Natural history of segmental lesions in primary pulmonary tuberculosis

Long-term review of 383 patients

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Morrison, J. B. (1973). *Archives of Disease in Childhood*, 48, 90. **Natural history of segmental lesions in primary pulmonary tuberculosis: long-term review of 383 patients.** A long-term follow-up of 383 children suffering from primary pulmonary tuberculosis with consolidation-collapse of lung segments supported the view that early surgical treatment is not necessary in the majority of patients. Only 21 children required thoracotomy; of these, 5 were observed for 8 to 12 months, the remaining 16 for periods of 1 to 9 years before operation was undertaken. With modern chemotherapy, supplemented perhaps by early steroid treatment in the more severe cases, a favourable outcome can be expected.

Before the advent of chemotherapy and modern anaesthesia, which made thoracotomy and lung resection a relatively safe procedure, it had been noted in this hospital that many children suffering from primary pulmonary tuberculosis with consolidation-collapse of lung segments recovered well on conservative treatment. In 1952, Thomas advised the surgical evacuation of enlarged mediastinal tuberculous glands with or without the resection of diseased lung, an idea subsequently expanded by Jacobs (1958). This conception of treatment, though questioned by Adler and Richards (1953) and Macpherson, Zorab, and Reid (1960), has never been refuted by any long-term follow-up of a large series of children, and therefore this study was undertaken. At a time when tuberculosis, as stated by Crofton and Douglas (1969), is still a major cause of death and disability in the world as a whole, with 10 to 12 million active cases of pulmonary tuberculosis and 1 to 2 million deaths per year, it seems appropriate to present our findings.

Material and methods

All children suffering from primary pulmonary tuberculosis with consolidation-collapse of lung segments discharged from this hospital for the 8 years 1952 to 1959 were followed up through their local chest clinics. The majority of these children came from Manchester, the children's part of the hospital having been built in 1931 for the specific purpose of long-term

treatment of pulmonary and nonpulmonary tuberculosis, combining the facilities of a hospital with full educational opportunities made available by a staff of 10 teachers. The hospital is situated on the North Wales coast 350 feet above sea level and some 70 miles away from Manchester. No attempt was made to distinguish, as did Adler and Richards (1953), between atelectasis and consolidation, as this distinction can be difficult to define precisely when a small volume of lung tissue such as a bronchial segment is involved. In many children both collapse, as evidenced by subsequent aeration of the lung, and consolidation, as shown by later calcification of caseous areas, coexisted. Where there was doubt as to the necessity for surgical intervention, it was agreed with the referring chest physician that should the child suffer a relapse after discharge, or should a large and possibly caseous area of consolidation persist, then the child should be referred back to the hospital for further treatment.

Results

Age and sex. 383 children were followed up for periods ranging from 9 to 17 years and, as is evident from Fig. 1, the majority were under 6 years of age on entry to the study. 60% were male, a manifestation of the tendency for boys to show greater glandular enlargement than girls. 230 children were under 6 years of age, and in this group the greatest enlargement of bronchopulmonary glands relative to body size occurs so that segmental and lobar bronchi are most liable to be compressed.

FIG. 1.—Age grouping of 383 patients.

A contact history was obtained in 72% of patients, usually in a near relative suffering from open pulmonary tuberculosis. It was not possible to determine the exact time of consolidation-collapse in relation to the primary infection, but this usually occurred within a few months of infection.

TABLE I
Symptoms

Symptom	No. of patients
None	103
Cough	179
Chest pain	29
Sputum	18
Wheeze	12
Dyspnoea	5
Malaise	69
Fever	62
Anorexia	46
Weight loss	37
Erythema nodosum	36
Night sweats	10

Symptoms and signs (Table I). In 103 patients no symptoms or signs were evident and the lesions were found on routine contact examination. Otherwise symptoms were protean in their manifestations, the commonest being cough 179 patients, malaise 69, fever 62, anorexia 46, and weight loss 37. Erythema nodosum occurred in 36 patients and chest pain in 29. Wheezing was present in only 12 children, but on rare occasions it could be severe and associated with a cough reminiscent of whooping cough. Sputum was present in 18 patients but usually gastric lavage had to be done to obtain material for culture of tubercle bacilli. Dyspnoea was present in only 5 patients.

Though, on occasions, signs of obstructive

emphysema or of consolidation were present, signs were usually minimal. However, complications of primary infection (Table II) might produce

TABLE II
Complications

Complication	No. of patients
Pleurisy	39
Emphysema	18
Bone and joint	17
Miliary	16
Miliary and meningitis	5
Meningitis	5
Glands	4
Eyes	2
Abdominal	2
Ears	1

marked signs. The commonest complications were pleurisy 39 patients, emphysema, which was of an obstructive nature 18, bone and joint lesions 17, and miliary tuberculosis 16. In 10 patients meningitis occurred and in 5 of these it was associated with miliary disease.

In order to assess whether chemotherapy had any influence on the frequency of the development of complications, a histogram (Fig. 2) was constructed.

FIG. 2.—Complication rate in years 1952-1959.

This showed that, except for the years 1955, 1956, and 1959, there was a general tendency for the complication rate to fall. In 1959 the total number of patients involved had fallen to 15 and of these, 3 developed complications. In 1958, 3 out of 30 patients developed complications and it is probable that had there been a higher total number of patients for 1958 and 1959 the percentage of complications could well have been lower. The figures show that between 1952 and 1958 there was a drop from 26% to 10% in the rate of complications,

but in 1959 with only 15 patients the complication rate was 20%.

Gastric lavage. The usual practice was to carry out this investigation on two or three occasions during the first few days after admission before starting chemotherapy. Only 36% of patients had a positive culture for tubercle bacilli.

Segments involved. The commonest segments to be involved were the anterior segment of the right upper lobe (63), the right middle lobe (61), and next the anterior segment of the left upper lobe (43) (Fig. 3). The right lung was involved

FIG. 3.—Segments involved.

more often than the left both as regards single and multiple segment involvement. Single segment involvement occurred in the right lung in 170 cases and in the left lung in 106; multiple segment involvement occurred in 68 cases in the right lung and in 39 in the left lung.

Bronchoscopy and bronchography. As these procedures require general anaesthesia in young children neither was performed very often. Only 12 children had bronchoscopies and of these 2 showed a normal appearance, 5 showed oedema of the mucosa around the involved segmental orifice (in 1 there was a block by external gland pressure,

in another a block by granulation tissue), and in 3 a stricture was present; 1 of the 3 with a stricture also had a sinus.

Four bronchograms were normal, 2 showed crowding of bronchi, 3 showed crowding with slight dilatation of bronchi, 8 revealed a block, in 3 there was bronchiectasis, and in 1 child a second bronchogram showed apparent return of dilated bronchi to normal.

Both bronchoscopies and bronchograms were done at varying times in the illness and this accounts for some of the differences found.

Sedimentation rate. In 183 children this was measured using the Westergren method. In 91 it was below 10 mm, in 81, 10 to 30 mm, and in 11 was over 30 mm at the first hour reading. Usually those children showing a raised ESR also had some pyrexia. As recovery proceeded, the ESR fell over a period of 3 to 9 months except in patients developing a pleural effusion in whom the fall was slower.

Fever. This occurred in only 62 children and was usually associated with a complication, though some children with persistent segmental lesions showed a mild pyrexia of 37.2 to 37.8 °C (rectal) for the first 2 to 3 months of treatment. Weight gain was usually rapid whether a mild fever was present or not and this was often remarked upon by the parents who could see a rapid change in their children's appearance in the atmosphere of a country hospital.

Chemotherapy (Table III). By present-day

TABLE III
Chemotherapy

Drugs not used	60 patients
Drugs used	323 patients
Courses of drugs used	No. of patients
Calciferol	34
Calciferol and PAS	29
PAS	28
INAH	33
Streptomycin	14
PAS and INAH	137
PAS and streptomycin	67
INAH and streptomycin	124
PAS, INAH, and streptomycin	9
1 course of drugs	197
2 courses of drugs	96
3 courses of drugs	29
4 courses of drugs	9
5 courses of drugs	2

FIG. 4.—Duration of chemotherapy.

standards this was extremely short, and Fig. 4 illustrates that many patients had such treatment for only 3 to 6 months. 60 children were not given drugs, either in the city hospitals from which most of them had come or in our own hospital. Other children had short courses of drug treatment before admission and drugs were sometimes discontinued after admission particularly in the early years of the study. On occasion drugs were given singly but this practice in general did not find favour with chest physicians so much as with paediatricians who were inclined to prescribe isoniazid (INAH) alone because of the objectionable taste of PAS and the necessity for giving streptomycin by injection. Calciferol was used because, after a vogue for the use of calciferol in the treatment of enlarged cervical glands in the late 1940s, we argued that it could be beneficial for children with enlarged mediastinal glands, particularly when the glands were slow to resolve. In 1952, the late Professor Charles Cameron of Edinburgh, in a personal communication, confirmed this finding. As the years passed, better chemotherapy was given for longer periods. However, as other investigators such as Lincoln *et al.* (1956) have found, chemotherapy often seemed to have little or no effect on the segmental shadow. The writer has noted that if the segmental shadow is extending, then adding streptomycin to PAS and INAH already being given may effect an improvement in the x-ray. Table III shows further the number of times on which calciferol, PAS, INAH, and streptomycin were used singly or in combination in 323 patients. In 138 patients, calciferol, PAS, INAH, or streptomycin used singly, or PAS and calciferol combined, were given. Various combinations of PAS, INAH, and streptomycin were used also, and in all, 161 courses of PAS and INAH, 70 courses of PAS and

streptomycin, 138 courses of INAH and streptomycin, and 9 courses of PAS, INAH, and streptomycin were used. A single course of drugs was used in 197 patients, 2 courses in 96 patients, 3 courses in 29 patients, 4 courses in 9 patients, and 5 courses in 2 patients.

Of the patients who had a relapse and required further chemotherapy 6 had no drugs initially, 1 had calciferol, 3 had PAS and calciferol, 1 had PAS, 1 had PAS and INAH, and 2 had PAS, INAH, and streptomycin.

Of the 21 patients requiring surgery, 1 had no drugs initially, 2 had calciferol, 2 had PAS, 2 had PAS and calciferol, and 1 had INAH, whereas the remaining 13 had combined drug treatment with PAS, INAH, and streptomycin. It appears, however, that even with periods of 4 to 10 months pre-operative chemotherapy, active tuberculous lesions sometimes showing tubercle bacilli on direct smear are found, and consolidation-collapse may persist for long periods.

Duration of consolidation-collapse. In 227 patients it was possible to define fairly accurately when the consolidation or collapse began to clear in serial x-rays, whereas in other patients this was a rather gradual process and more difficult to assess. Fig. 5 shows that there were two peaks, one at 2½

FIG. 5.—Beginning of clearing of consolidation-collapse.

months and the other at 7½ months from the onset of the condition, when x-ray clearing began to occur. It may be that these two peaks represent different pathological processes, the early one being due to the clearing of an atelectatic area and the later one representing clearing of tuberculous consolidation, atelectasis being present only to a minor degree.

FIG. 6.—Duration of consolidation-collapse and duration of stay.

Fig. 6 shows that maximal clearing for most patients was reached about 10 to 12 months from the onset of the condition, though some patients took 12 to 24 months to show marked resolution. The duration of stay was somewhat longer than the duration of the segmental lesion, with the majority of children being discharged by 14 months from the admission date. No doubt this seems a very long time by present standards but, as this hospital was specifically designed and equipped to deal with long-stay patients before and at the time of this study, it seemed to be a reasonable method of treatment, and this is borne out by the good late results. The psychological upset of a hospital stay seemed to be minimal and no doubt this was in part due to an understanding nursing staff backed up by a good teaching staff, children being admitted to nursery schooling at 3 years of age.

Operations. Only 21 children (5.2%) had major surgery performed. Of these, 4 were aged 3 to 6 years, 7 were 7 to 9 years, 4 were 9 to 12 years, and 6 were over 12 years at the time of operation. In 10 patients lobectomy was done, in 7 a segmental resection, in 1 lobectomy plus removal of glands, in 2 segmental resection plus removal of glands, and in 1 glands only were removed after which an atelectatic lobe re-aerated. Operation was not normally undertaken within a year of coming into hospital and most of the children were over the age of 6 before surgery was done. This policy was particularly adhered to after a severe case of laryngeal oedema necessitating tracheostomy resulting from a difficult endotracheal intubation in a child of 4. Thereafter, it was decided that children having persistent lesions might be allowed home if they

were otherwise well, and that the chest physician responsible for their care would send them back to the hospital if the necessity arose later. In 3 patients a solid caseous area of disease was found, in 3 a fibrotic shrunken lobe or segment, in 7 atelectasis and bronchiectasis, in 2 an infiltrated lobe, and in 5 a tuberculous abscess.

Post-discharge complications (Table IV). 17 children had a flare-up in the collapsed segment after discharge, and one had a flare-up elsewhere in the lung (Table IV). Of these, 12 patients

TABLE IV
Post-discharge complications

	No. of patients
<i>Pulmonary</i>	
Flare-up in collapsed segment	17
Flare-up elsewhere in lung	1
Of these, operation required	6
<i>Extrapulmonary</i>	
Facial lupus	1
Erythema nodosum	1
Bone and joint . .	1
Tuberculous meningitis	1
Post-tuberculous meningitis { epilepsy	1
{ giddiness	1
	2

resolved their lesions without surgery. Extrapulmonary complications occurred in 4 patients and 2 had late complications of tuberculous meningitis treated earlier in the course of their illness. 14 patients had an occasional cough, 7 occasional sputum, and 3 wheeze. One of the patients who complained of wheezing had asthma.

Final results

In 1965, that is, 6 to 13 years after discharge, the general health and the chest condition of 338 patients (88%) was satisfactory and was not giving rise to symptoms requiring any treatment. If one deducts those patients having occasional chest symptoms such as cough, sputum, or wheeze, then 324 patients were fit and well. 41 could not be traced. 4 died, 2 from tuberculous meningitis early in the disease, 1 from a road accident after discharge, and 1 from appendicitis with peritonitis. Deducting those children who required surgery, the number of patients successfully treated medically, excluding the 2 tuberculous meningitis deaths, was 303. We believe that the majority of the untraced 41 were also well.

Full radiological clearing occurred in 173 patients (45%). Some of these patients showed full

clearing plus a calcified primary focus, or calcified glands, or calcified primary complex. Fibrotic scars were seen in 84 patients (23%), and a calcified focus, calcified glands, or complex in 14; other calcified foci with or without calcified glands were also seen in a further 18 patients. Persistent atelectasis occurred in 8 patients and in 2 of these calcified glands were present. Calcified foci at the site of the collapsed segment were noted in 27 patients, and calcified foci at the site of the collapsed segment plus calcification in the glands in 5. Double or triple primary complex was noted in 7 patients and persistent emphysema in 2 patients.

The clearing of calcification in whole or in part from the lungs and/or lymph nodes of 68 children is a most interesting finding, which has been discussed in detail elsewhere (Morrison, 1970). In brief, by 1968 full clearing of calcification had occurred from the lungs of 24 children and from the lymph nodes of 13 children, and partial clearing had occurred from the lungs of 17 children and from the lymph nodes of 14 children.

Discussion

In 1920, Eliasberg and Neuland coined the term 'epituberculosis' for the condition of consolidation-collapse in primary pulmonary tuberculosis and stated that, 'the man who concludes that a serious form of tuberculosis is present will be surprised for clinical recovery is frequent'. Though Thomas (1952) had arrived at the decision that children could not be regarded as having a benign disease, our experience before this led us to a similar conclusion to that of Eliasberg and Neuland. Thomas advocated surgical management for children who had not responded to the conservative therapy of bed rest and antituberculous chemotherapy. From a study of the case histories which he quotes, the period of conservative treatment, 2½ to 9 months, was not particularly long when one considers the length of time during which changes can occur in tuberculous lung lesions, particularly in the evolution of the primary complex. Sweany (1941) has illustrated how the evolution of the primary complex goes on over a period of many years; though it was once thought that calcification was a sign of healing in tuberculosis, calcification may be absorbed and over a period of 10 to 20 years bone may be laid down. Hence a decision to operate in children having less than 12 months' treatment seemed to the writer to be premature. Though the logic of removing massively diseased glands cannot be gainsaid where the right surgical facilities are available, nevertheless the difficulties of the task in young children can be considerable; among

the initial 37 children operated upon in the series reported by Thomas (1952), one died of haemorrhage.

The pathology of the condition has been well reviewed in articles by Adler and Richards (1953), Seal and Thomas (1956), and Macpherson *et al.* (1960). It seems from Fig. 5 that we are dealing with two pathological processes which overlap in many cases, namely atelectasis and consolidation, which may proceed to caseation and calcification. Probably those children showing early clearing of consolidation-collapse at 2½ months have mainly atelectasis, while those showing clearing at 7½ months mainly have a true tuberculous pneumonia, either caseous or noncaseous, or a mixture of these conditions. This will depend on whether the lymph nodes rupture back into the bronchi, though consolidation round a tuberculous focus can occur, and in sensitized animals has been produced by the intravenous injection of tubercle bacilli by Nichols (1905).

The present findings and conclusions, though not of so much importance as they might have been 20 years ago for Great Britain, are nevertheless relevant for those areas where childhood tuberculosis is still a problem. This applies not only in the developing countries but even in the U.S.A., where, for instance, Giamonna *et al.* in 1969 described 9 cases of massive hilar lymphadenopathy among 35 children with active primary pulmonary tuberculosis seen during a single year in Florida. Only one of these children had surgical treatment for persistent atelectasis and calcification. It seems that simple measures such as removing the child from a poor environment combined with antituberculous chemotherapy will, in the majority of children, achieve satisfactory resolution of the tuberculous process given adequate time, and surgery will rarely be required.

Gerbeaux, Masse, and Baculard (1957) believe antituberculous chemotherapy plus steroids may play a useful part in hastening resolution and preventing later complications. At the present time a few children, usually of immigrant stock, are being admitted to this hospital who have had a preliminary short course of steroid treatment in a city hospital. Rebound lesions may occur on stopping steroids but even when this does not occur the segmental lesion may still be slow to resolve unless treatment is started at a very early stage in its evolution. Though it is tempting to use steroids when one observes the rapid resolution of areas of consolidation-collapse in some patients, a controlled trial over a period of 12 to 24 months might well reveal as little difference in the progress

FIG. 7.—Case 1, female, aged 9 years. (a) Segmental shadow in axillary area of left upper lobe; (b) partial resolution at 3½ months from onset; (c) at 4 years and 6 months there is only slight residual linear streaking at the site of the lesion. Treatment: INAH 200 mg daily with PAS 10 g daily for 12 months. Streptomycin also given for first 4½ months of treatment.

of the lesions as was observed in the treatment of adult type pulmonary tuberculosis in the Scottish survey of Horne (1960). Nemir *et al.* (1963), reporting on 42 children with primary tuberculosis with lymph node involvement, treated 21 patients with prednisone and found that as compared with

21 control patients there was no significant alteration in the course of the disease. Giamonna *et al.* (1969) found no improvement or regression of lymphadenopathy in one child in their series who received prednisone.

Fig. 7 to 9 illustrate the process of resolution in

FIG. 8.—Case 2, female, aged 9½ months. (a) Consolidation in right upper lobe; (b) marked calcification in this lesion and in a right paratracheal lymph node at 1 year 10 months from onset. Note also marked calcification in spleen, in abdominal lymph nodes, and in liver. Calcification also evident in a node at root of neck on right side. (c) At 9 years 11 months marked resolution of right upper lobe lesion with further contraction and clearing of calcification in right upper lobe and paratracheal lymph node. Treatment: 6 weeks streptomycin 200 mg daily before admission. Streptomycin 200 mg daily for 4½ months at 9 months from onset of spinal lesion.

FIG. 9.—Case 3, male, aged 8½ months. (a) Marked obstructive emphysema of left lung with mediastinal displacement and depression of left dome of diaphragm. Area of consolidation-collapse in anterior segment of left upper lobe. Improvement in degree of obstructive emphysema occurred by 4 months from onset; (b) at 11 years only a small calcified focus remained in left midzone. Treatment: PAS 2½ g daily and streptomycin 400 mg daily for 7 weeks before admission.

3 typical instances. In Case 1 (Fig. 7) radiological clearing is shown to occur in a relatively short time in a straightforward case of consolidation-collapse. In Case 2 (Fig. 8) the slower clearing of consolidation which has become partly calcified is illustrated. In Case 3 (Fig. 9) the resolution of gross obstructive emphysema is shown. Chemotherapy by modern standards in all of these children, particularly the last, was very short indeed. It may be that chemotherapy is continued nowadays for an excessively long time and that the physician forgets the part played in healing by the natural defences of the body which, before chemotherapy, were frequently sufficient to produce healing both in childhood and adult type pulmonary tuberculosis.

The importance of this study is to stress that the place of surgical interference in this condition, whether it be minimal by bronchoscopy or major by thoracotomy, is strictly limited. Bentley and Grzybowski (1954) found that active endobronchial measures were undertaken in only 8 out of 29 patients bronchoscoped in their series of 169 children with segmental lesions; in these 8 patients there was no evidence that the course of the lesion was thereby influenced. The necessity to give general anaesthesia in young children and the often predictable nature of the findings, which bronchoscopy in other series failed to benefit, led the writer to avoid bronchoscopy and broncho-

graphy in all but a few young children. Macpherson *et al.* (1960) adopted a similar policy.

One cannot help but agree with Bentley and Grzybowski (1954) that while specimens removed at operation, particularly in the early stages of the disease, may show severe and extensive pathological changes, this does not of itself justify the need for surgery. They note that even in a severely ill child with suppurative pneumonic changes behind a bronchial obstruction, antibiotics and bronchoscopy will generally lead to clinical recovery. They did not find that any child with a segmental lesion succumbed to the illness, and the risk of developing haematogenous dissemination was not greater than in simple primary pulmonary tuberculosis. Added weight to the argument not to operate early is the observation by Dunnill (1962) that at birth there are 20 million alveoli present but that by 8 years they have increased to 300 million. In our series, 270 children were under 6 years of age on entry to the study and early surgery would have deprived them in many instances of lung tissue capable of growth. The main indications for major surgery appear to be the following. (1) Gross obstructive emphysema if thought to be life-threatening because of stridor and cyanotic attacks. This condition however can resolve given time, and resolution may well be hastened by steroids. (2) Persistent segmental lesions after 2

years. (3) Bronchiectasis with symptoms. The indications as set out in Miller, Seal, and Taylor's book (1963) are rather more comprehensive, but no long-term follow-up of the children operated on has been published and one wonders how many might have cleared their x-rays on longer conservative treatment. Our pathological findings show an almost equal number of patients with tuberculous consolidation, abscess formation, or infiltration of a segment or lobe, compared with those showing a fibrotic shrunken segment or lobe, or atelectasis with or without bronchiectasis.

Brock in 1950 stated that 'to operate in the presence of active lymphadenitis is unjustifiable. If the process is given time to resolve under expectant treatment the patient may be left with little residual disease or disability.' The same view seems to hold good in 1972 and is in keeping with that originally put forward by Eliasberg and Neuland (1920).

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