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OBSERVATIONS ON THE TREATMENT OF PULMONARY TUBERCULOSIS AT THE PRESENT TIME*

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[WITH SPECIAL PLATE]

In previous Mitchell Lectures the emphasis has usually been on some aspect of tuberculosis as seen through the eyes of a physician engaged in clinical practice. In selecting a subject I was aware that the late Dr. F. G. Chandler talked on the diagnosis and treatment of pulmonary tuberculosis in 1940, but so much has changed in the intervening 14 years with the advent of specific antibacterial therapy and the advances thereby made possible in thoracic surgery that I felt my observations on the present state of therapy in this disease might not be out of place. I shall deal with my own clinical material and with work in this country of which I have at least some slight personal knowledge.

We all admit that preventive medicine does far more in the eradication of tuberculosis than the puny efforts of the clinician in dealing with the sick; in Scandinavia, certain provinces of Canada, and some parts of the United States it would appear that clinical tuberculosis will disappear in the near future, as smallpox and diphtheria have in Great Britain.

The mortality from respiratory tuberculosis has shown a steady decline for the past century, save for the two world wars, but the fall since 1948 has been striking. From 1931 to 1939 the average total annual death rate for England and Wales was about 25,000; from 1940 to 1944 the figure was approximately 22,000, but in 1945 it was 20,000, and by 1953 it was just under 8,000. Whether this abrupt fall is related to antibacterial therapy is for the statistician to decide. The notification of new cases remains high—in the neighbourhood of 50,000 per annum since 1947—but has dropped from about 48,000 in 1952 to 41,000 in 1953. The number of non-notified deaths from respiratory tuberculosis is still high, even though it has fallen from 3,530 in 1937 to 2,239 in 1952 and 1,751 in 1953. Papworth has shown us that in the known case simple hygiene to prevent spread of infection is highly efficacious; it is the undiagnosed positive case which is the danger.

With mass radiography and improvement in the standard of chest clinics, the type of case seen at a London chest hospital has altered appreciably of late years, but the management of the symptomless case remains a real problem. Apart from cases found by mass radiography,

pulmonary tuberculosis seems to be changing its character, and we know that over 45% of probationer nurses and first-year medical students are Mantoux-negative when they first attend hospital.

Bed Rest

In recent years one of the greatest advances has been the Medical Research Council's trials of chemotherapy, with simultaneous clinical and scientific observations on large numbers of patients with similar types of disease, using control cases, and with a panel examining results dispassionately. For this we owe much to the late Dr. Marc Daniels. In the first streptomycin trials in 1947-8 the control cases were given six months' proper bed rest, and the improvement in a proportion of these was impressive. Dr. Wallace Fox, in a personal communication, has told me that 17 of the original 52 control (acute bilateral) patients are still alive after five years; most of these were not given chemotherapy for the first two years, although many had collapse measures.

In my experience, in the newly diagnosed case the incidence of "extension" of disease during the period of a few weeks while the patient is awaiting admission to hospital is alarming. Explicit and simple instructions on the details of bed rest at home must be given to the patient. My directions are that he must have the foot of the bed raised on two bricks and use no more than two pillows; he is allowed up once a day only, for toilet purposes and to wash and shave, otherwise he must lie in bed throughout the twenty-four hours, including meal-times, save for using a chamber for emptying the bladder.

In cavitated disease, postural retention as practised extensively by Dillwyn Thomas at Sully Hospital, Glamorgan (Thompson, Savage, and Rosser, 1954), with the patient lying in a simple plaster cast and with the foot of the bed raised, at the correct inclination for six to twelve weeks, is a real advance in treatment, especially when combined with chemotherapy. Although cavities rarely close permanently, they usually decrease markedly in size and the surrounding exudative disease becomes more proliferative. Cough and sputum disappear quickly as a rule. The lung is then in a better state for further treatment and less extensive surgical measures are required.

Antibacterial Therapy

The discovery of streptomycin by Waksman and his colleagues (Schatz, Bugie, and Waksman, 1944) and the experimental work and clinical trials of Hinshaw and his co-workers (1944, 1945, 1946) have revolutionized the treatment

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of pulmonary tuberculosis, not only as regards medical treatment, but by allowing more extensive surgical measures by collapse or resection with a greatly diminished risk of broncho-pleural fistula and dissemination of the disease. Another advance was the discovery that the combination of *p*-aminosalicylic acid (P.A.S.) with streptomycin materially decreased the incidence of resistant strains of bacteria to both drugs. In 1951 isonicotinic acid hydrazide (isoniazid) was discovered. This powerful, cheap, and relatively simple drug can be taken by mouth, and again the incidence of resistant organisms is diminished when it is combined with either of the other drugs.

Obviously new and possibly more efficient drugs will be produced; the clinician tends to become confused with the rapid changes taking place these days. The principle of testing under scientific control the value and dangers of new therapeutic agents is of the greatest value, and it behoves us not to discard a well-tried combination of drugs until there is good evidence that a new combination is more efficient and less toxic.

On looking back over the milestones in therapy during the past 30 years—insulin, liver extract, sulphapyridine, penicillin, and cortisone in Addisonian crisis—I still treasure the moment of doubting amazement when I saw the results of streptomycin treatment in the group of young patients with acute exudative disease who were in the Brompton Hospital during the Medical Research Council's trials from 1947 to 1953. The following is an example of such a case.

Case A.—A girl aged 18 years was admitted to the Brompton Hospital in January, 1949, with four months' history of cough, night sweats, and loss of weight. She was acutely ill with tuberculous bronchopneumonia: temperature, 103° F. (39.4° C.); pulse, 120; respirations, 30. She was given streptomycin, 1 g. daily, with P.A.S., 15 g. daily for 14 weeks. In January, 1950, a left pleuropneumectomy was performed, and she was subsequently sent to a sanatorium for six months. She is well and working four years later. (Plate, Figs. 1-3.)

When participating in the treatment of this girl I was thrilled by the vista of what might be accomplished in the future treatment of pulmonary tuberculosis. Such a prospect, coupled with the advent of lobar and segmental resection after chemotherapy, may have blinded us to the value of the older and tried forms of treatment, however. There is a tendency in some countries to accept the view that the proper treatment of pulmonary tuberculosis is a prolonged course of rest with chemotherapy followed by the resection of the remaining areas of nodular caseous disease. The rather scathing term "pimpectomy" has been used by some clinicians who feel that the pendulum of resection has swung too far.

Thoracic surgery has had an immense influence in giving us knowledge of pathological processes in the lungs at an earlier stage than is seen at necropsy. As a class, thoracic surgeons are highly trained and very able; they handle the lungs in life and can correlate the x-ray appearances with the actual lesions found. It is therefore not surprising that the thoracic surgeon should have great influence in advising in and organizing the treatment of pulmonary tuberculosis. Perhaps it is not untimely to suggest that we physicians, in publishing the results of medical treatment, should use the same factual presentation as our surgical colleagues.

In the treatment of pulmonary tuberculosis we have three main weapons in addition to the long-established principles of rest, diet, fresh air, and graded exercise: (a) antibacterial drugs without collapse therapy; (b) collapse treatment, either medical or surgical, in which the diseased lung remains in the body and possibly acts as a stimulus to antibody formation; and (c) resection of the diseased part, which may act as a reservoir of subsequent infection. Any of these three may be used singly or in combination. We must be clear as to our aims in treatment, which are: (1) permanent healing of the lesions; (2) minimal loss of respiratory function; and (3) the attainment of these in the shortest time. The treatment of tuberculosis is long in any case, and un-

necessary months of idleness may have serious effects on morale and on domestic happiness.

Artificial Pneumothorax Therapy

I want to review our results by medical collapse measures alone, before antibacterial therapy was introduced, so as to have a base-line for the comparison of treatment to-day. The true value of artificial pneumothorax therapy is difficult to assess from the voluminous literature, because of variations in the classification of the extent of disease and an often inadequate follow-up. A paper by Foster-Carter, Myers, Goddard, Young, and Benjamin (1952) on cases in the Frimley Sanatorium furnishes some sort of yardstick. The paper covers the five-year period 1937-42 and 1,153 patients, of whom 955 had cavitated disease, and approximately 99% were followed up for at least eight years. Classification was according to the number of zones in the postero-anterior radiograph on admission; this was shown by Hartley, Wingfield, and Burrows (1935), on their experience of 2,759 cases at Frimley, to be probably the most reliable classification on which to base prognosis. It is as follows: Class I, not more than one zone involved; Class II, unilateral or bilateral disease not involving more than three zones; and Class III, four or more zones involved.

The average period of stay in the Brompton Hospital was 40 days and in Frimley Sanatorium 140 days, amounting to about seven months' institutional treatment in all. No doubt the criticism could be made that these cases are a selected group, as Frimley did not take bed-rest cases, and that Class III (advanced) cases diagnosed radiologically were not really so "advanced" as those transferred to other sanatoria where bed-rest patients were accepted. Obviously a ten-year follow-up would have been better than one of eight years. Be that as it may, the figures show a fair proportion of Class III cases. A further point is that these patients were under the control of different physicians at the Brompton Hospital, whose opinions varied widely as to the use of collapse measures, division or not of adhesions, and duration of treatment. This paper is, however, impressive in that the numbers are sufficient, with nearly 99% of cases followed up for eight years, and the results statistically significant. I am grateful to the authors for allowing me to quote from it.

Of 256 patients with cavitated disease, who had *no collapse therapy* at any time, 113 (44%) survived eight years; 93 (82%) of these were working and 62 were known to have a negative sputum. Of 83 patients in Classes I and II, 74% survived eight years, and of 173 in Class III, 33% were alive after that period. Thus it is clear that the extent of the original disease is of more importance than the size of the cavities. Of the 616 cases of cavitated disease reported in the much-quoted paper by Barnes and Barnes (1928), 130 were followed up for five years; of these, 79% were in Class III and 85% had large cavities; the five-year survival rate was only 10%. The Frimley figures give a less gloomy picture: of 104 Class III patients with large cavities 33% survived five years and 23% eight years.

In non-cavitated disease artificial pneumothorax treatment appears to be of little benefit. Of 130 patients treated without collapse therapy 88.9% survived eight years, although 24 (18%) required collapse therapy later. Of 62 patients treated by unilateral pneumothorax, 87% survived eight years and 35% needed further collapse. It is possible that the physician selected the less favourable cases for collapse therapy. The point I want to emphasize is the relatively good prognosis in non-cavitated disease without antibacterial therapy.

Of 457 patients with cavitated disease treated by unilateral artificial pneumothorax 316 (69%) survived eight years; 423 (93%) of these cases came into Classes II and III. An eight-year survival rate of 82% was obtained in 240 cases in Class II, and in 48% of 183 cases in Class III.

The striking finding of the Frimley investigation—in my view a most unexpected one—is the good result attained by

what I would call "contra-selective collapse." The authors define three grades of collapse resulting from artificial pneumothorax: (a) "satisfactory"; (b) "adherent satisfactory," with disappearance of the cavity; and (c) "adherent unsatisfactory," in which the cavity fails to close within one year. A further surprising fact is that extension of disease to the opposite lung occurred in 25% of the "satisfactory" group, 23% of the "adherent unsatisfactory" group, and only 11% of the "adherent satisfactory" group. This might be just a chance happening and is difficult to explain on other grounds.

Empyema occurred in 17% of the whole series, with 14% in the "satisfactory" group, 9% in the "adherent satisfactory" group, and 36% in the "adherent unsatisfactory" group, which again shows the danger of maintaining treatment when the cavity fails to close. The results eight years after termination of the pneumothorax show that 64% of the "satisfactory," 60% of the "adherent satisfactory," and about 28% of the "adherent unsatisfactory" group were well and working.

The deductions I draw from this important paper are as follows: (1) The grading according to zones in the radiograph gives a good indication of prognosis. (2) A satisfactory collapse in which the cavity closes gives much better results than are obtained without collapse therapy. (3) An artificial pneumothorax which fails to close a cavity in a reasonable time is dangerous. (4) The incidence of empyema is 17%, which is too high; it occurs particularly in the group with persistent cavities.

I have analysed a series of my own cases, 62 in all. So far as I am aware this includes every case admitted to the Brompton Hospital under my care in which I recommended pneumothorax treatment during the six years 1942-7 inclusive; these cases are therefore not included in the Frimley report. The series is too small to be of any statistical value, and in addition seven patients have not been traced.

The results, which are analysed in Table I, were good in 36 and bad in 11, and there were 10 deaths. I believe in attaining an anatomically perfect collapse where possible, and adhesion section was performed in 35 out of 47 cases,

TABLE I.—Results of Artificial Pneumothorax in Cases Admitted to the Brompton Hospital During 1942-7

	Non-cavitated, Sputum Negative	Class I	Class II	Class III	Total
Failed A.P. ..	—	—	5 (1 died)	2 (1 died)	7 (2 died)
Lost touch ..	—	1	5	1	7
A.P. maintained ..	—	1	—	—	1
Result good ..	7	11	11	7	36
Treatment failed ..	—	—	6 (5 died)	5 (3 died)	11 (8 died)
Total ..	7	13	27	15	62 (10 died)

Years after termination of A.P.	Good Results				
Over 4 ..	7	6	6	5	24
3 to 4 ..	—	2	4	1	7
1½ to 3 ..	—	3	1	1	5
Total ..	7	11	11	7	36

yet empyema occurred in only 2 of the 47 patients, who were all followed up for at least eighteen months after termination of the pneumothorax. In both cases a suspended cavity was obvious and the pneumothorax should have been terminated within a few weeks. I can also endorse the observation by F. H. Young (1949) that cases under the care of one physician throughout do better than those under multiple control.

Phrenic Paralysis with Pneumoperitoneum Treatment

Banyai (1946) introduced this treatment about 1934 and is enthusiastic as to its value. Many papers on its applica-

tion have been published, but in this country at any rate it is employed chiefly as a preliminary treatment for acute exudative disease, to give some rest to the lung before more definite collapse measures are undertaken. I have used it in a limited number of (generally advanced) cases since 1942, and feel that its value, particularly when it is combined with chemotherapy, is perhaps not sufficiently appreciated. I have had no experience with pneumoperitoneum without phrenic paralysis.

As in pneumoperitoneum the pleural surfaces are not separated, the complications seen with artificial pneumothorax—such as fluid, empyema, haemothorax, and frozen lung—do not occur. Serious complications are rare—less than 5%. As with pneumothorax treatment, a certain amount of skilled supervision is required to attain the objective aimed at—relaxation and rest of the lung selected for phrenic paralysis. This entails a careful search for an accessory phrenic nerve at the time of the phrenic crush and suitable refills to keep the paralysed diaphragm high in the chest, to the level of the third rib or intercostal space in front as seen in the ordinary postero-anterior radiograph; also recrushing the nerve if the hemidiaphragm recovers too early. Careful assessment is needed at a suitable time, usually between six and nine months, to ascertain whether the aims of treatment, especially cavity closure, have been attained; if not, further treatment should be instituted. Lateral radiographs and also tomographs are necessary to decide the progress of the lesion, as pneumoperitoneum affects mainly the posterior part of the lung.

All but two of my 68 patients who have undergone this procedure at the Brompton Hospital have been followed up to date. Apart from four cases in which the pneumoperitoneum was induced by other physicians but supervised by me, the treatment has been given on my recommendation in all cases. Treatment has been abandoned for at least eighteen months, and no patients have been given chemotherapy as part of their treatment. My registrars, Dr. K. J. Gurling and Dr. W. H. Helm, have reviewed the case sheets and original radiographs with me, so as to obtain an unbiased assessment of the extent of the original disease and the results of treatment. When the original films were not available, owing to the fire at the Brompton Hospital in 1950, we have taken the radiologist's report or my own notes on the original films.

Table II gives the over-all results obtained in the 68 cases, divided into Classes I, II, and III and "lower-lobe cavities." In 32 the results were classified as "good," in 20 as "failed,"

TABLE II.—Over-all Results in 68 Cases Treated by Phrenic Paralysis and Pneumoperitoneum

Class	No. of Patients	Results of Treatment				Received Other Treatment	Final State			
		Good	Failed	Non-proven	Lost		Well and Working	Disease Progressive	Died	Lost
I ..	6	3	1	2	—	3	6	—	—	—
II ..	24	10	9	4	1	7	18	1	4	1
III ..	26	10	7	8	1	12	16	2	7	1
Lower-lobe cavities	12	9	3	—	—	3	9	2	1 (non-tb)	—
Total	68	32	20	14	2	25	49	5	12	2

and in 14 as "non-proven"; 2 have been untraced for one and a half years. With further treatment in 25, 49 of the patients are well and working and have negative sputum. Table III gives a detailed analysis of 65 cases.

The 6 cases in Class I need little comment. In Case 1 the patient, a business man, had to travel by air, and a thoracoplasty was therefore performed. In Case 4 an artificial pneumothorax was induced because the physician did not believe in pneumoperitoneum treatment. In Case 6 a

TABLE III.—Detailed Analysis of the 65 Cases Treated by Phrenic Paralysis with Pneumoperitoneum

Case No.	Age and Sex	Standard of Treatment	Duration (Years)	Result	Years After Termination	Further Treatment and Remarks	Final State
CLASS I							
1	31 M	Good	5/12	Non-proven	3½	R. thoracoplasty	Well
2	29 M	Poor	3½	Good	1		"
3	25 M	Good	5	"	1½		"
4	26 M	Poor	9/12	Non-proven	7½	R. artificial pneumothorax with fluid	"
5	20 F	Good	3½	Good	1		"
6	44 F	Fair	4/12	Failed	2½	L. plombage	"
CLASS II							
1	40 M	Good	1	Non-proven	9½	Pneumoperitoneum added to R. artificial pneumothorax. Subsequently relapsed more than once. Working 1953	Well
2	18 M	Poor	4/12	Good	11	Well 10 years. ? Smouldering disease 1 year	"
3	18 M	Fair	4½	"	5		"
4	29 M	Good	2½	"	6		"
5	20 M	Poor	8/12	Non-proven	8	Extensive bilateral infiltration with R. pleural effusion	"
6	16 M	"	3½	"	½	Left sanatorium when radiograph satisfactory. Did not attend chest clinic. Died suddenly	Died
7	34 M	Very poor	2½	Failed	2½	Died. Cavities closed temporarily. Should have had thoracoplasty	"
8	27 F	Good	3½	Good	3½	L. artificial pneumothorax abandoned before pneumoperitoneum started	Well
9	39 M	Poor	2	"	4		"
10	45 M	Good	10/12	"	6½		"
11	27 F	"	4½	"	2½		"
12	22 F	"	4½	"	2		"
13	27 F	Fair	1½	Failed	4½	Pneumoperitoneum abandoned for ulcerative colitis after 18 months. R. thoracoplasty	"
14	18 F	Good	4/12	"	5½	R. thoracoplasty	"
15	20 F	"	3/12	"	4½	Cavity bigger with pneumoperitoneum, but closed with artificial pneumothorax. Abandoned 1½ years	"
16	38 F	Poor	3	Good	2½		"
17	37 M	Good	5/12	Non-proven	4½	Sputum positive at 5 months. Bilateral artificial pneumothorax maintained	"
18	34 F	"	1½	Failed	1	Died. Cavity closed 1 year but reopened. R. thoracoplasty. Died 1 year	Died
19	21 M	Fair	1½	"	3½	Difficult patient: ceased treatment. Bilateral disease. Long chemotherapy	Well
20	41 M	Good	1½	"	2½	L. thoracoplasty. Prolonged chemotherapy. Sputum positive. 2 years after	"
21	30 M	"	7/12	?	2	Abandoned on ship after 7 months	Lost 2 years
CLASS III, GROUP A (with Aim of Cure without other Treatment)							
1	18 F	Good	4½	Good	5		Well
2	21 M	"	2	Failed	6	R. thoracoplasty 1948. L. artificial pneumothorax 1950-3	"
3	24 M	"	½	Non-proven	7½	Bilat. artificial pneumothorax 4 years. R. upper lobectomy 1952	"
4	44 M	Fair	1½	Failed	4½	R. thoracoplasty 1949	"
5	19 F	Poor	3½	Good	1½	Chemotherapy, 42 g. Streptomycin	"
6	20 F	Good	½	Non-proven	3½	L. artificial pneumothorax. Persists 1954	"
7	19 F	"	4½	Good	3	L. thoracoplasty 1951. Sputum positive	"
8	26 M	Poor	6	Failed	6	R. thoracoplasty 1953. L. artificial pneumothorax maintained	Fair
CLASS III, GROUP B (with Aim of Curing One Side)							
1	46 M	Good	2	Failed	2	Died 1947. Alcoholic	Died
2	21 F	Poor	4	Good	4½	R. plombage 1949	Well
3	53 M	"	4/12	Failed	3	Died 1949. Disliked refills. Downhill course after pneumoperitoneum stopped	Died
4	28 F	Good	1½	Good	6	R. thoracoplasty 1948	Well
5	35 F	Fair	5/12	Failed	½	Died 1948. Gross cavitated disease. Enteritis 6 months	Well
6	22 F	Poor	4½	Good	3½	R. thoracoplasty 1951. Sputum negative	Well
7	27 M	Good	1½	Failed	1½	Died 1951. L. artificial pneumothorax plus empyema	Died
8	20 F	"	3	"	1½	Deteriorating	Ill
CLASS III, GROUP C (preparatory to Surgical Treatment of Same Side)							
1	22 F	Good	8½	Good	1½	R. artificial pneumothorax. Empyema. Wash-outs	Well
2	30 F	Fair	1½	Failed	½	L. thoracoplasty 1946. Died 1947	Died
3	28 F	Good	1	Good	6	Abandoned treatment after one year	Well
4	63 M	Fair	½	Non-proven	7½	Slowly progressive	Ill
5	37 M	Very poor	1½	"	—	Died. Treatment poor	Died
6	34 M	"	1½	"	—	Treatment very poor	Lost 1½ years ? Dead
7	20 F	Fair	½	Failed	6½	Cavity bigger. L. thoracoplasty 1949	Well
8	23 M	Good	1½	Good	5½	R. thoracoplasty 1948. Spread L. in 1953	Well
9	31 M	Poor	6/52	Non-proven	3	Died 1951. Disease progressive	Died
10	22 M	Good	2½	Good	3	R. artificial pneumothorax. L. thoracoplasty 1951	Well
LOWER-LOBE CAVITIES							
1	45 F	Good	½	Good	5	Patient stopped refills at 6 months. Well April, 1954	Well
2	20 F	"	4	Failed	5	Cavity blocked: reopened at 4 years. Lobectomy Feb., 1949	"
3	27 F	"	4½	Good	4	Also large cavity R. apex. Phrenic evulsion	"
4	15 F	Poor	5½	"	2½	L. artificial pneumothorax 5½ years	"
5	27 M	"	8/12	Failed	7½	Pneumoperitoneum abandoned too soon. L. extrapleural artificial pneumothorax. Mixed empyema. R. thoracoplasty 1949. Sputum positive	"
6	20 F	Good	1½	Good	7	L. artificial pneumothorax failed; pneumoperitoneum added and cavity closed. R. artificial pneumothorax for cavity. Fresh disease L. upper lobe after 1½ years	"
7	30 F	"	1½	"	3½	Haemoptysis persisted. Sputum negative. R. lower lobectomy Nov., 1948. Cavity closed. Died acute enteritis 1952	Died
8	38 M	Fair	3	Failed	4½	Patient abandoned refills. Cavity reopened May, 1950, with spread to R. lower lobectomy Jan., 1951—further disease L. upper lobe. Chemotherapy	Fair
9	16 F	Good	5	Good	2½	Round foci on R. cavitated. L. lower lobectomy Nov., 1951. Cavity well shut off; R. still smouldering	"
10	35 F	"	5	"	2½	Lower-lobe cavity healed. Smouldering L. apex—plombage 1953	Well
11	16 M	Fair	2½	"	5½		"
12	16 F	Good	3½	"	1		"

pleural effusion occurred before treatment, with the formation of a thick-walled apical cavity. In Class I the results were : 3 good, 2 non-proven, and 1 failed.

The 21 cases in Class II were treated with the aim of cure without further treatment. The results were : good, 9 ; failed, 7 ; non-proven, 4 ; and untraced, 1. The final state is more cheerful in that after treatment 17 patients are well and working, 3 have died, and the other is untraced. The remaining 3 cases of the 24 in Class II were treated in preparation for surgical treatment on the same side, and are therefore not included in Table III. The first patient had a left plombage in 1951 and is now well ; the second, a diabetic girl of 27 years with extensive bilateral cavitation, has had a left extrapleural pneumothorax and a right plombage, but is going downhill. The history of the third case is as follows :

Case B.—The patient, a woman of 39 with chronic unilateral cavitated disease, developed a tuberculous bronchopneumonia following a large haemoptysis and the left lung was virtually destroyed. Streptomycin treatment had to be stopped after a fortnight owing to the development of severe toxic reactions to the drug. With a left phrenic crush and pneumoperitoneum the diaphragm was kept high and the disease controlled. Owing to the presence of disease on the right side it was necessary to wait for eighteen months before a left pneumonectomy could be performed, but during most of this time she was free of cough and sputum and doing her housework, and by the end of the period she had regained her normal weight. Unfortunately, when on holiday she was given a refill at a strange clinic, where she had a syncopal attack. This was thought to be due to an air embolism, and the refills were abandoned forthwith without any consultation. The patient died three months later with enormous cavities on both sides. Diagrams of the radiographs are shown below.

The above case illustrates the dangers of dual control, and, moreover, shows the importance, when surgical treatment

successful, the treated lung standing up to surgical collapse of the contralateral side ; the other 5 were failures. In Group C, of 10 cases, 4 were classed as successful ; 2 of these patients recovered without further treatment. There were 4 non-proven cases and 2 failed. Three cases required thoracoplasty. As in all of the 68 cases the pneumoperitoneum has been abandoned for eighteen months or longer there are no cases in Group D.

An example of the few cases in which a permanent pneumoperitoneum has been maintained is described below. (See Plate, Figs. 4-6.)

Case C.—A man aged 28 years with severe diabetes, Kimmelstiel-Wilson syndrome, and gross hypertension. The extent of the disease and subsequent progress are shown in the radiographs. He has never had antibacterial therapy. For some four years he has been clinically well, without cough or sputum, and is earning his living. I have refused the repeated requests of his chest physician to subject this patient to a thoracoplasty to close the cavity on the left side.

The last part of Table III shows the results in 12 patients with lower-lobe cavities, which are notoriously difficult to close ; 3 of these had had unsuccessful pneumothorax therapy previously. Results were successful in 9. In Case 7 the patient died of acute enteritis four years after a lobectomy, performed because haemoptysis persisted in spite of pneumoperitoneum treatment. The resected specimen showed that the original cavity had closed and the bleeding had been caused by an area of bronchiectasis.

The patient in Case 2, a girl of 20, had a large cavity which became "blocked" ; she remained well and free of sputum for four years with the pneumoperitoneum, but then "spread" occurred near the cavity and a left lower lobectomy was performed. Five years later she is well and working, having had two children in this time. This case taught me that when a cavity becomes "blocked" but does not progressively decrease in size, resection should be carried out, say after a year.

In Case 5, a male aged 27, the pneumoperitoneum had been abandoned too soon, as clinical and radiological examination indicated that healing was taking place. Subsequently the patient went through a whole series of surgical operations.

Plombage

The late Dr. F. G. Chandler (1940) has said that the thoracoplasty is "a terrific and mutilating operation, one that offends the aesthetic sense and craftsmanship of the surgeon." With the modern thoracoplasty few would now subscribe to this view, particularly as most surgeons use general rather than local anaesthesia, which was not the rule some years ago. The mortality

is now less than 5% with experienced surgeons, but the immediate post-operative pain and the common complications, such as atelectasis of the lower lobe and fluid formation, call for fortitude from the most courageous patient. The waiting period for the second stage, and occasionally the third, calls for even more courage. In my experience thoracoplasty still gives most reliable and lasting results, and patients may be seen attending for an annual check, year after year, in good health, in full work, and with minimal deformity. In spite of these good results, however, one feels at times that one is using a sledgehammer to crack a nut.

Like Chandler I had hoped that some form of plombage with a non-irritant substance would be devised, and that—although it contravenes a principle of surgery by leaving a foreign body in the tissues—something better than the old wax plomb would be found.

Wilson in 1948 showed in animals that "lucite" spheres caused little irritation or reaction in the tissues. Trent, Moody, and Hiatt in 1949 published a damning report on

Diagrams of radiographs in Case B. (a) Condition before treatment (October 20, 1950): grossly diseased cavitated left lung. (b) During treatment (May 4, 1951): left diaphragm up to level of second rib; patient without symptoms, doing full day's housework. (c) Condition on day of death (October 21, 1952), three months after treatment had been abandoned: "destroyed" left lung; gross cavitated disease in right.

has been decided upon, not to abandon the pneumoperitoneum until the patient is actually in a surgical bed.

In Class III, the advanced cases, there are 26 patients who offer a challenge to the clinician for any form of therapy. The aim in these cases was to see how many can be salvaged rather than successfully treated. With chemotherapy, of course, the outlook is better, but these patients did not have this help. I divided them into four groups, as a bald statement of success or failure does not give a fair picture of what may be done : Group A—with the aim of cure without other treatment ; Group B—with the aim of curing one side preparatory to collapse or resection on the opposite side ; Group C—with the aim of temporary treatment preparatory to collapse or resection on the same side ; and Group D—the pneumoperitoneum is maintained indefinitely, as the condition of the patient or the extent of the disease does not allow of major surgery.

In Group A there are 8 cases : 3 were successful, 3 failed, and 2 were non-proven. After further treatment all patients are well and working. In Group B 3 of the 8 cases were

51 cases in which lucite spheres were introduced into the extrapleural space. Woods, Walker, and Schmidt (1950) in the United States, and Lucas and Cleland (1950) in this country, have reported favourably on the use of extrafascial stripping as for a Semb thoracoplasty and then introducing lucite balls (at first hollow, but now solid and sterilizable by boiling), of which they have had considerable experience.

Mr. W. P. Cleland, who has carried out the plombage in most of my cases, has kindly let me have his results to date in 186 of his own cases treated three or more years ago, starting about 1948. Of these only about 56% were good risks and some 12% were designated as "scrapheap" cases. His figures are as follows :

Good results without further treatment	..	..	No. of Cases
" " " " " "	..	..	104 } 134
" " " " " "	..	..	30 } (72%)
Unsatisfactory:			
Persistent cavitation	..	..	8
Active disease	..	..	3
Sinuses, etc.	..	..	4
Untraced	..	..	18
Died (from unrelated causes, 8)	..	..	19
Total	..	..	186

There were 13 cases with space infection. Of these, 2 were pyogenic; one had a thoracoplasty and the other was treated by general and local chemotherapy; both patients are now well. The other 11 cases had late tuberculous infection, the majority with sterile pus; of these, 2 died from conditions unrelated to their infection, 3 had sinuses, and 6 are well.

Table IV gives details of the 27 cases for which I recommended lucite plombage. The results were good in 20 and moderate in 2, and there were 5 failures. Of the 3 deaths, one patient (Case 7) died from an anaesthetic preliminary to a pneumonectomy, one (Case 22) from epilepsy when cured of her tuberculosis, and the other (Case 23) from carcinoma of the bronchus. Complications were not serious.

It is still early, the longest period since operation being five years, to be sure that the foreign body in the chest will not give trouble, but I am hopeful. From the patient's point of view the advantages of this operation are three-

fold: (1) it is a one-stage procedure; (2) it is not followed by chest deformity; and (3) it has a relatively low complication rate with absence of post-operative shock and severe pain in the majority. From the point of view of the physician there is a fourth advantage—the patient can have the operation in a "medical" ward and so avoid the wait of six to twelve months for a surgical bed.

Resection

In some countries, particularly the United States, resection has become the accepted form of treatment after a long course of antibacterial therapy, varying from six months to two or even three years. Its use may be considered broadly under two headings: (a) *direct* therapy, in which the diseased and usually functionless portion of lung, which has previously caused symptoms, is removed, thus eliminating a reservoir of future infection; and (b) *prophylactic* therapy, by which I mean removal of parts of damaged lung not at the time causing symptoms but which are considered to be potential sources of infection at a later date. Certain discrete round foci or bronchiectatic segments of the upper lobes are examples. In regard to direct therapy, the older school argue, from previous experience of collapse therapy, that the diseased lung left in the chest acts as a stimulus to specific immunity, while the younger school have greater regard for the theory of removing "the factory." Controversy over prophylactic resection of apparently benign lesions still continues.

From my own impressions as opposed to factual data I regard bronchiectasis in the upper lobe, collapsed by disease or therapeutic procedures, as a benign condition in all but a small minority of cases, and bronchography shows that it is very common. According to Clegg (1953) discrete round foci may be of three types: (a) small areas of tuberculous pneumonia; (b) cold abscesses within the bronchi; and (c) blocked cavities.

In this country Ronald Edwards (Bickford *et al.*, 1952), of Liverpool, who published his first 200 results in 1950, and later Dillwyn Thomas (Thompson *et al.*, 1954) of Sully

TABLE IV.—Results of Extrafascial Apicolysis with Lucite Plombage

Case No.	Age and Sex	Complications	Sputum After	Result	Time After Operation (Years)	Further Treatment	Final State
CLASS I							
1	19 M	Cavity patent. Closed 3/12 posture	Nil	Good	3½	3/12 postural treatment	Well
2	57 M	Small effusion	Negative	"	4	—	"
3	37 F	—	"	"	3½	—	"
4	38 M	—	"	"	2½	—	"
5	44 F	—	Positive (culture)	"	2½	—	"
6	21 M	—	?	"	1½	—	"
CLASS II							
7	28 M	—	Positive	Failure	1½	Anaesthetic death at operation for R. pneumonectomy	Dead
8	19 F	—	Negative	Good	4½	—	Well
9	32 F	Fluid: one aspiration	"	"	5	—	"
10	26 F	Pyogenic empyema	"	"	4½	—	"
11	22 M	Fluid and atelectasis. Thrombosis arm vein	Positive	Failure	4½	R. thoracoplasty	Well. Sputum positive
12	37 M	Fluid and atelectasis. Thrombosis arm vein	Positive	"	3½	L. upper lobectomy	Well. Sputum positive
13	40 F	Fluid: four aspirations	Nil	Good	4½	—	Well
14	29 M	Atelectasis few days	?	"	1½	—	"
15	41 F	{ Nil } bilateral	Negative	"	{ L. 1½ R. 1½ }	—	"
16	21 M	Pneumothorax. Haemorrhage into space	"	"	1½	—	"
17	44 F	Fluid: two aspirations	"	"	1½	—	"
18	30 M	" " "	"	"	1½	—	"
19	30 F	" " "	"	"	1½	—	"
CLASS III							
20	27 M	Pneumothorax and atelectasis. Fluid: two aspirations	Negative	Good	5	R. artificial pneumothorax 5 years. Abandoned 1 year	Well
21	21 F	Fluid: two aspirations	Positive	"	5	Plombage repeated June, 1950	Died of "epilepsy"
22	25 F	—	"	Fair	2½	R. pneumonectomy Dec., 1950	" " carcinoma
23	40 M	Fluid: two aspirations	"	Failure	1½	—	Well
24	33 F	—	"	Fair	3	—	"
25	35 F	Haemothorax: one aspiration	Negative	Good	2½	—	"
26	68 M	—	Positive	Failure	1½	—	Fair. Sputum positive
27	28 M	Pneumothorax: atelectasis R.	Nil	Good	1½	—	Well

Hospital in Wales, with their assistants have performed a large series of resections, although most thoracic surgeons are undertaking a greater or less number according to their views on the pathogenesis and progress of tuberculosis of the lungs. The tendency now is that with lobectomy or resection of more than one segment of a lobe it is probably wise to prevent over-inflation and possible "reactivation" in the remaining lung by some operation to reduce the size of the hemithorax. This may be done at the time of the original resection or at a later date; in either case it adds something to a simple thoracotomy.

Mr. Edwards has kindly allowed me to quote these figures of his results. Of 1,023 patients, 20 died within three months of operation, an immediate mortality of 1.95%. In a four-year follow-up of 112 cases there are 61 pneumonectomies with 4 deaths and 4 with late exacerbations of disease; 49 lobectomies with one post-operative death and 5 exacerbations; and 2 segmental resections with 1 exacerbation. After four years 95% of the 112 patients are well and working.

By 1952 the percentage of segmental resections performed had increased to approximately 66% of all resections. Up to March, 1952, after 259 segmental resections, only one post-operative death and two empyemata had occurred.

Thompson and Savage, working with Dillwyn Thomas at Sully Hospital, report for the five-year period to June, 1953, 266 cases of resection of various types with an operative mortality of 1.88% and "apparently arrested" disease in about 97%. It is too early yet to assess final results.

For what it is worth I present my own small series of resections. By nature I am conservative, and while welcoming advances in treatment I am inclined to wait and see the results of innovations in the cases of more enterprising physicians. Of 11 pneumonectomies, mostly with "destroyed" lung, results were good in 9. There were 2 deaths, one from acute bronchitis 2½ years after, the other from epilepsy one year after; the latter has already been referred to under "Plombage." Of 21 lobectomies, results were good in 18 and poor in 2; there was one failure. Only 4 had post-operative collapse to decrease the size of the hemithorax. Of 8 segmental resections, results were good in 6 and bad in 2.

Conclusion

In this paper I have given certain figures, which I believe to be reliable, concerning artificial pneumothorax and pneumoperitoneum treatment without antibacterial therapy. Now that antibacterial therapy is available the results of surgical intervention are much better, as also are those of medical collapse. With medical collapse and chemotherapy, in my experience, many patients with minimal or moderate disease can safely return to their homes and occupations within eight to twelve months.

In the Frimley series from 1937 to 1942 quoted above the incidence of empyema was 17%—an appalling figure. If this is the true risk at the present time, then it is no wonder that artificial pneumothorax is much less used than in the past. The results in suitable cases five years after refills have been discontinued are very good, however. Of my own series of 62 patients treated with artificial pneumothorax from 1942 to 1947 it is possible, but I think unlikely, that in each of the seven untraced cases an empyema developed. Of 47 cases followed up for at least eighteen months after the pneumothorax was abandoned, only in two did empyema develop; both of these were badly selected cases in which treatment should have been abandoned forthwith.

I now teach my students that the indications for artificial pneumothorax are very limited and that the treatment should be used only in the following circumstances: (1) when the clinical duration of disease is at least four months and chemotherapy has been given for a further four weeks; (2) when cavities are less than 4 cm. in diameter; (3) when there is no clinical or radiological evidence of endobronchial

disease; and (4) when it is estimated that after the lung has healed it will fill the hemithorax without risk of over-inflation or displacement of the mediastinum. I further impress upon them that they should not hesitate to abandon an artificial pneumothorax that has been started if conditions are unfavourable.

We physicians unfortunately often deal with advanced cases quite unsuitable for pneumothorax or surgical treatment at that stage. In these cases the use of chemotherapy with postural retention for two to three months, followed by phrenic crush and pneumoperitoneum, will give an idea of future possibilities. A plombage on the worse side at the appropriate time may in some of these rather hopeless cases enable the patient to get back to a useful life within twelve to eighteen months. It is perhaps not sufficiently appreciated at the present time that pneumoperitoneum with phrenic paralysis added to antibacterial therapy has real value.

The following is a typical case (see Plate, Figs. 7-9).

Case D.—An officer in the Merchant Navy aged 27 years had been a contact of his brother and sister, both of whom had cavitated disease. In June, 1950, radiological examination showed bilateral disease with cavitation. The patient was admitted to a sanatorium, where he was given bed rest with streptomycin, 54 g., and P.A.S.; a right artificial pneumothorax was attempted and abandoned. In June, 1951, he was sent home. From December, 1951, to April, 1952, he was in the Brompton Hospital with a positive sputum. He was treated by postural retention for six weeks and then had a left phrenic crush with pneumoperitoneum; during this time he received streptomycin, 87 g., with P.A.S. He returned to a sanatorium for five months and was then readmitted to the Brompton Hospital on September 1, remaining there till November 5. His sputum was still positive on culture. Tomography revealed a small cavity at the right apex. On October 1 a right lucite plombage was performed, after which he was dyspnoeic for some days. Sputum disappeared soon after this, and he has been doing part-time work since December, 1953. Pneumoperitoneum treatment continues. The total dose of streptomycin received by this patient was 182 g.

Bacteriologists and morbid anatomists in this and other countries are investigating the finding in many resected specimens that large numbers of bacilli are present in some lesions and none in others; only a small proportion of these bacteria will grow on the artificial media now in common use, and may fail to infect or kill laboratory animals.

Dubos (1953), in his summing up of a discussion on the subject at the twelfth Conference on the Chemotherapy of Tuberculosis held in February, 1953, in the United States, comments on these facts. Bacilli are found more often in cavitated lesions than in closed necrotic foci; these bacilli may be dormant and not necessarily dead. A low-oxygen, high carbon-dioxide content is known to inhibit the growth of tubercle bacilli *in vitro*, and these are just the conditions found in closed necrotic lesions. Breakdown products of necrotic tissue such as spermine and spermidine, and enzymes such as lysozyme, also inhibit bacterial growth *in vitro*. Bacilli may, however, persist in the tissue-cells and lymph nodes of men and animals in spite of prolonged chemotherapy.

Further research is required both by laboratory workers and by clinicians who will make accurate observations on the anatomy, pathology, and bacteriology of these pulmonary lesions, follow up the patients, and publish their findings.

There is no doubt that in the right type of disease resection is a fundamental treatment which has come to stay—and rightly so. At present I am uneasy about the policy of some surgeons in removing apparently "benign" lesions on the supposition that these may break down at some future date.

When one ponders over the problem of pulmonary tuberculosis one is always brought back to the question of immunity. Why should the rat be immune and not the guinea-pig? Recently I have been studying sections of lung

taken at biopsy from patients with miliary shadows in the lungs. Some of these cases are diagnosed on all available evidence as "sarcoidosis," and others as benign chronic miliary tuberculosis; a small group seems to be "on the fence" between the two. I have a feeling that further experimental study of the syndrome called "sarcoidosis" may provide a clue to the problem of immunity in tuberculosis.

Summary

The treatment of pulmonary tuberculosis is reviewed in the light of recent advances.

The aims of treatment are: (1) permanent healing of the lesions; (2) minimal loss of respiratory function; and (3) the attainment of these in the shortest time.

In addition to the long-established principles of rest, diet, fresh air, and graded exercises there are three main therapeutic weapons: (1) antibacterial drugs without collapse therapy; (2) collapse therapy, either medical or surgical; and (3) resection of the diseased portion of lung.

The value of the various forms of treatment is assessed on the basis of results obtained by the author and by other workers in Great Britain.

The finding that large numbers of tubercle bacilli are present in some lesions and none in others is referred to, and the need for further research into this question is stressed.

Further experimental study of the syndrome called "sarcoidosis" may provide a clue to the problem of immunity in tuberculosis.

My grateful thanks are due to my registrars, Dr. J. K. Gurling and Dr. W. H. Helm, for their valuable assistance in reviewing the records of my cases; also to my secretary, Miss Hope Daniel, for her persevering efforts in following up the patients.

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In his Report for 1953, Dr. Stuart Laidlaw, Medical Officer of Health for the City of Glasgow, writes: "One can readily imagine the public outcry had diphtheria immunization been available only to the well-to-do. But it is little encouragement to those protagonists of free preventive measures that so few avail themselves of the opportunities offered. Public apathy is not restricted to diphtheria immunization alone. Only 17% take advantage of free infant vaccination, though Glasgow is a seaport town with an air terminal. Many contacts of open cases of tuberculosis decline to be x-rayed. Many parents ignore the opportunity of B.C.G. protection for children of school-leaving age. There is also the unsatisfactory response by expectant mothers to the offers of free dental treatment and supplementary vitamins despite the fact that these provide additional safeguards to themselves and the unborn child."

CURRENT THERAPY IN PULMONARY TUBERCULOSIS IN THE UNITED STATES*

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[WITH SPECIAL PLATE]

The study forming the subject of this lecture was carried out under the auspices of the Committee on Non-Surgical Collapse Therapy of the American College of Chest Physicians to determine the kind of therapy advised as the initial treatment in different cases of pulmonary tuberculosis by physicians who are recognized experts in this disease. Ten representative cases were selected. They were of ordinary forms of tuberculosis that might be seen any day in such a physician's office. They differed as regards age, race, sex, and type of disease, but had no unusual or bizarre complications. All had positive sputum. They could be grouped, according to the classification of the National Tuberculosis Association, into minimal, moderately advanced, and far advanced. These patients had been known to us for a long time. It was endeavoured to make the initial problem as simple as possible. A similar study was carried out on these same ten cases in 1948.

The method of investigation was as follows. A brief case history with a single chest radiograph of each case was sent, with an accompanying questionnaire, to the one hundred physicians selected as representative of the top clinical thinking in their respective areas throughout the United States. The questions asked were: (1) Would you use bed rest alone as therapy for this type of case? (2) Would you add drug therapy? (3) Would you use collapse therapy? (4) Would you use surgery? (5) With the therapy indicated above, how long would you keep this patient on complete bed rest and in a sanatorium? In general, complete bed rest is interpreted as strict rest in bed with no bathroom privileges; the patient is not allowed out of bed at all for any reason. Modified bed rest is indicated as such.

In what follows the replies to the above questionnaire are analysed.

Drug Therapy

Drug therapy will be discussed for all of the cases together, because the same practitioners recommend practically the same dosages throughout the ten cases and most of them say they would start chemotherapy immediately. The length of time chemotherapy would be continued varied considerably, however, for the different patients.

Antimicrobial therapy is now generally accepted by the vast majority of chest physicians as part of the routine treatment of pulmonary tuberculosis, whatever the extent of the disease. Such therapy would be used as part of the basic treatment by 97%, with variation, according to the extent of the disease, only from 93% for minimal disease to 99.5% for far advanced disease. The drugs of choice were limited to streptomycin, *para*-aminosalicylic acid (P.A.S.), and isonicotinic acid hydrazide (isoniazid). Practically all the physicians would use combined and continuous therapy, with a marked preference for streptomycin plus P.A.S. A majority favoured the intermittent use of streptomycin in a dosage of 1 g. twice weekly, with P.A.S. by mouth to tolerance—about

*Based on the Fourth Varrier-Jones Memorial Lecture, given at Manson House, London, on May 14, 1954.

J. L. LIVINGSTONE: OBSERVATIONS ON THE TREATMENT OF PULMONARY TUBERCULOSIS
AT THE PRESENT TIME

FIG. 1.—July 11, 1949.

FIG. 2.—December 29, 1949.

FIG. 3.—February 19, 1954.

FIGS. 1-3: Case A.

FIG. 4.—July 10, 1948.

FIG. 5.—February 12, 1952.

FIG. 6.—May 5, 1954.

FIGS. 4-6: Case C.

FIG. 7.—December 6, 1951.

FIG. 8.—September 29, 1952.

FIG. 9.—May 6, 1954.

FIGS. 7-9: Case D.