the one who died from carcinoma of liver.

**DISCUSSION**

It is generally believed that the indications for surgical treatment of pulmonary tuberculosis are rapidly fading from the control program. In so far as standard drug therapy is successful, the place of surgery would obviously be expected to play a proportionately smaller part. When, however, the standard drugs lose their effect before the disease gets under control, the patient finds himself at a decided disadvantage. A survey was carried out by the Hong Kong Government and the British Medical Research Council (1964) to determine the incidence of drug resistance in Hong Kong. Their finding revealed that 20 per cent of the patients attending the Chest Clinics for the first time were producing organisms resistant to one or more of the standard drugs. These patients stated that they had not received any previous antituberculosis drug. Those who gave a definite history of previous chemotherapy on their first visit to the Clinics, showed a much higher incidence of drug resistance. In this group, 70 per cent were producing organisms resistant to one or more of the standard drugs. These findings indicate the difficulties liable to be encountered in the further management of large number of patients in Hong Kong. If they fail to derive benefit from second-line drugs and if their disease is not amenable to surgical treatment, their future is, indeed, in jeopardy.

The patients in the present series may be taken to represent those with the more chronic and irreversible forms of the disease. Many had histories of several years' duration and it was obvious that no radical radiologic change could be expected to take place by chemotherapy alone. It had been our experience with second-line drugs that patients with the most extensive disease showed the least response while those whose lungs were least involved fared best. We believe that the addition of surgery can make a marked difference to the chances of recovery when indications exist and the presence of resistance to the standard drugs calls for consideration of surgical treatment. At best, the second-line antituberculosis drugs are more expensive, more toxic and less acceptable to the patients over a long period.

In our series there were 45 patients who had failed to show any response to the second-line drugs even after six months. In our experience, patients whose sputa did not convert in the first couple of months' treatment either never converted or reverted to positive after a period. We believe that surgery had an even more pressing place in such patients even though the risk of complications may be greater. In addition to pyrazinamide and ethionamide, these “failed” cases were given an additional drug, i.e., kanamycin, cycloserine, etc., during the period of surgery. It was in this group that the seven patients failed to convert their sputa postoperatively.

The timing of surgery for patients with drug resistant infection can sometimes be difficult. On the one hand, one likes to get the disease process as much under control as possible before surgery and on the other hand, it is advisable, for obvious reasons, to do the surgery before the organisms have developed resistance to the second-line drugs. As it is the common practice to continue chemotherapy for a year or so after surgery, it is important that the organisms retain their sensitivity. In these patients with long-standing histories, there are often scattered residual areas of disease which are at least potential sources of reactivation.

The initial treatment of pulmonary tuberculosis with standard chemotherapy
seems very elementary, yet it is regrettable easy to fall by the wayside. Irregularity or intermittency in the administration of the drugs paves the way for untold, but largely preventable, trouble.

**Summary**

Resection for first line drug resistant pulmonary tuberculosis was performed on 208 Chinese patients in Hong Kong. The chemotherapeutic regimen prescribed as a surgical cover was a combination of pyrazinamide and ethionamide.

Recovery was uncomplicated in 170 patients (82% per cent). Second thoracotomy was performed on 29 patients for fistula or leaks (16); postoperative hemorrhage (11); unexpanded lobe (1); and empyema (1). Recovery in these 29 patients was thereafter uneventful.

There was no death attributed to surgery or to the disease, but one patient died three months postoperatively from carcinoma of the liver.

Jaundice attributed to pyrazinamide occurred in one patient after four months' treatment and the drug was withdrawn. The patient otherwise pursued an uneventful course.

The sputum remained positive postoperatively in seven patients, but three of these later converted. Four patients (2 per cent) failed to become sputum negative and so they are considered as treatment failures.

**Resumen**

En 208 pacientes chinos en Hong Kong afectos de tuberculosis resistente a las drogas primarias se practicaron resecciones quirúrgicas pulmonares. El régimen terapéutico de protección durante la etapa quirúrgica consistió en una asociación de Pirazinamida y Etnonamida.

En 107 pacientes (82%) el restablecimiento tuvo lugar sin complicaciones. Hubo necesidad de practicar una segunda toracotomía en 29 sujetos. Debido a fistulas en 16, a hemorragias postoperatorias en 11, a falt a reexpansión lo -bar en 1 y empiema en 1. Todos los 29 se restablecieron posteriormente.

No se registró muerte alguna debida a la tuberculosis o a la intervención quirúrgica, pero uno de los pacientes murió a las tres meses debida a cáncer del hígado. Hubo un caso de ictericia que sobrevino a los cuatro meses de iniciado el tratamiento con Pirazinamida y que se normalizó con la supresión de la droga, siguiendo después un curso favorable.

La expectoración continuó siendo positiva post-operatoriamente en 7 casos, 3 de los cuales divinieron mas tarde negativos. En cuatro casos no se logró la conversión del espusto, por lo que pueden ser considerados como fracasos terapéuticos.

**Zusammenfassung**

Be 208 chinesischen Patienten in Honkong, die gegen die Tuberkulostatika erster Ordnung resistent waren, wurde eine Resektionsbehandlung der Lungentuberkulose durchgeführt. Die chemotherapeutische Vorbehandlung, unter deren Schutz die Operation ausgeführt wurde, bestand in einer Kombination von Pyrazinamid und Ethionamid.

Bei 170 Patienten (82%) war die Heilung unkompliziert. Eine zweite Thorakotomie wurde an 29 Patienten durchgeführt wegen: Fistel oder Drainage (16); postoperative Blutung (11); atelektitischen Lungenlappen (1); und Empyem (1). Die Heilung dieser 29 Patienten war anschließend ungestört. Es trat kein Todesfall auf, der mit der Operation oder der Grunderkrankung in Verbindung stand, es starb lediglich - Patient 3 Monate postoperative an einem Leberkarzinom. Ein Ikerus, der auf Pyrazinamid zurückgeführt wurde, trat bei einem Patienten nach 4-monatiger Behandlung auf. Das Medikament wurde abgesetzt. Im übrigen war der weitere Verlauf bei diesem Patienten unkompliziert. Das Sputum blieb bei 7 Patienten postoperativ positiv, von denen 3 später negativ wurden. 4 (2%) wurden nicht negativ und wurden deshalb als therapeutischer Mißerfolg betrachtet.

**Referencia**


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