ASPIRATION IN THE TREATMENT OF PRIMARY TUBERCULOUS PLEURAL EFFUSION

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One of the after-effects of primary tuberculous effusion is persistent pleural thickening, which may be slight and manifested by a radiological abnormality only, or so marked as to cause deformity of the thoracic cage and scoliosis of the spine.

Whatever its degree, pleural thickening is likely to result in impaired pulmonary function, and even those cases which show minimal x-ray changes, or none at all, may still show some impairment of lung function due to the pleural symphysis which has occurred.

What has been termed an "active" form of treatment, consisting of repeated aspiration of the pleural cavity, together with postural treatment and physiotherapy, has been suggested by Birath (1952) and Mackay-Dick and Rothnie (1954) as a method of reducing the incidence of pleural thickening after pleural effusions. Mackay-Dick and Rothnie claimed that not only was the incidence of thickening reduced but also that patients on this form of treatment fared better in the early stages than those not so treated, in that they felt better, looked better, and ate better, and their fever subsided more rapidly.

There are, however, disadvantages associated with aspiration of the pleural cavity. Thus Pagel, Simmonds, and Macdonald (1953) pointed out that puncture of the pleura may excite further exudation of fluid, and Emerson (1955) found that the E.S.R. rose and fluid re-accumulated after therapeutic aspiration. Robson (1952) stressed the danger of pulmonary oedema occurring if much fluid is removed quickly at one time, and Hudson (1957) stated that, other things being equal, fluid should not be removed, because of its high antibody content. It has also been said that the "natural splintage" of the lung afforded by the fluid should not be upset by aspirating it. Until recently, the general consensus of opinion has been in favour of not aspirating pleural effusions except for diagnosis, for the relief of dyspnoea or pressure symptoms, or for the removal of a small amount of fluid when the effusion has persisted for some weeks (Mackenzie, 1952; Pagel *et al.*, 1953).

It seemed to us that, although good results had been obtained with the "active" form of treatment advocated by Mackay-Dick and Rothnie, the place in it of repeated aspiration was still in doubt, and in view of the possible disadvantages associated with aspiration we felt that this aspect of treatment required further study. Accordingly, we carried out a trial in which the results of treatment were compared in two groups of patients, one receiving repeated aspirations and the other no further aspiration after that for diagnosis. Fifty-two

patients were included in the trial, all of whom were soldiers aged 17-24 who developed primary tuberculous pleural effusion during their Army service. All were admitted to the Connaught Hospital (Army Chest Centre) between October, 1955, and November, 1956.

Diagnosis

Each patient had postero-anterior and lateral radiographs taken on admission. Tomography was carried out later on every case. Parenchymal lesions, typical of primary foci, were noted in four patients. The other 48 had no radiological evidence of parenchymal disease throughout the period of the trial. No instance of effusion secondary to adult-type tuberculosis was included in the series.

The diagnosis of primary tuberculous effusion was based on three main findings. (1) Typical onset and course, with the absence clinically and radiologically of other possible causes of effusion such as pneumonia, upper respiratory infection, emboli, bronchiectasis, or trauma. (2) Positive Mantoux or Heaf reactions. Six patients were Heaf-positive grade 3. The remaining 46 were all Mantoux-positive, 27 of them to 1/10,000 old tuberculin (1 T.U.). (3) Examination of pleural aspirate, which was performed on every patient. Only those showing the typical straw-coloured predominantly lymphocytic fluid which was sterile on culture for pyogenic organisms were included. Direct film examination of pleural fluid and sputum for tubercle bacilli was carried out on every case, but not all cases transferred from other hospitals had had culture or guinea-pig inoculation techniques applied. Of the 52 cases, pleural fluid culture was positive in six cases and guinea-pig inoculation positive in three. No positive findings were reported from sputum, laryngeal swabs, or gastric washings.

Routine Treatment Common to all Patients

The standard treatment consisted of streptomycin, 1 g. daily, and isoniazid, 100 mg. twice daily, this regime being continued until 100 g. had been given, when the dose was reduced to 1 g. on alternate days with continued daily isoniazid. A total of 140 to 150 g. of streptomycin was usually reached during treatment. Three patients had started treatment with P.A.S. instead of isoniazid before admission; they were continued on this regime. Vitamins A, D, and B complex and ferrous sulphate were given throughout treatment. Bed rest was continued for three months in every case. Those patients still showing pyrexia or a raised erythrocyte sedimentation rate at the end of this time were treated on further bed rest until these had subsided. Upgrading occupied a further three months, by the end of which time patients were up to all meals and had carried out graduated walking exercises. Breathing exercises directed to the improvement on the affected side of diaphragmatic and chest-wall movement were carried out by all patients; these were begun when the temperature had become normal. Patients were encouraged to spend rest periods, each of an hour twice a day, lying with the unaffected side arched over a pillow, in an endeavour to stretch the affected side and prevent rib-crowding. This regime was applied to all patients who completed their treatment at the Army Chest Centre.

Thirteen patients in this series were transferred to other sanatoria during treatment, but none before aspiration therapy had been completed and their temperatures and E.S.R.s had returned to normal. Their radiographs at the six months' stage were made available to us by the chest physicians concerned. The main difference between these patients and those remaining at this hospital for the whole of the follow-up period occurred in the type of chemotherapy they received. Both the drugs used and the dosage schemes employed varied to some extent from our practice. Of the 13 patients concerned, however, all received streptomycin, and the total dose after six months' treatment varied between 84 and 180 g., the average being 153 g.

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Aspiration Technique

All patients with pleural effusions were subjected to an initial diagnostic aspiration of not more than 100 ml. Thereafter, those patients admitted to the series were either not aspirated again (these comprised group A) or they were aspirated repeatedly (group B). In the latter, as much fluid as possible (but not more than 2 pints—1,140 ml.) was removed on the first occasion, and aspiration was repeated (normally on successive days) until no more fluid could be obtained. In a few patients aspiration was repeated on alternate days or on every third day, but never less frequently than that.

Aspiration technique followed normal practice. The site of aspiration was determined clinically and radiologically. After local analgesia, fluid was removed through a 13 s.w.g. needle by a 30-ml. syringe fitted with a two-way tap.

In group B, 1 g. of streptomycin in 10 ml. of water was instilled into the pleural cavity after each aspiration. This was the only difference in chemotherapy between the groups. In group A failure of the fluid to absorb spontaneously after a period of one month was regarded as an indication for therapeutic aspiration, and this was carried out on three patients in the group.

Allocation of Patients to Groups

Patients were allocated to one or other of the two groups as follows. Those who were admitted direct to this hospital were placed alternately in one group or the other as they were admitted, and treatment was continued accordingly. Patients transferred from other hospitals and already under treatment were allocated to one group or the other according to whether their previous treatments had been by single diagnostic or repeated aspiration.

Certain patients admitted with pleural effusion from other hospitals had to be excluded from the series because their aspiration or drug regimes had not been in accordance with those practised at this centre; there were 21 of these. Otherwise, every case of pleural effusion admitted between October, 1955, and November, 1956, which satisfied the diagnostic criteria indicated above, was included in the series.

Comparison of Groups

Group A, treated by single aspiration, comprised 19 patients. Of these, seven were admitted to this hospital within a few days of onset of symptoms, and were allocated by the alternate admission method. The remaining 12 had begun treatment elsewhere, but their diagnosis and treatment fulfilled the criteria for admission to the series. Group B, treated by repeated aspirations, comprised 33 patients, eight admitted direct and 25 secondarily.

Table I shows the number in each group divided according to the maximum effusion size, in which there was no significant difference between the groups. The size of the effusion was estimated from the radiographic appearance as follows: large if the bulk of the fluid extended above a horizontal line through the lower border of the second rib anteriorly; medium if above a similar line through the

TABLE I

Effusion Size:	Small	Medium	Large	Total
Group A	5	9	5	19
„ B	10	14	9	33

TABLE II

	Group A	Group B
Initial mean E.S.R. ..	34.2±9.6	37.5±11.2
Mantoux-positive at 1 T.U. ..	10 (53%)	17 (52%)
Findings of <i>M. tuberculosis</i> ..	3 (16%)	6 (18%)

fourth rib; and small if below this line. Thin lateral prolongations of fluid above the main bulk of the effusion were discounted.

Table II shows initial similarities between the groups as regards mean E.S.R., Mantoux state, and positivity of pleural fluid and sputum. The groups were similar also as regards age, sex, and treatment received (other than the aspiration regime).

As some of these patients began treatment in other hospitals before being transferred to this centre it might be thought that differences in aspiration technique would introduce differences between the groups. However, we found that those patients admitted primarily to this centre, to whom this objection could not apply, showed results similar to those obtained from the series as a whole. Furthermore, those patients whose initial treatment differed from our own practice were excluded from the trial.

In each group, two patients showed on x-ray examination parenchymal lesions which were considered to be primary foci. No complications occurred in group A, but therapeutic aspiration was carried out once on three patients in the group who had failed to show any spontaneous absorption of fluid after one month's treatment. The only complication which occurred in group B was one small pneumothorax, following aspiration, which had absorbed completely after eight weeks and which required no treatment.

The number of aspirations performed in Group B is shown in Table III. The average number of aspirations performed on each patient was 4.2. The majority (17) of the patients had three aspirations.

TABLE III

No. of aspirations	2	3	4	5	6	7	8	9
„ „ patients	3	17	3	2	3	—	3	2

Assessment of Progress

Progress was assessed on the length of time the temperature and E.S.R. remained raised, the radiological appearance after six months' treatment, and the duration of the effusions.

Duration of Raised Temperature.—Twice-daily recordings were available in all but five cases. Patients were regarded as apyrexial when their temperature remained consistently below 99° F. (37.2° C.). It was found that the temperature fell to normal in group A in a mean of 30.4±8.2 days from the date of the first aspiration, and in group B in a mean of 30.2±16.2 days. This difference is small, but it is a significant one having regard to the standard deviations. The longest duration of pyrexia in group A was 42 days and in group B 80 days. The three patients in Group A who required therapeutic aspiration showed no rise in temperature after their aspirations.

TABLE IV.—Mean E.S.R.

		Weeks After First Aspiration										
		0	1	2	3	4	5	6	7	8	9	10
Group A		34.2	35.1	25.0	21.3	20.0	15.8	15.2	11.1	7.9		
„ B		37.5	40.0	40.0	36.1	32.0	28.8	24.3	24.5	20.0	15.8	9.1

Duration of Raised E.S.R.—The E.S.R. was recorded weekly until it had remained normal on three consecutive occasions. Thereafter it was estimated monthly. The E.S.R. was regarded as normal when it was below 10 mm. in one hour (Westergren). Table IV shows that the mean E.S.R. fell to normal in group A in eight weeks and in group B in 10 weeks, measured from the date of first aspiration. Two of the three patients in group A who required therapeutic aspirations showed a marked rise in E.S.R. after re-aspiration.

Degree of Residual Opacity after 6 Months' Treatment.—Radiographs taken six months (plus or minus three

weeks) after treatment was begun were reviewed and residual opacities assessed as follows: First-degree opacity was when not more than the costophrenic angle was obliterated and there was no diaphragmatic elevation or tenting; third-degree opacity was when there was thickening, rib-crowding, and scoliosis of a degree meriting consideration for decortication; second-degree opacity comprised all intermediate cases. The results are shown in Table V. It will be seen

TABLE V.—Degree of Opacity After 6 Months' Treatment

Degree:		1	2	3
Group A (19 cases)		14 (73.7%)	5 (26.3%)	
„ B (33 „)		21 (63.6%)	11 (33.3%)	1 (3.1%)

that 73.7% of group A and 63.6% of group B either had no thickening at all or at most showed minimal changes consisting of an obliterated costophrenic angle only, without diaphragmatic elevation or tenting. These patients are regarded as having made satisfactory progress. Patients having moderate or severe pleural thickening after six months' observation comprised 26.3% of group A and 36.4% of group B. The difference is not statistically significant having regard to the number of patients in each group.

Duration of Effusion.—Every patient was radiographed on admission, and this was repeated monthly, or more often if fluid was absorbing rapidly. A clinical impression was gained that, while repeated aspiration often resulted in an early rapid reduction in effusion size, residual pleural thickening was often marked and cleared slowly; in group A, fluid seemed to clear more completely once resorption had begun. This impression was confirmed when the rates of clearing in the two groups were compared (Table VI).

TABLE VI.—Patients Showing More than First-degree Opacity

		Months of Treatment from Date of First Aspiration											
		1		2		3		4		5		6	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Group A		14	73.7	12	63.2	7	36.8	6	31.6	5	26.3	5	26.3
„ B		22	66.6	14	42.4	13	39.4	12	36.4	12	36.4	12	36.4

Discussion

This trial on a small series of primary tuberculous pleural effusions shows that in the repeated-aspiration group of cases the E.S.R. declined more slowly than in the single-aspiration group, whilst the temperature fell slightly more quickly.

The effect of repeated aspiration in prolonging the duration of an elevated E.S.R. was commented on by Emerson (1955), but it is important to remember that in our series the comparison is between single aspiration on the one hand and repeated aspiration with intrapleural streptomycin on the other.

The slightly more rapid fall of temperature in our repeated-aspiration group confirms the findings of Mackay-Dick and Rothnie (1954), although we found the advantage in this respect of that group over the single-aspiration group to be small.

So far as the rate of clearing is concerned, our conclusion is that effusions treated by repeated aspiration tend to clear more rapidly in the early stages than those left to absorb spontaneously, but by the six-months stage there is little difference in the amount of residual pleural opacity.

Insufficient time has elapsed for a conclusion to be reached on the effect of repeated aspiration on the incidence of subsequent tuberculosis, but during the six-months follow-up period no patients in either group developed fresh evidence of tuberculosis.

Aspiration of the pleural cavity causes the patient some discomfort and may give rise to complications; it should not, therefore, be performed unnecessarily. Although our results show little apparent advantage in repeated aspirations, we formed the clinical impression that many patients,

especially those with large effusions, felt better if their effusions were aspirated early on, even although this subjective improvement was not matched by objective criteria; in view of this we felt that a compromise between the two methods might prove the ideal form of treatment—that is, an initial large aspiration (at the time of the diagnostic one) and no aspiration thereafter.

It had originally been our intention to include in the trial a third group of patients who had one large initial aspiration performed at the time of diagnostic aspiration and who were not aspirated further, but we had insufficient cases to include this group in the series. The results in those patients who were treated in this way were good, however, and during the past eight months this method has been our standard practice. Later, it is hoped to collect similar data on this group for comparison with the results of the present trial.

Summary

A comparison has been made between the use of single and repeated aspiration in the treatment of primary tuberculous pleural effusion.

Of the 52 patients included in the trial, 33 were treated by repeated aspiration and 19 by single diagnostic aspiration.

The results were compared in terms of duration of pyrexia, and elevated E.S.R., rate of clearing of effusion, and residual opacity after six months' treatment.

There was a slightly shorter duration of pyrexia and a prolonged duration of raised E.S.R. in the repeated-aspiration group.

Although the repeated-aspiration group tended to clear rapidly in the early stages, there was no significant difference between the groups in the amount of pleural opacity remaining at six months.

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The Tobacco Manufacturers' Standing Committee, in its report for the year ended May 31 last, states that experiments have been carried out in the industry's laboratories to find substances that might be used to reduce the minute quantities of benzpyrene in cigarette smoke. Two such substances have been found—copper nitrate and platinum diamminonitrite. An earlier claim that the addition of 4% ammonium sulphamate to cigarette paper has a similar reducing effect was not substantiated, though the addition of relatively large amounts of ammonium sulphamate to the tobacco itself did reduce the benzpyrene content of the smoke. Besides benzpyrene a number of other polycyclic hydrocarbons have been found in cigarette smoke, and they are being investigated. Tests continue to show that, since the virtual elimination of the use of arsenical insecticidal sprays on tobacco crops, traces of arsenic have almost disappeared from cigarettes made in Britain. A new research project is to be the study of the principles of "smouldering combustion, particularly in relation to forced air supply in products such as tobacco." The report may be obtained from the committee's offices, 6-10, Bruton Street, London, W.1.