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HOSPITAL TREATMENT OF PULMONARY TUBERCULOSIS

A FOLLOW-UP STUDY OF PATIENTS ADMITTED TO EDINBURGH HOSPITALS IN 1953

BY

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This paper reviews the outcome of all cases of adult pulmonary tuberculosis admitted in 1953 to the three tuberculosis hospitals within the City of Edinburgh. The patients have been followed up to the end of 1956, and have therefore been observed for three to four years. Most admissions came via the main chest clinic, which at that time had its own medical staff carrying no responsibility for hospital beds. Waiting-lists were long, and before admission many of the patients had received treatment by regimes of chemotherapy which would now be regarded as undesirable. This accounts for the presence of drug resistance in a significant proportion of the admissions. An element of selection operated because of the size of the waiting-list. Patients responding well to domiciliary and clinic care were not usually admitted to hospital; disappointing clinical response or compelling social factors were often the indication for admission. Some of the patients were admitted virtually moribund.

A reorganization of the tuberculosis service in Edinburgh was being planned in 1953 and came into effect in 1954 (see Discussion). As a step in this reorganization all the patients admitted in 1953 remained after their discharge under the supervision of the clinicians responsible for their hospital care.

The 305 patients studied comprise 156 males and 149 females. The youngest patient was aged 11. Table I shows the age distribution of the patients and

TABLE I.—*Age Distribution and Extent of Disease of Patients With Pulmonary Tuberculosis Admitted in 1953 to Edinburgh Hospitals*

Extent of Disease	Age in Years						All Ages
	11-19	20-29	30-39	40-49	50-59	60+	
Far advanced	14	26	33	24	18	17	132
Moderately advanced ..	16	57	28	27	11	4	143
Minimal	3	13	9	4	1	0	30
All cases	33	96	70	55	30	21	305

the extent of their disease (classification of National Tuberculosis Association of America*). The condition of the patients and their progress since discharge was assessed as at December 31, 1956. If patients had left the area up-to-date information was requested from the

clinician to whose care they had passed. There were five patients whose follow-up was incomplete, and these had been observed for periods varying from 11 to 24 months. The remaining patients had been under observation for three to four years.

Bacteriology

On admission at least three specimens of sputum were examined by smear and culture. If sputum was unobtainable laryngeal swabs or gastric lavage specimens were cultured. Positive cultures were submitted to tests for sensitivity to streptomycin, P.A.S., and isoniazid.

Positivity.—Of the 305 admissions 251 (82%) were bacteriologically positive before treatment. It is probable that this percentage would have been higher had not some patients received drugs before admission to hospital with less adequate preliminary bacteriological search.

Drug Sensitivity.—At the time of admission the organisms of the 251 patients with positive bacteriology showed the following sensitivities: sensitive to three standard drugs (streptomycin, P.A.S., and isoniazid), 190; resistant to one of the drugs, 30; resistant to two of the drugs, 19; resistant to three of the drugs, 8; undetermined, 4. Drug resistance could be explained on the basis of unsatisfactory previous chemotherapy in all but eight patients, in whom no history of previous drug treatment could be elicited. It was assumed that they had been infected by a drug-resistant organism. All of these eight patients (3.2% of the cases with positive sputum) had organisms resistant to P.A.S., and the organisms of two were also resistant to streptomycin.

*N.T.A. Classification (1950):

Minimal.—"Slight lesions without demonstrable excavation confined to a small part of one or both lungs. The total extent of the lesions, regardless of distribution, shall not exceed the equivalent of volume of lung tissue which lies above the second chondro-sternal junction and the spine of the fourth or body of the fifth thoracic vertebra on one side."

Moderately Advanced.—"Slight disseminated lesions which may extend through not more than the volume of one lung or equivalent in both lungs. Dense and confluent lesions which may extend through not more than the equivalent of one-third the volume of one lung. Total diameter of cavities less than 4 cm."

Far Advanced.—"Lesions more extensive than moderately advanced."

Treatment

Hospital Stay.—In December, 1956, four of the admissions of 1953 were still in hospital. Among the patients discharged the average stay was ten months.

Chemotherapy

All patients, with seven exceptions, received chemotherapy. One of the exceptions had been rendered resistant to P.A.S. and isoniazid before admission, and it was thought wise to carry out thoracoplasty without hazardous streptomycin in case resection should subsequently prove necessary. The thoracoplasty controlled the disease. One patient had minimal disease adjudged probably inactive, and drugs were withheld. This patient subsequently relapsed. Five other patients, in a moribund condition when admitted, died without receiving drugs.

Where the patient's organisms were sensitive to the main drugs, regimes of chemotherapy did not differ appreciably from those we use currently. The usual combinations were: (1) Streptomycin 1 g. daily + sodium P.A.S. 5 g. four times daily. (2) Streptomycin 1 g. daily + isoniazid 100 mg. twice daily. (3) Isoniazid 100 mg. twice daily + sodium P.A.S. 10–20 g. daily (two or four doses of 5 g.). (4) A combination of all three drugs, usually as the initial treatment pending the results of sensitivity tests; if these proved satisfactory either streptomycin or P.A.S. was stopped.

In some cases streptomycin was given intermittently (twice or thrice weekly) in combination with daily P.A.S. We have since abandoned this practice, as we believe it carries the danger of the patient's organisms becoming resistant first to P.A.S. and then to streptomycin. There is published evidence of the danger of giving streptomycin intermittently with isoniazid (Medical Research Council, 1953).

In some patients we were faced with the problem of resistance to both streptomycin and P.A.S. In these cases isoniazid was combined with oxytetracycline. The combination of viomycin and oxytetracycline was used for patients resistant to all three of the standard drugs.

Our chemotherapeutic management differed in one important respect from our current practice in that some patients were given drugs for shorter periods than we would now regard as advisable. The importance of this emerges in the study of relapses (see below).

Minor Collapse Procedures

Five patients (less than 2% of all patients) received treatment with artificial pneumothorax, and 31 (10%) had a pneumoperitoneum induced as a definitive measure and not merely as a preliminary to major surgical measures.

Major Surgery

During their first period of hospital treatment 122 patients (40% of admissions) underwent major thoracic surgical procedures. They comprised 54 males and 68 females. Thirty-four (28%) were over 40 years of age, and eight (7%) over 50. Of those with far-advanced disease 42% received major surgery, the figures for those with moderately advanced and minimal disease being 44% and 13% respectively. Twenty-two patients had organisms resistant to two drugs or more at the time of surgery. Among the 122 surgically treated cases there were 102 who underwent single procedures; of the 20 patients undergoing multiple procedures nine had surgery directed to both lungs.

The operative procedures, numbering 144, were: 1-stage thoracoplasty, 50; 2-stage thoracoplasty, 4; pneumonectomy, 8; resection of a lobe or more, 37; resection of segments or less, 43; resection of empyema and portion of lung, 2. Six of the thoracoplasty operations were carried out as a preliminary to planned later resection. Thoracoplasty was required in two patients to close a residual space after resection.

Only surgical measures carried out during the first admission as a patient in 1953 are included in the above analysis. Eight patients were submitted to surgery following readmission, and five of these had not had previous surgery.

Results

The progress of the 305 patients up to December 31, 1956, is summarized in Table II. (The subsequent progress of the patients who relapsed is discussed in a later section.)

TABLE II.—*Pulmonary Tuberculosis Admissions to Edinburgh Hospitals in 1953. Outcome of Treatment, Related to Use of Major Chest Surgery and Sensitivity of Organisms to the Three Standard Drugs While in Hospital*

State at Discharge	Later Fate	Patients Having						Totals	
		Organisms Sensitive to at Least Two Drugs			Organisms Resistant to at Least Two Drugs				
		Major Surgery	No Surgery	All Cases	Major Surgery	No Surgery	All Cases		
Sputum-negative	Remaining well	95	131	226	13	1	14	240 18 6	264
	Relapse	2	13	15	3	0	3		
	Death (all causes)	0	5	5	1	0	1		
Sputum-positive	Still positive	0	0	0	1	0	1	1 1 5 0	7
	Lost sight of	0	1	1	0	0	0		
	Now negative and well	0	4	4	1	0	1		
	Death (all causes)	0	0	0	0	0	0		
Died in hospital (all causes)		3	16	19	3	8	11	30	
Still in hospital		0	0	0	0	4	4	4	
Totals		100	170	270	22	13	35	305	

In this table the expression "sensitive organisms" indicates that the patient's organisms were sensitive in hospital to at least two of the three standard drugs, or that organisms had never been cultured. Resistance to one of the drugs did not exclude a patient from this category, as treatment by a standard and reliable combination of drugs was still possible. A patient's organisms were held to be "resistant" if resistance was shown to be present to at least two of the standard drugs during his period of hospital stay. The same definitions apply to the words "sensitive" and "resistant" when used later. It was, of course, possible for a patient to pass from the "sensitive" to the "resistant" group after discharge from hospital. Similarly, some patients in the "no surgery" category had surgical treatment at a second admission because they had left hospital with their disease uncontrolled or had relapsed after discharge. Table II should be interpreted with these possibilities in mind.

Relapse was defined as evidence of resumed activity of disease after apparent quiescence had been achieved. Such evidence consisted of radiological deterioration, reversion to positive bacteriology, or the development of overt non-pulmonary tuberculosis.

Four of the 305 patients had not been discharged from hospital by the end of December, 1956. All four had been admitted with far-advanced tuberculosis and resistant organisms, and, while the clinical condition of two had not obviously altered, two were undergoing gradual deterioration. All were deemed unfit for surgery, and attempts to treat them by a variety of drugs had so far proved unsuccessful.

Bacteriological State at Time of Discharge.—Thirty deaths occurred in hospital and 271 patients were discharged alive, four still being in hospital. Six of the survivors, sputum-negative at the time of discharge, died later from non-tuberculous causes. Among the 271 living discharges there were seven patients whose sputum was still positive (2.6%). One of these patients, who had undergone pneumonectomy but had a persistent broncho-pleuro-cutaneous fistula, was

allowed home with the acquiescence of his physician. Our sputum-positive admissions included 187 patients who (a) had drug-sensitive organisms, (b) received treatment with a satisfactory combination of standard drugs as described earlier, and (c) survived the early post-admission period. With one single exception these patients had been rendered culture-negative within six months of starting drugs; the exceptional case converted to the negative state during the eighth month.

Irregular Discharge.—Discharges against medical advice totalled 12 (4% of discharges) and accounted for six of the seven discharges with positive sputum. Reference is made later to the subsequent progress of these patients.

Deaths

Thirty-six of the 305 patients admitted (12%) had died before the end of December, 1956. The causes of death are shown in Table III:

TABLE III	
Related to Tuberculosis (26)	
Directly attributable	20
Indirectly	2
Early post-operative	4
Due to Non-tuberculous Conditions (10)	
Bronchogenic carcinoma	3
Oesophageal	1
Leukaemia	1
Respiratory failure due to ankylosing spondylitis	1
Cerebral haemorrhage	2
Chronic nephritis	1
Cardiovascular degeneration	1

Of the 20 patients whose deaths were directly attributable to tuberculous disease, 15 died from progressive tuberculosis without any obvious associated condition; one developed congestive failure; one had severe associated emphysema; two had amyloid disease; and one died from haemoptysis. The six deaths indirectly related to tuberculous disease included four post-operative deaths (three from pulmonary insufficiency and one from haemorrhage); one death from torsion of the spleen with retroperitoneal haemorrhage, a complication of pneumoperitoneum treatment; and one death from pneumonia in a patient whose tuberculous disease had been controlled at the cost of extensive fibrosis and grossly impaired lung function.

The time of death after admission is given in Table IV. It will be seen that 9 of the 20 patients whose direct cause of death was tuberculosis died within four weeks of admission.

TABLE IV.—Time of Death Related to Admission

Period After Admission in Months	Deaths Directly Due to Tuberculosis	Deaths from All Causes
<1	9	12
1-3	2	6
6-11	2	3
12-17	2	6
Over 18	5	9
Total	20	36

At admission the organisms of the 20 patients whose deaths were directly attributed to tuberculosis showed the following sensitivities: sensitive to streptomycin, P.A.S., and isoniazid, 7; resistant to streptomycin, P.A.S., or isoniazid, 5; resistant to two or more of these drugs, 8.

Of the 12 patients whose organisms were sensitive to at least two of the standard drugs, seven were admitted in a moribund state and died within a month of admission. Another patient, considered to be beyond redemption, was given drugs for only a month. Two further deaths from cardiac failure and amyloid disease occurred in patients whose tuberculous disease was still active at the time of death. Another death from respiratory failure and anoxia was in the main due to associated emphysema, and this patient had been sputum-negative for some months before death. The twelfth patient died from progressive tuberculosis with organisms resistant to all three drugs; the fact

that she had been infected with an organism primarily resistant to P.A.S. was not appreciated at the time of admission, and the chemotherapeutic combinations used were inadequate.

Relapse

Relapse followed in 18 of the 264 patients discharged with negative sputum (7%). In 16 the relapse consisted of a deterioration of the lung condition: 13 had a radiological extension associated with reversion to positive sputum, one had radiological extension only, and two developed a positive sputum culture without apparent radiological change. One patient developed overt spinal tuberculosis and one superficial glandular tuberculosis.

Factors in Relapse Rate

Some factors were examined which might have an influence on relapse rate.

Irregular Discharge.—Six patients taking their discharge against advice had become sputum-negative in hospital, but two of them relapsed.

Drug Resistance.—Resistance to two or more of the three standard drugs was present at the time of relapse in four patients (one-fourth of the patients with relapse of pulmonary disease). Three of these were known to have resistant organisms while they were in hospital; but in one resistance became apparent only after discharge. The combination of P.A.S. with intermittent and not daily streptomycin may have been responsible. If it is accepted that this patient had resistant organisms at discharge despite negativity, the relapse rate among sputum-negative discharges with drug resistance was 22% (4 out of 18), as compared with 6% (14 out of 240) among sensitive cases.

Duration of Chemotherapy.—Table V is concerned only with surviving patients whose organisms remained sensitive to at least two of the standard drugs, allowing treatment

TABLE V.—Showing Incidence of Relapse Among Survivors With Organisms Sensitive to Two or More of Standard Drugs, Related to Initial Extent of Disease and Duration of Chemotherapy

Duration of Chemotherapy in Months	Extent of Disease							
	Far Advanced		Moderately Advanced		Minimal		All Groups	
	No.	Re-lapses	No.	Re-lapses	No.	Re-lapses	No.	Relapses
<3	4	2	4	1	6	2	14	5 (35.7%)
3-5	3	2	4	0	5	0	12	2 (16.7%)
6-8	4	0	23	2	4	0	31	2 (6.5%)
9-11	11	1	31	3	6	0	48	4 (8.3%)
12-17	26	1	43	0	4	0	73	1 (1.4%)
18-23	14	0	12	0	0	0	26	0
24+	21	0	14	0	2	0	37	0
Total	83	6 (7.2%)	131	4 (4.6%)	27	2 (7.4%)	241*	14 (5.8%)

* The number of patients discharged sputum-negative with known or presumed sensitive organisms was 240. Two patients discharged sputum-positive had sensitive organisms and achieved negativity with continued chemotherapy as out-patients, and are included in the Table. One patient is omitted from the Table because he took drugs very irregularly after discharge and no reasonably accurate assessment of the duration of chemotherapy was possible. No relapse cases have been omitted.

with reliable combinations of streptomycin, P.A.S., and/or isoniazid. The relapse experience is shown for groups receiving chemotherapy for different periods. Although the figures are small there is a definite trend, with an inverse relationship between relapse experience and duration of chemotherapy. Five out of 14 patients receiving drugs for less than three months relapsed. Among the 63 patients treated for more than 18 months no relapses occurred, and there was only one relapse among the 136 patients given drugs for more than a year. The actual duration of chemotherapy in this case was 15 months. While the patients receiving the longer periods of drug treatment have had a shorter average period of observation since drugs were stopped, this would not by itself explain the different relapse experience.

The duration of drug treatment appears even more important when considered in relation to the extent of disease.

Extent of Disease

In the pre-chemotherapy era the relationship between the original extent of lung disease and the likelihood of later relapse was well recognized. Such a relationship was not immediately apparent in a study of our drug-sensitive cases. Table V shows that relapse was observed in 7.2% of patients with far advanced disease, 4.6% of moderately advanced cases, and 7.4% of minimal cases. Also apparent from the table, however, is the trend towards longer periods of drug treatment with more extensive disease.

The percentage relapse rates in the final column of Table V were used to calculate the number of relapses which would be expected in the far-advanced, moderately advanced, and minimal groups if extent of disease had no relation to later relapse experience. The "expected" relapses among far-advanced cases were 3.5 (actually observed 6), among moderately advanced 6.8 (observed 6), and among minimal cases 3.8 (observed 2). The calculations are consistent with the hypothesis that the worse prognosis associated with more extensive disease was masked by the use of relatively longer periods of chemotherapy.

Major Surgery

The part played by thoracic surgery can perhaps be best assessed by considering patients with sensitive and resistant organisms separately (see Table II).

Patients with Resistant Organisms

Among 22 resistant cases undergoing surgery there were four deaths (two post-operative, one from progressive tuberculosis, and one from pneumonia). Among the 18 survivors 16 were discharged sputum-negative, but three relapses occurred. The 13 resistant cases not submitted to surgery had a much less favourable experience. Only one was discharged sputum-negative, and eight have died as a result of their tuberculosis.

Patients with Sensitive Organisms

Of 100 patients with sensitive organisms receiving surgery, 97 were discharged sputum-negative and only two of these relapsed. Out of the 144 patients not treated surgically and discharged sputum-negative, 13 relapsed.

The more favourable experience of the surgically treated patients with sensitive organisms cannot be wholly attributed to surgery. In 1953 there was a waiting period for surgery, and in consequence surgically treated patients received on average longer periods of chemotherapy. To adjust for duration of chemotherapy and extent of original disease, separate tables in the same form as Table V were constructed for surgical and non-surgical patients and were used to calculate "expected" relapses in the corresponding groups of surgically treated patients. By summation it was found that the "expected" number of relapses among the surgical patients, assuming no effect from surgery, was 4.5. This compares with the observed number of two relapses. The difference is slight and the value of surgery *per se* in patients with drug-sensitive organisms cannot be considered to have been proved. But these calculations do not take into account the factor of clinical selection for surgery. Presumably many of the patients with sensitive organisms were submitted to surgery because there were features which suggested a greater likelihood of relapse, though, on the other hand, some might have been denied surgery because of poor respiratory function.

Later Fate of Patients Who Relapsed

Seventeen of the 18 patients who relapsed were readmitted and one was treated at home. All received further chemotherapy, and five had surgical procedures. By December, 1956, all but one had been rendered sputum-negative. Thirteen were at work and two were fit for work but in

normal retirement. (Two patients, in hospital in December, 1956, have since been discharged and are also at work at the time of writing.)

Later Fate of Patients Sputum-Positive on Discharge

The seven patients who were discharged with positive sputum (six of them against advice) were all given further treatment. The six irregularly discharged patients had sensitive organisms while in hospital, and two achieved bacterial negativity and quiescence of disease without further treatment than chemotherapy, for which one was readmitted. Three patients, two of whom had developed resistant organisms while out of hospital (almost certainly from failure to take drugs as prescribed), were rendered sputum-negative with the aid of surgery. One patient left the district on discharge and was still sputum-positive eight months later, since when no knowledge concerning him has been available.

The condition of the single sputum-positive patient given a regular discharge has not altered.

General Assessment of Patients at December 31, 1956 Bacteriological

Six of the 269 survivors (2.2%) were known to be sputum-positive in December, 1956. Five of these patients were in hospital, four having been under continuous hospital treatment and one having been readmitted following relapse. Only one patient was at home with a known positive sputum.

Work Status

A survey of 269 patients in December, 1956, gave the findings shown in Table VI:

TABLE VI

Fit for work:		
Working or normal retirement	243	250 (93%)
Unemployed	7	
Unfit for work because of tuberculosis:		
At home	5	11 (4%)
In hospital	6	
Unfit owing to non-tuberculous disease	8	(3%)

By the time of writing two of the patients in hospital in December, 1956, had been discharged and were at work, so that only 3.4% of the surviving patients were unfit for work as a direct consequence of tuberculosis.

Discussion

In the past 10 years any attempt to assess results in the treatment of pulmonary tuberculosis has suffered from an important difficulty. A major criterion of success is the absence of relapse, so that a reasonable period of follow-up is essential; but at the end of such a period the original methods of treatment are apt to be out of date. Our assessment of the results of hospital treatment of patients admitted in 1953 has the advantage that, though we have been able to follow up our patients for a minimum of three years, our general methods of chemotherapy have not radically changed during that period. By 1953 Medical Research Council trials, and studies in our own hospitals, had established combinations of drugs which prevented the emergence of drug-resistant tubercle bacilli in almost all patients, provided they had not previously received unsatisfactory chemotherapy or been infected with resistant organisms. We were also beginning to appreciate the advantages of chemotherapy on a prolonged basis, even though the duration of treatment given to our 1953 patients was not always as long as would be our current practice.

The proportion of patients treated surgically in 1953 was much higher than would now be the case in our hospitals. This can be attributed in part to the higher prevalence of drug-resistant organisms among admissions in 1953, and we had not yet acquired as much confidence as we now possess in the ultimate results of chemotherapy unaccompanied by other measures.

Deaths

Although the overall mortality among our patients was 12%, some was attributable to non-tuberculous disease, and

the true death rate from tuberculosis was 8.6%. When post-operative deaths and deaths related to tuberculosis but not directly attributable are excluded, it is noteworthy that nearly half of the tuberculous deaths occurred within a month of admission—that is to say, in patients admitted moribund. Eight of the 20 patients dying directly from tuberculous disease had organisms which were resistant to two or more of the standard three drugs on admission.

The main factors contributing to our tuberculous deaths were therefore delayed admission and drug resistance. Both these factors should be preventable or almost so, and we believe that under present conditions deaths due to progressive tuberculous disease should be few indeed. No doubt the pulmonary fibrosis associated with the healing of the tuberculous process will claim its ultimate toll of death from cor pulmonale, and we may also expect an occasional death from the acute, almost accidental, complications of lung tuberculosis—haemoptysis and spontaneous pneumothorax.

Post-operative death rates have little meaning except in reference to the type of the patient submitted to surgery. Our surgical patients included a relatively large proportion of seriously ill cases whose outlook without surgery was regarded as hopeless. A sixth of them had organisms resistant to two or more of the standard drugs. Our surgical colleagues deserve great credit for their willingness to come to our aid in the treatment of some desperately ill patients. In the circumstances the early post-operative mortality of 3% (patients and not procedures) was remarkably low.

Relapses

In most reports relating to the prognosis of tuberculosis the majority of relapses have been observed within two years of leaving hospital. Our relapse rate among survivors was 7%, which compares favourably with other published reports but is still, we believe, unsatisfactorily high.

Our analysis of relapses indicates the importance of drug resistance as a factor. When resistance to two or more of the standard drugs was present before apparent quiescence with negative sputum was obtained, relapse followed in 22% of patients, while among sensitive cases the proportion relapsing was 6%.

In our patients with drug-sensitive organisms the most important single factor in reducing the risks of relapse appeared to be the duration of chemotherapy. The recognized relationship between relapse and extent of original disease was concealed by the tendency to give longer drug treatment to patients with more extensive disease. No patient receiving more than 15 months of chemotherapy relapsed. The shorter the period of drug treatment the greater was the likelihood of relapse. This inverse relationship between relapse and duration of chemotherapy is entirely consistent with other investigations carried out in Edinburgh. Ross and Kay (1956), studying patients whose cavities had closed under chemotherapy, did not observe any relapses among patients whose drugs had been continued for more than six months after cavity closure. Stewart and her colleagues (1956), in their studies of resected lung specimens, found an inverse relationship between the duration of effective chemotherapy and the recovery of viable tubercle bacilli from the lung.

The Role of Surgery

Our drug-resistant cases submitted to surgery fared vastly better than did our other drug-resistant patients. Patients who were denied surgery were, of course, more gravely ill. Even so, the results of surgical treatment in drug-resistant cases leave us in no doubt that drug resistance, far from being a contraindication to surgery as so commonly suggested, constitutes in fact a compelling argument for its use, if the patient is reasonably fit. While some of the recently introduced drugs are less efficient than streptomycin, P.A.S., and isoniazid, operative procedures can be carried out successfully under their cover.

The place of surgery in the treatment of patients with sensitive organisms is less certain. Our surgical patients did well and only 2% relapsed. In addition to surgery, however, they received longer periods of chemotherapy than did the non-surgical patients, and we were unable to exclude the possibility that prolonged chemotherapy and not surgery *per se* was responsible for their favourable experience. It can be argued that the group of patients with sensitive organisms submitted to surgery were chosen because the clinicians regarded relapse as a probable event without its use, and that in consequence the low relapse rate observed among the surgical patients is sufficient evidence of the value of surgery. But we cannot be certain that the clinicians were correct in their judgment. Experience in the pre-chemotherapy era has led us to view features such as unclosed and blocked cavities with the utmost suspicion and as indications for surgical treatment, but the possibility exists that the use of modern drugs for prolonged periods may have robbed even these of their menace. The place of surgery needs reappraisal in the light of new developments. Retrospective studies suffer from the inescapable element of selection, and the value of surgery could best be defined by controlled trial, with random allocation of patients to surgical and non-surgical groups when the clinicians thought such a course justifiable, and with both groups receiving similar chemotherapy on a prolonged basis.

Resettlement of Patients

Our patients may be considered to have done well in re-establishing themselves in society after discharge. In December, 1956, only 4% of the survivors were unfit for work by virtue of tuberculosis, and among those capable of work less than 3% had failed to find employment.

The tuberculosis hospital has an important part to play in reducing the pool of known infectors at large in the community. As few patients as possible should be discharged in an infectious state. Seven of our patients (2.6% of survivors) were discharged with a positive sputum, but six of them had taken their own discharge. Irregular discharge is obviously an important problem but should be less frequent under present conditions than it was in the past. Improved prognosis, shorter hospital stays, and financial aid must all help to reduce the incidence of irregular discharge. We are unaware of any earlier reported hospital series with as low an irregular discharge rate as the 4% observed.

Patients discharged irregularly or with positive sputum remained under our clinical supervision and some were re-admitted. The response to further treatment measures was satisfactory and at the time of follow-up only one of our series of patients was known to be outside hospital with a positive sputum, though we lacked information about another one who was positive but had left the district and was untraced.

In the patient with drug-sensitive organisms the attainment of sputum negativity poses little problem. Even in far-advanced cases sputum conversion can confidently be expected if a reliable and appropriate combination of drugs is administered (Horne and Grant, 1956). All patients meeting these conditions among our admissions of 1953 achieved the culture-negative state, and, with the exception of the patient who converted in the eighth month, all became negative within six months of starting drugs.

Current Tuberculosis Practice in Edinburgh

Reorganization of the Edinburgh tuberculosis services in January, 1954, resulted in the allocation of both clinic and hospital duties to all consultants. The arrangements allowed each patient to remain under the care of the same consultant from entry to the register until his removal. We believe that the continuity of supervision thus achieved has been to the benefit of the patients, and there has been a more rapid turnover of hospital beds. A hospital waiting-list of 375 patients in March, 1954, had been all but eliminated a year later.

Any patient with a positive sputum is normally admitted to hospital and retained at least until the sputum becomes negative on culture. Patients with negative bacteriology, mild disease, and insignificant symptoms are often treated on an out-patient basis and are usually allowed to continue at work. Very few patients are treated at home on bed rest.

In the case of previously untreated patients admitted to hospital it has been our practice for some time to initiate treatment with all three standard drugs. It is known that a small but important proportion of new tuberculous cases have been infected with tubercle bacilli resistant to one of the main drugs (Thomas *et al.*, 1954; Fox *et al.*, 1957). The number with organisms resistant to two drugs is much smaller. A two-drug regime involves the risk of losing the benefit of a second drug should it be combined with a drug to which the patient's organisms are already resistant. The danger of reducing resistance is not completely circumvented by the use of a triple-drug regime, but on balance there are advantages in its use.

Patients under 40 years of age receive streptomycin 1 g. in a single injection daily, together with sodium P.A.S. 5 g., and isoniazid 100 mg., both given twice daily by mouth. If sensitivity tests on pre-treatment cultures are satisfactory in respect of all three drugs, either P.A.S. or streptomycin is withdrawn. Our standards of drug sensitivity are high, and any degree of resistance above the threshold of experimental error is considered of potential clinical significance. Solid media are used for sensitivity tests (Stewart, 1955).

Because of the increased risk of vestibular disturbance patients over 40 years of age are not given streptomycin daily, but as 1 g. three times weekly in combination with P.A.S. and isoniazid. When the patient is discharged from hospital, treatment is usually continued with P.A.S. and isoniazid because of the inconvenience of giving streptomycin injections on a domiciliary basis. The P.A.S. and isoniazid are given in the same doses as before in the form of cachets containing both drugs, so that the patient cannot take one drug without the other.

We are wary about resorting to drugs claimed by the manufacturers to be effective substitutes for the standard drugs and advocated because of lower toxicity. We believe that such drugs should not be used routinely until they have been shown to produce adequate blood or urine levels of their active components. The drug claimed to possess a new action should be submitted to a carefully conducted trial before it is accepted for routine use.

Even the minimal case receives uninterrupted chemotherapy for at least a year. In general our practice is to give drugs for at least a year after sputum conversion, cavity closure, or operation, whichever is the latest. Severe cases, or patients with residual open cavities, are treated for at least two years.

Patients admitted desperately ill in grave danger of early death are treated with corticosteroids in addition to chemotherapy. Subjective improvement is more rapid and survival of the patient may be obtained until the effect of the chemotherapeutic drugs is apparent. The place of corticosteroids in routine treatment has been recently assessed (Research Committee of Tuberculosis Society of Scotland, 1957). Corticosteroid drugs must, of course, always be covered by chemotherapy to which the patient's bacilli are sensitive.

Mild cases with negative sputum treated at work without hospital admission usually receive P.A.S. and isoniazid in combined cachet form. The vital importance of taking drugs regularly and in the prescribed dosage is explained carefully to patients receiving treatment out of hospital. Even so, an occasional bitter experience has taught us not always to rely on a patient's veracity, and it is wise to check the urine for P.A.S. from time to time (Simpson, 1956).

Artificial pneumothorax has been abandoned, and the place of pneumoperitoneum in routine treatment is under assessment. Cavities which fail to close on chemotherapy are usually dealt with by resection, but if this entails a significant operative risk we are prepared to treat the patient with chemotherapy

alone. Some of the excellent results in such patients have already been reported (Douglas and Horne, 1956). We seldom recommend resection of lesions without overt cavitation unless we suspect that the patient will fail to co-operate adequately in a prolonged chemotherapy programme after discharge. Totally destroyed lungs, extensive basal tuberculous bronchiectasis, and narrow stricture of a lower-lobe bronchus we regard as definite indications for resection. It is our opinion that surgery has its largest part to play in the treatment of patients who are producing organisms rendered resistant by previous unsatisfactory chemotherapy. In these patients various forms of "salvage" chemotherapy have to be employed, mainly with the object of making the patient fit for operation and preventing post-operative complications (Crofton, 1955; Stewart *et al.*, 1954; Murdoch and Stewart, 1956; Stewart *et al.*, 1957).

We consider that the weapons now available are sufficient to command recovery in nearly all newly diagnosed cases of pulmonary tuberculosis. One hundred per cent. success is not an unreasonable target. Failure can almost always be traced to errors committed by the doctor or by the patient, the doctor failing to prescribe reliable combinations of drugs or the patient failing to take his drugs as prescribed. It should not be accepted with complacency, and its explanation should be assiduously sought.

Summary

The types of treatment given to 305 patients with pulmonary tuberculosis admitted in 1953 to the Edinburgh tuberculosis hospitals are described and the results achieved are assessed up to December, 1956.

The death rate from tuberculosis was 8.6%. Drug resistance and admission in a moribund state accounted for most of the tuberculosis deaths in this series. As these are largely preventable, deaths from progressive tuberculosis should be rare.

Of the survivors 7% relapsed during the period under review. Important factors in determining relapse were drug resistance and the duration of chemotherapy. There have been no relapses among 63 patients with sensitive organisms receiving more than eighteen months' chemotherapy.

The condition of the patients in December, 1956, is described with particular reference to their employment status and infectiousness. Only 4% of survivors were unfit for work by virtue of tuberculosis.

Our current practice in the treatment of pulmonary tuberculosis is summarized.

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