The Treatment of Pulmonary Tuberculosis Amongst Africans in Bulawayo

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PART II

Antituberculous Drug Therapy

Drug treatment schedules were based initially on those recommended by the Medical Research Council (Great Britain) trials of 1948 to 1955.[1] These incorporated the principles of giving two drugs together (never one singly), of giving adequate doses (streptomycin 1 gram daily; P.A.S. 20 grams if combined with streptomycin or 10 grams if combined with I.N.H., and I.N.H. 200 mg. daily). In addition, rotation of the three drugs in pairs at three-monthly intervals was practised as a measure to reduce the emergence of resistant strains.

It was recognised that the most potent combination therapeutically was streptomycin and I.N.H., with the combination I.N.H. and P.A.S. almost as good.

When in 1958 it became obvious that some patients were presenting with organisms already resistant to one or more drugs (either due to previous inadequate treatment or to initial infection with a resistant strain), the drug routines were further modified in that all the three drugs were given initially for a period. Thus treatment schedules during this period under review were modified to some extent with the passage of time.

At first, rotation of the three primary drugs (streptomycin, P.A.S., I.N.H.) was practised: then in 1956 out-patient treatment compelled the adoption of the combination P.A.S.-I.N.H. without rotation. Then in 1958, with the adoption of sputum cultures and resistance testing on all new patients admitted, treatment was initiated with all three drugs until the resistance test returned. Treatment was then reduced to two drugs in fully sensitive cases, although for in-patients the sequence of all three drugs for three months, followed by streptomycin and I.N.H. for a further three months before reduction to P.A.S. and I.N.H., was instituted. If a patient became an out-patient at an early stage, then he was placed on the P.A.S.-I.N.H. combination straight away.

Drug Resistance

Although from 1958 a sputum specimen from all new admissions was sent for culture and sensitivity testing, many of them were failures in that the organism failed to grow or was overgrown with fungal contaminants.

Of those tests reaching a successful conclusion, it was found that in many cases the laboratory report of resistance did not agree with the clinical findings. Many cases reported on as resistant did in fact respond to the drugs.

Thus in most cases the practical guide as to the presence of drug resistance remained the clinical one.

Drug resistance during this period was of course to the primary drugs—that is, streptomycin, I.N.H. and P.A.S. The secondary drugs used on drug-resistant cases during this period were Viomycin, Cycloserine and Terramycin.

Clinical resistance was viewed from two aspects. Firstly, there was the stage of suspicion of the presence of resistance. This was defined as when a patient failed to improve after six months' treatment (other factors excluded). Drug resistance was then suspected. Or when a patient under treatment relapsed after some initial improvement (other factors excluded), drug resistance was then suspected. At this stage any surgical measure contemplated would be carried out as soon as possible under secondary drug reinforcement cover and sputum cultures would be requested.

Secondly, there was the stage of confirmed clinical resistance—confirmed by time. This was defined as either persistent sputum positivity present in spite of one year's continuous adequate supervised treatment with the primary drugs, or as relapse of a patient whilst under continuous adequate supervised treatment with a sputum reverting from a negative to a positive state present continuously for six months.

The second stage was defined mainly to cover those cases not suitable for salvage surgery, and where secondary drugs were not available for treating them, in order to give a date on ethical grounds on which the primary drugs could be withdrawn.

In all cases a history of previous treatment was taken as a warning that drug resistance was likely to develop, and treatment would be planned with this in mind.

In January, 1959, there were 10 of these clinically-resistant cases in the wards, five of them having confirmatory laboratory reports. This number should be related to at least two years' admissions—that is, to at least 1,000 cases or 1 per cent. of admissions.

Out of the 10 cases, eight had a history of previous inadequate treatment at other institutions, mainly due to the patient absconding. One had a history of previous inadequate treatment at Mpilo due to absconding and the tenth patient had no previous history of treatment and might well have been infected initially with a resistant strain.

Other Non-Specific Drugs Used in Treatment

As a routine, all cases on admission received vitamin supplements and iron for the first month. Thereafter these were continued as indicated on clinical grounds and by haemoglobin estimations. Cortisone was used on severely ill patients on admission, usually for one to two weeks, selection of patients and duration of treatment being dictated largely by availability of the drug. The occasional lung case with meningitis would receive longer treatment with cortisone of a month or more. Largactil became the routine treatment for all cases showing psychotic tendencies.

All patients had a stool and urine examination as a routine on admission and received appropriate treatment for any worm infestation found.

Duration of Treatment

Drug treatment with the specific drugs was continued without interruption until the patient's disease was quiescent and, to minimise relapse, for an additional period of nine months after quiescence. Quiescence was defined at Mpilo as follows:

(a) Sputum had become and remained negative for three consecutive months. Each month a minimum of three stained smears were examined.

(b) Radiologically the disease had improved and reached a stationary phase present for three months.

(c) Clinical state and serial monthly weight and E.S.R. estimations had similarly improved and reached a stationary phase.

To reach this stage required from six to 12 months. To this was added the extra period

of nine months, bringing the average total treatment to 18 months.

Additional treatment of a further three months or so would be given to cases with residual cavitation or gross destruction and to patients whose work involved a high risk to others, such as teachers and bus conductors. After completion of treatment the case was followed up with three-monthly examinations of chest X-ray, sputa, weight and E.S.R., increasing to six-monthly. After two years of surveillance following quiescence the case was labelled "arrested"; after five years of quiescence it was labelled "recovered." Many of our patients successfully attended for review over the years and are now in their fourth and fifth year of surveillance.

As was to be expected, however, when Mpilo first opened in 1954 there was great difficulty in persuading the patients to remain even three months in hospital, although, surprisingly enough, they were quite happy to come back for follow-up reviews. Gradually the patients were educated to accept longer and longer periods of hospitalisation. In September, 1955, the average duration of treatment (over the period January, 1955, to June, 1956) was male 4.1 months and female 6.3 months each. As a measure of the acceptance of treatment over this period of January, 1955, to April, 1956, when the average time spent in hospital of all patients was six months or less, the following figures relating to absconding patients are of interest:—

	Male	Female
Patients absconding	14 (7.2%)	2 (4%)
Normal discharges	180	47

In 1958 the average treatment in hospital (where treated from beginning to end as an in-patient) had crept up to 18 months. The numbers then absconding from all centres in Bulawayo were 24 males and 38 females, which, related to 588 discharges in the year, gives a percentage of 10 absconding.

The rise of 3 per cent. or so in the absconding rate is thus balanced against a 200 per cent. increase in the length of time spent in hospital.

Bed Rest

In 1954 and 1955 bed rest was considered an important aspect of treatment, and at Mpilo a strict sanatorium regime was enforced. This involved total bed rest initially, proceeding through various stages of up periods combined with rest periods to full ambulation. Toilet privileges were allowed, however, to all except the very ill patient.

In 1955, owing to pressure on beds, the out-patient treatment of patients with homes in Bulawayo was commenced. Two streams of patients thus developed: those who were retained in hospital throughout and were subjected to a more physically restful though regimented life, and those who after a preliminary period in hospital were discharged to out-patient treatment involving possibly long walks to hospital, certainly day-long ambulation in the home, combined with a sub-normal diet and other adverse living conditions.

It gradually became obvious that these out-patients, in spite of their grim handicaps, progressed to just as satisfactory an end-state as the in-patient. The eventual end result was the same, although it appeared to require an extra few months of treatment for the out-patient to reach this state than for the in-patient.

As a result of this observation measures were relaxed to some extent. Patients were allowed up for longer periods and at an earlier state.

Postural Retention or Recumbency

This procedure was practised extensively in 1954 and 1955. The patient was arranged in bed so that any unilateral cavity was placed in the most dependant position. Deflation of the cavity was accelerated and the spread of infection to the contralateral side minimised.[2]

Gradually, as confidence grew in the effectiveness of the primary anti-tuberculous drugs, and coincidental with the relaxation in bed rest, this measure fell into disuse, except occasionally as an attempt to control persistent bleeding from a cavity.

As with a pneumoperitoneum, however, the procedure is being resurrected and its use is now indicated in some drug-resistant cases.

Pneumoperitoneum

In 1955 a pneumoperitoneum, combined with a phrenic crush when indicated, was carried out almost as a routine on all admissions. The procedure was thought to benefit all cases by "cooling down" the acute disease and to benefit specifically cavitated disease of moderate size,

particularly those in the apex of the lower lobe and in the posterior segment of the upper lobe.

Gradually it became obvious that the drugs alone, combined with postural retention where necessary, could achieve equally good results without the aid of a pneumoperitoneum. Consequently in 1956-57 the pneumoperitoneum was abandoned as a general measure and only used selectively with a phrenic crush to attempt closure of cavities persisting after a reasonable trial of chemotherapy and bed rest. In 1957-58, as further confidence was gained in the benefits of these anti-tuberculous drugs, the use of a pneumoperitoneum in persistent cavities was abandoned, for evidence accumulated that many of these cavities could be rendered sterile by prolonged chemotherapy and the danger of relapse consequently reduced.

The main use now for a pneumoperitoneum is in the control of persistent haemoptysis and in drug-resistant cases.

Artificial Pneumothorax

In the period 1955-58 artificial pneumothorax was used selectively in suitable cases to control persistent apical cavitation. With the advent of chest surgery there was no longer a need for this use of an artificial pneumothorax. Resection was employed in its place. Only recently the only remaining case of a pneumothorax at Mpilo was abandoned after four years of refills. He was a school teacher who refused surgery for his persistent upper lobe cavitation.

Surgical Treatment

Surgical treatment for pulmonary tuberculosis at Bulawayo was mainly that of lung excision. Because of the possible danger of antagonising African opinion, thoracoplasty operations were not advocated. Even so, however, the majority of the patients refused resection when offered, perhaps one in six accepting.

Two streams of "surgical" patients thus developed. There were the few cases who accepted surgery when offered. This included those with persistent cavitation or destroyed lobes or lungs on one side, with no disease or controlled minimal disease in the contralateral lung. Sputum would be negative following nine to 12 months of chemotherapy. Resection of the residual disease would be carried out and drugs continued for a further 12 months. Then there would be the other stream of patients with similar lesions who would be offered surgery, but who would refuse to have the operation. These cases would then continue with their drugs alone.

After a time it became apparent that the group of "surgical" patients refusing surgery appeared to fare as well as those who accepted surgery as judged by general well-being, by time of return to work and by relapse rates as judged over two or three years.

Consequently, in drug sensitive cases, the attitude adopted was to recommend surgery to the patient where this was indicated. Should the patient refuse surgery, then there was no great disappointment, as it was felt that perhaps the alternative of drugs alone might offer him almost as good a prognosis.

With drug-resistant cases, however, the position was different. Surgery in many cases might offer the only hope of cure and in others might offer the only hope of attaining sputum negativity, even if only temporarily.

So in cases with drug resistance to two or three of the primary drugs, surgery where feasible would be advocated. In cases where drug resistance was only threatened and not yet established (gross unilateral disease showing no response to treatment after three to six months), surgery would be seriously considered at an earlier stage than in the above clean cases.

Unfortunately the drug-resistant case was not usually suitable for resection, the disease being too widespread in both lungs.

Taking all the above factors into account, it is understandable how, out of 572 cases admitted in 1959, only five patients eventually reached the operating table. Four of these were men and one was a woman. Out of the five, four were fully drug sensitive and one was a drug-resistant case.

Response to Treatment as Judged by Cavity Closure and Sputum Conversion

Cavity Closure

In 1956 all X-ray plates of patients who had completed their treatment for pulmonary tuberculosis and were filed under the letters A, B, C and D were examined. Out of 55 sets examined, 28 had cavities on admission to hospital.

Of these 28 sets, 21 (75 per cent.) closed on medical treatment as revealed by posterio-anterior and lateral films; three cases failed to close and four cases were doubtful.

The average time of closure was four months. One case closed at one month, another at 11 months. The maximum number closed at three months. These figures, though small, tally fairly closely with other published results of that period. For example, Hoyle and Nicholson [3] in England obtained 70 per cent. closure and Tyrell [4] in Glasgow 65 per cent.

Sputum Conversion

At Mpilo every patient has three sputa examined each month by the Ziehl-Neelsen technique with a standard five-minute search. When all three sputa are negative on three consecutive months the patient is labelled sputum negative.

In 1956 the notes of all patients admitted to hospital between 1st December, 1955, and 31st May, 1956, were examined. Out of 87 records, 46 (53 per cent.) were found to be sputum negative after three months' treatment and 92 per cent. after six months' treatment. The bulk of the conversion occurred during the second, third and fourth months.

Hoyle and Nicholson found 74 per cent. sputum negative at three months, 84 per cent. at six months and 92 per cent. at nine months. The Medical Research Council [5] in England found 75 per cent. negative at three months.

As confidence grew in the response of the patient's lesion to the anti-tuberculosis drugs, it was usual to expect every patient's sputum to become free of the organism. If, after a year's treatment, sputum conversion had not occurred, drug resistance was invariably the cause.

Out-Patient Treatment of Active Pulmonary Tuberculosis

In January, 1956, treatment of active cases of tuberculosis as ambulant out-patients was commenced so that the ever-increasing pressure on the beds could be relieved.

Naturally, only those patients with some sort of home in Bulawayo could be treated as out-patients and this greatly limited the field. On an average about 60 per cent. of the patients on admission were domiciled in Bulawayo, the rest being from rural areas. Of these 60 per cent., not all could return to their original home after a stay in hospital, but a surprisingly large proportion of them did manage to find accommodation with friends or relatives, and in our need we did not enquire too closely into the suitability of these homes.

Help was given to these out-patients and their dependants by the Government through the native commissioner by the distribution of minimum subsistence rations and by the issue of bus warrants. The municipalities helped with rent remissions where patients were municipal householders, and the Red Cross and R.A.P.T. and the African Welfare Society helped where they could with clothing and fuel.