MODERN PRACTICE
IN
TUBERCULOSIS

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CHAPTER 1

PRIMARY TUBERCULOSIS

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EXCEPT for those people living in more or less isolated communities, most of the population of the British Isles become infected by tubercle bacilli at some time in their lives. Published records of surveys of tuberculin testing in England show that about 80 per cent of young adults have positive tuberculin tests. It therefore follows that primary tuberculous lesions have developed in that proportion of the population during infancy, childhood, adolescence or early adult life. Among those known to be in contact with cases of active tuberculosis, a much greater number have primary lesions. In the Prophit Survey (1948) it was found that, in the contact group of 18–20 years of age, 95·6 per cent had positive tuberculin tests. In the Brompton Hospital records (1931) there were 70 per cent positive in the contact group of 0–5 years of age, 75 per cent in the 5–10 years and 76 per cent in the 10–15 years age group.

In Great Britain it is probable that in the population as a whole, primary infection is usually of human origin and tubercle bacilli gain entry by inhalation and consequently it is usual to find the primary lesion in the lungs.

The study of primary tuberculosis in adults has, up to the present, been limited. There is evidence to suggest that the behaviour of primary lesions in many adults may differ from that of primary lesions in childhood.

Primary tuberculous lesions in children may develop and heal, or become arrested, without any but pathological evidence and this is the usual course of events. In other children, x-ray examination may show changes in the thorax due to primary lesions and, in yet others, clinical symptoms and signs accompany the primary lesion. It is obvious that it is only the latter group which present themselves as patients, those in the other groups being people in apparent good health and the primary lesion is only discovered on routine radiological examination or, by inference, from positive tuberculin tests, or when autopsy is performed following death from other causes than tuberculosis.

The pathological changes have been studied either by means of experiments in which animals were infected by tubercle bacilli, or in series of post-mortem examinations in which death has been due to some other cause than tuberculosis and in which primary tuberculous lesions have been found in various stages of development and healing. Such a series of autopsies in children has been described by Blacklock (1932). Zarfl (1913) has given an account of a primary lesion in its early stages found in a child who died at the age of twenty-four days.

From these accounts and from those of Ghon (1916), Parrot and others, the course of primary lesions can be followed. Primary lesions are more commonly single than multiple. The first lesion in the lung is probably that of reaction to a foreign body but at an early stage numerous tubercle bacilli are found in the lung

lesion. A small area of tuberculous broncho-pneumonia develops with caseation. The typical lesion, the average size of which Blacklock compares with that of a hazel nut, becomes encapsuled by fibrous tissue and demarcated from the surrounding normal lung tissue. The only spread of the tuberculous process is along the lymphatic channels. Soon after tubercle bacilli reach the lung parenchyma, they are found also in the lymph glands which drain the portion of the lung in which the primary lesion is situated. Small tubercles may be present immediately outside the fibrous capsule, the tuberculous process probably being conveyed along lymph ducts. The lymph glands become enlarged and contain caseating material. The reaction to the tubercle bacillus in children, especially in young children and infants, is more evident in the lymph glands than in the lung itself. The usual course is for the lung lesion to heal with disappearance of caseous material; in some cases there is no recognizable evidence of the lesion after healing, in others there is a fibrous scar, and in others, calcium is deposited in the lung lesion and in the lymph glands leaving a more permanent and obvious testimony of the primary tuberculous complex. Primary lesions usually develop in the sub-pleural region. They may involve the pleura and not infrequently there is an area of pleural thickening over the lung lesion. The site of the primary lesion varies. Both Ghon and Blacklock found the lesion most frequently in the right upper lobe and least often in the right middle lobe.

This localization of the primary complex in the lung and glands with subsequent healing does not always take place. Primary infection may in a short space of time lead to an acute illness ending fatally with miliary tuberculosis and meningitis. Between the two extremes of the small, silent lesion and the acute fatal illness are to be found many degrees of departure from what might be considered the normal reaction to infection. It is often difficult to define the exact stage at which the primary lesion gives rise to a morbid condition and to say when the individual is suffering from tuberculosis.

Certain conditions appear to favour the development of the more extensive lesions and complications. The age at which infection takes place is accepted by most as being significant. In infants and young children up to about the age of three years, the primary lesion is liable to develop complications. In adolescents and young adults there is evidence to suggest that the primary lung lesion may not remain localized but may spread into the surrounding tissue.

Those children who are in contact with heavily infected active cases and are exposed to repeated doses of infected material and who live with the tuberculous person in poor accommodation tend to develop lesions which are liable to give rise to recognizable clinical and radiological changes.

Certain illnesses, especially measles and whooping-cough, may have a deleterious effect on the course of the primary lesion, as does malnutrition. Different races and certain families appear to react unfavourably to primary tuberculous infection.

COMPLICATIONS OF PRIMARY LESIONS

Pulmonary lesion

When for one or more of the above reasons the primary pulmonary complex does not follow the usual course, it may be found that, instead of the localized lesion

with its surrounding capsule of fibrous tissue, there is an extensive area of tuberculous broncho-pneumonia. Broncho-pneumonia may also develop as a result of aspiration of tuberculous material from a tuberculous lymph node which has ulcerated into the lumen of a bronchus. Tuberculous broncho-pneumonia may give rise either to an acute and often fatal illness or else there may be a subacute condition with few and indefinite symptoms and ultimate recovery. It is difficult to say what determines the acuteness or otherwise in each case but the acute type of illness is found more frequently in infants.

In the acute type the child is severely ill and there is a high swinging temperature and rapid respiration. Cough may or may not be present. At first there may be little to distinguish the condition from a non-tuberculous broncho-pneumonia, the physical signs and radiological appearance having at this stage no special characteristics to show the tuberculous aetiology. A history of contact with a case of tuberculosis and a positive result to a Mantoux test in the dilutions of Old Tuberculin, 1 in 10,000 or 1 in 1,000 in an infant or young child supports the diagnosis of tuberculosis. Another significant observation is the failure of the condition to respond to sulphonamide drugs or to penicillin. Although a few cases recover, usually the course of acute tuberculous broncho-pneumonia in children is a steadily progressive one. There may be periods when the condition is apparently stationary but the general condition steadily deteriorates and marked wasting develops. Further x-ray examinations show increasing lesions with evidence of cavities. Sputum as such is seldom obtained but gastric washings may contain tubercle bacilli on direct examination or culture. Streptomycin and *para*-amino-salicylic acid are now being used for these cases and it is likely that the outcome for some patients at any rate will be more favourable.

In the subacute type of broncho-pneumonia there may be few symptoms. The child comes under observation perhaps for general malaise, loss of weight or failure to gain weight, occasionally because of cough and sometimes simply for examination as a contact with no symptoms of sufficient severity or persistence to cause anxiety to parents. Physical and radiological evidence of broncho-pneumonia is found and tubercle bacilli may be recovered from gastric washings. The general condition of the child shows no marked wasting but there is always failure to gain weight satisfactorily, and often the weight is stationary for weeks or months. The temperature chart shows irregular pyrexia, the temperature rising to 99° or 100° F. for two or three days with intervals of several days when there is no pyrexia. The broncho-pneumonic lesion appears to remain unchanged over a period of weeks, or even two or three months, then there is steady resolution accompanied by an improvement in the general condition of the child. Radiographs show decrease and, in most cases, complete disappearance of abnormal shadows apart from evidence of calcified deposits in the lesion in some cases. Thus the recovery from an extensive tuberculous condition becomes complete.

In some cases, especially in older children, the primary lesion does not remain localized, but spreads and infiltrates the surrounding tissues and the condition becomes indistinguishable from the typical tuberculous infiltration found in adults.

Primary lesions in adults have not been studied to the same extent as in children. Such lesions have been investigated in certain groups of young adults in Great

Britain in the Prophit Survey. The distribution of the primary lesions found differed from that in children, these being more persistently found in the upper than lower zones. Morbidity following primary infection was relatively high but it is pointed out that there was repeated exposure to infection in many of these cases, which may have contributed to this higher morbidity incidence. In other countries, studies on a larger scale have been made of lesions following Mantoux conversion but it is difficult to differentiate, in adults, post-primary from primary lesions and the investigation of this subject is at present far from complete.

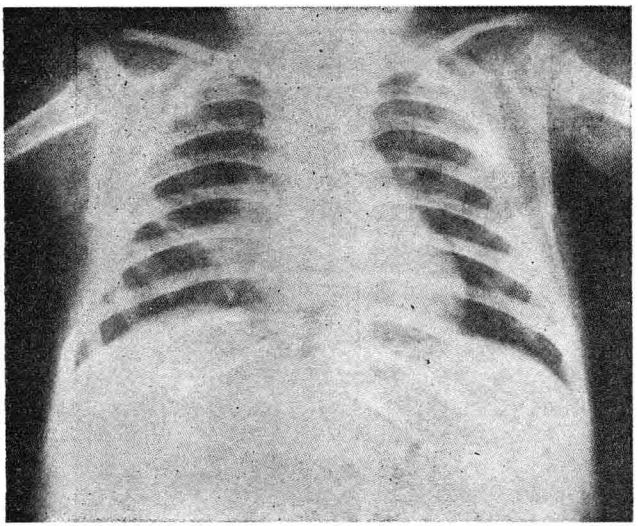
Glandular lesion

Although in most cases the lesions in the lymphatic glands do not give rise to symptoms or signs, they can be detected if of sufficient size by x-ray examination. In children, the lesion of the glands is usually more evident than the lesion in the parenchyma. Radiological signs of hilar adenitis may not develop for a few weeks after primary infection has taken place, and secondary effects resulting from tuberculous adenitis may be still further delayed (Fig. 1). When there are large caseating glands present, no abnormal clinical signs can be detected but there may be general symptoms of malaise, failure to gain weight and an irregular pyrexia as in the case of subacute broncho-pneumonia (Fig. 2).

The lymph glands which drain the region of the lung in which the primary parenchymal lesion is situated are always infected but others may be involved. Tuberculous caseating lesions may be present in the paratracheal glands of the same side, in the glands at the carina, and in hilar or paratracheal glands on the opposite side from the site of the primary lesion. Even when they are definitely enlarged, paratracheal glands and glands in the region of the carina may be difficult to detect in postero-anterior radiographs. Lateral pictures or tomographs are often of help in showing these lesions.

The lymph gland lesions themselves, although they may be extensive, may give rise to few symptoms and signs. They are, however, indirectly one of the most common causes of clinical manifestations in primary tuberculosis in childhood. The hilar glands involved are closely associated with the main bronchi and their branches, and pressure on these structures may cause diminution or occlusion of the lumen of a neighbouring bronchus. In other cases, the tuberculous process invades the bronchial wall and there is erosion of tuberculous material into the bronchial lumen. One of two things may follow, either tuberculous material may be aspirated into the distal part of the lung and a segmental patch of tuberculous broncho-pneumonia may develop, or the tuberculous material may block the lumen and there is atelectasis of the distal segment of lung. Broncho-pneumonia resulting from such aspiration has already been referred to; this complication appears to occur less frequently than the other, occlusion of the bronchus.

Collapse of part of the lung resulting from tuberculous hilar adenitis is probably one of the most likely complications of primary tuberculosis. The collapse of the lobe, being dependent on the glandular lesion and not the pulmonary part of the primary complex, does not necessarily affect the lobe which contains the primary lesion. The primary focus may be recognized, at the time or later when there is calcification, in another lobe or even in the opposite lung from the atelectactic lobe in cases where there has been spread of infection across the midline to glands in



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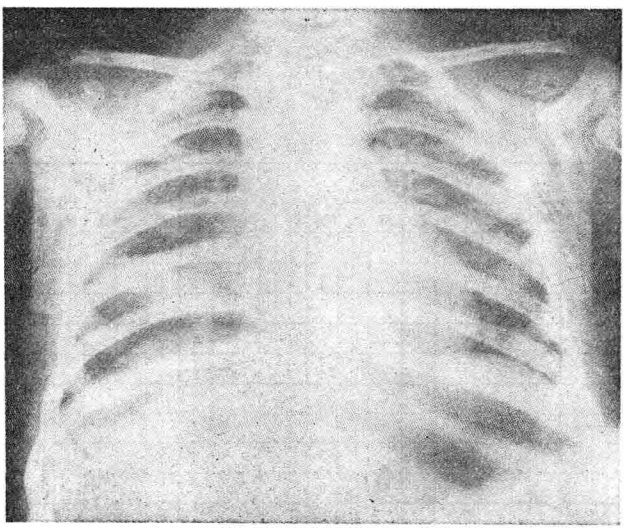

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FIG. 1.—Primary infection with Mantoux conversion known to have taken place between December 1936 and April 1937. At time of Mantoux conversion x-ray was normal. (*a*) July 1937. Showing enlarged hilar glands with partial collapse of middle lobe three months after Mantoux conversion. (*b*) December 1937. Increased collapse of middle lobe eight to twelve months after primary infection.

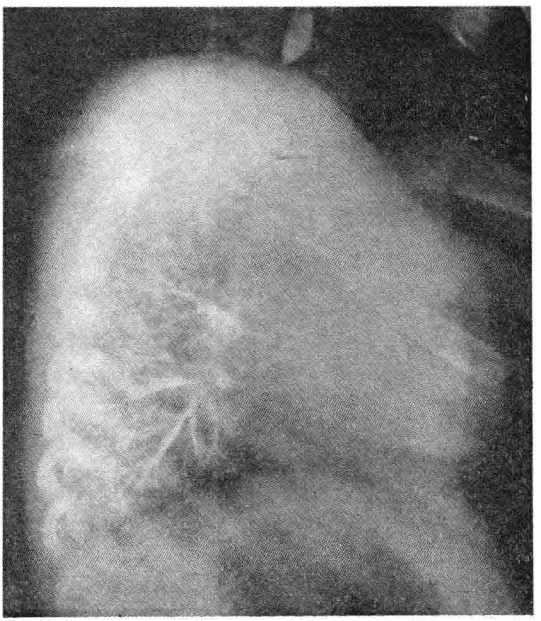

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FIG. 1.—(*contd.*) (*c*) April 1938. Bronchogram showing blocking of middle lobe bronchus.

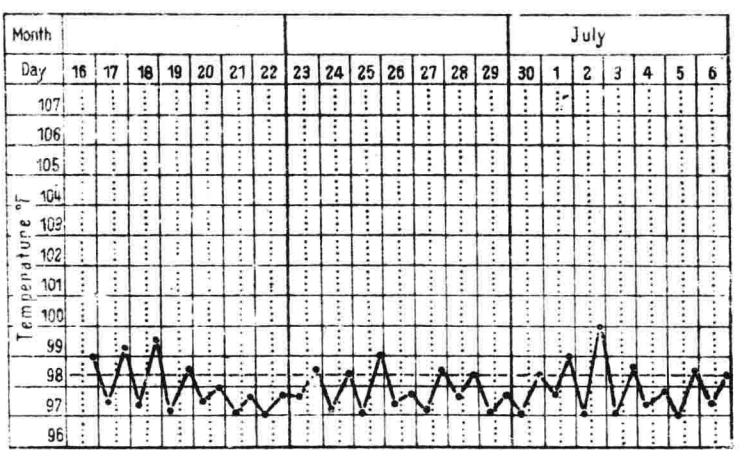


FIG. 2.—Temperature chart of girl aged 3 years with gross hilar adenitis following primary tuberculous infection.

the opposite hilum (Fig. 3). From the anatomical distribution of the glands at the hilum, it is to be expected that the middle lobe on the right side would be liable to be occluded. Richards (1944) found that the right middle lobe was affected in 23 out of 66 cases of collapsed lobes. In a series of 43 cases of collapse of lung associated with active primary tuberculosis at the Children's Contact Clinic at Brompton Hospital (1950), it was found that collapse occurred with equal frequency in right upper and right middle lobe, the incidence being 14 in each. Brock (1950) has found post-tuberculous bronchial stenosis or bronchiectasis in the middle lobe in 60 out of 93 cases.

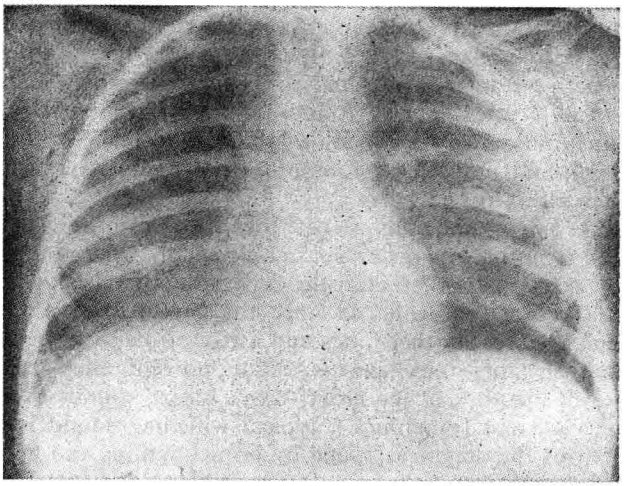
Occlusion of a bronchus and collapse of a lobe may not produce any symptoms or signs, but when symptoms do occur, spasmodic cough, wheezing respiration and breathlessness on exertion are characteristic. On examination it may not be possible to detect even large areas of collapse since the condition is often masked by compensatory emphysema in other lobes and a rise of diaphragm on the affected side. These compensatory mechanisms often prevent displacement of the mediastinum and of the apex of the heart. Weak breath sounds over the affected lobe may be detected and sometimes a typical whistling sound is heard. X-ray examination confirms the diagnosis, aided by bronchograms and bronchoscopy if necessary. By means of tomographs it is often possible to demonstrate the enlarged gland and narrowing of the adjacent bronchial lumen.

The ultimate result of the bronchial occlusion is uncertain. There may be regression of the lesion and the bronchus becomes patent with resulting re-expansion of lung which returns to normal. In other cases, the intrabronchial lesion disappears and the lumen opens up and becomes normal or has a persisting distortion or narrowing but the pulmonary collapse persists and there is a permanent atelectatic segment of lung. A third possible result is that bronchiectasis develops in the collapsed lobe. During the stage of active hilar adenitis it is difficult to predict how much re-expansion of the lung is likely to take place and how complete the recovery will be. Records from Brompton Hospital Contact Clinic (1950) show that if re-expansion takes place it usually does so within two years. Others have stressed the frequency with which bronchial dilatation is found in the collapsed lobes. There is no doubt that adenitis associated with primary tuberculous infection is an important aetiological factor in the development of bronchiectasis in later life.

Miliary tuberculosis

Both from the lung lesion and from the hilar glands, tubercle bacilli may be discharged into the bloodstream. Miliary lesions may be found in the lungs only, or there may be dissemination through the systemic circulation with scattered lesions throughout the body and the classical picture of acute miliary tuberculosis, with or without meningeal changes, develops.

Clinical, radiological and pathological findings suggest that disseminated lesions in small numbers occur not infrequently after primary infection. The comparatively few scattered miliary lesions do not give rise to any constitutional disturbance, but x-ray examination of the lungs may show evidence of miliary lesions which resolve without specific treatment. During the active stage of primary lesions, secondary blood-borne lesions may develop in the spine or other bones and



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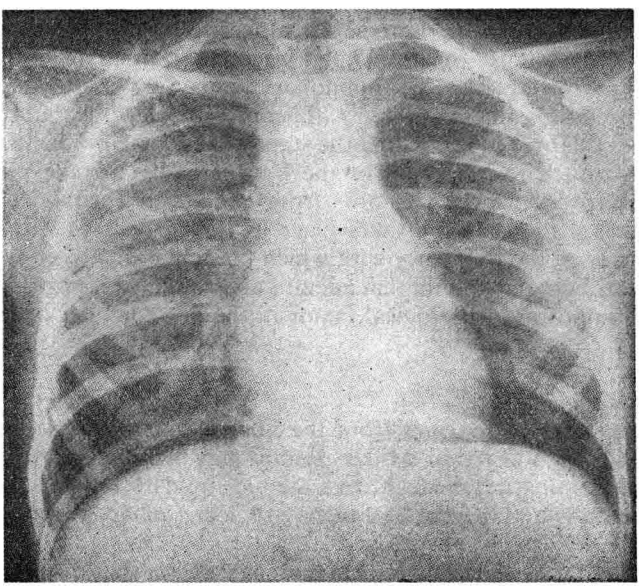

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FIG. 3.—(*a*) February 1932. Primary tuberculous lesion with enlarged right paratracheal glands and collapse of *middle lobe*. (*b*) February 1935. Healing lesion with calcified primary focus in right *upper* lobe and calcified lesion in glands at right hilum.

elsewhere, without the accompanying picture of classical acute miliary tuberculosis. These lesions may develop insidiously while a child is being treated by rest in bed for the original primary pulmonary lesion and may remain undetected until they are well established. These active haematogenous lesions are apparently more likely to appear in those cases in which there has been a big reaction to the primary infection either in the lung itself or in the glands, or in both. When resistance is lowered, especially by an attack of measles, secondary lesions or characteristic acute miliary spread may develop, even if the primary lesion is not a gross one.

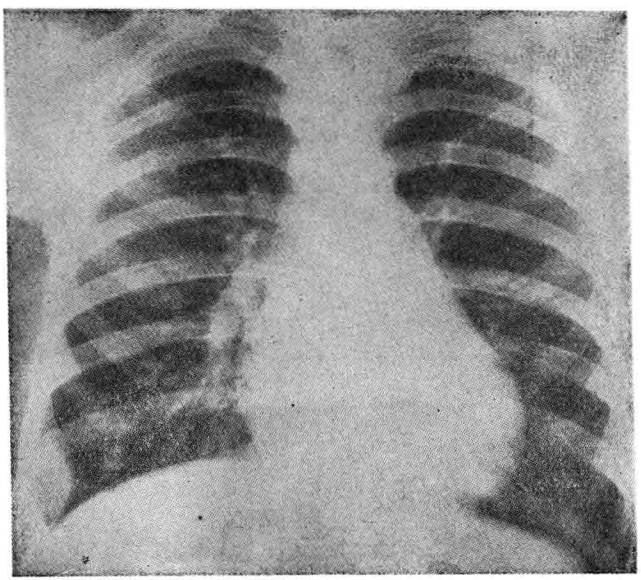

FIG. 4.—Calcifying primary lesion of right lower lobe, with resolving localized pleural effusion.

Pleural changes

The primary lesion is usually situated in the subpleural region, but in spite of this fact large pleural effusions are not often associated with primary tuberculosis in childhood. Other pleural changes more frequently found are thickening of the overlying pleura or small loculated effusions, especially in the interlobar regions (Fig. 4). When pleural effusion does occur in a child it may be quickly absorbed, lasting for little more than one week. The symptoms may be slight with little constitutional disturbance but usually there is a history of pain in the chest. The diagnosis of the tuberculous aetiology may be difficult and may only be established when the fluid clears and a primary complex is found in subsequent radiographs (Fig. 5).

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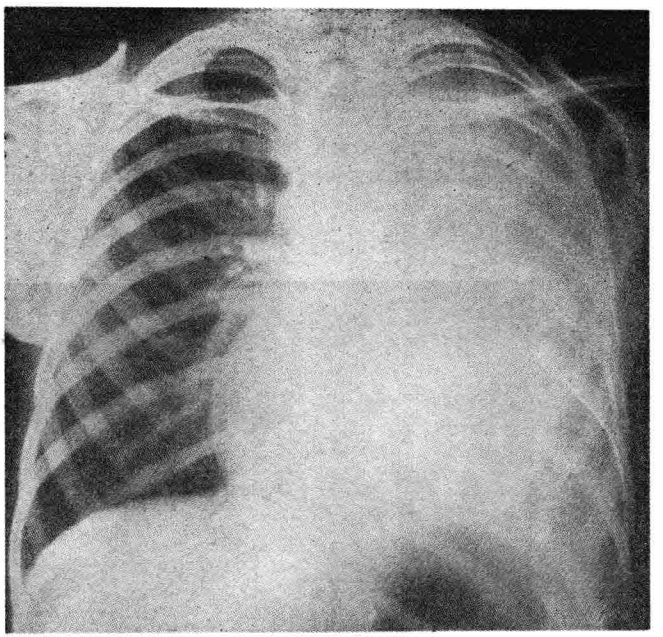

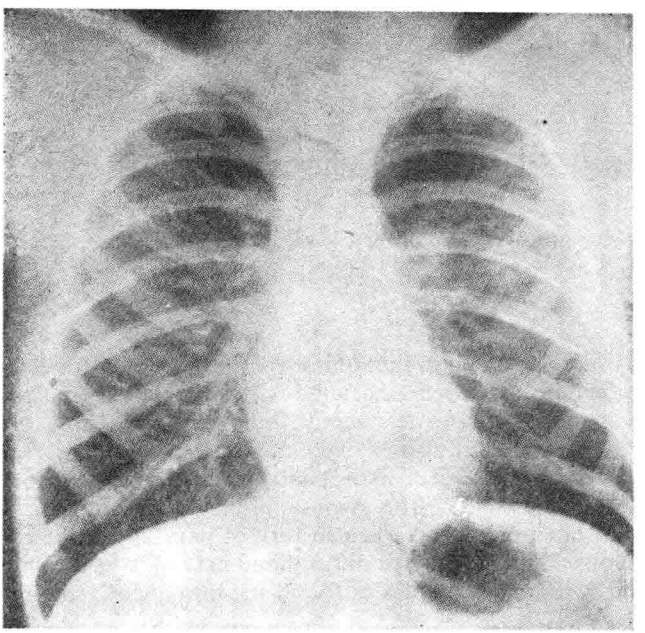

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FIG. 5.—(*a*) December 1947. Pleural effusion. (*b*) February 1948. Showing effusion cleared. Enlarged glands left hilum and early primary lesion left third intercostal space.

It is more usual in adults than in children to find large pleural effusions associated with primary lesions. In the Prophit Survey there were 25 cases of pleural effusion among 71 cases which showed clinical evidence of tuberculous lesions following Mantoux conversion.

Erythema nodosum

Erythema nodosum may accompany the early stages of primary lesions. The frequency with which it occurs in association with primary tuberculosis varies in different countries. In Great Britain erythema nodosum accompanies other infections than tuberculosis but the appearance of this condition always calls for a careful investigation of possible primary tuberculosis.

EPITUBERCULOSIS

In 1920 Eliasberg and Neuland described a condition found in children to which they applied the term epituberculosis. They considered the condition was certainly tuberculous and usually found evidence of tuberculous lesions elsewhere in the body. The children were found to have signs of extensive pulmonary lesions but they were not accompanied by any marked constitutional symptoms. Radiological examination showed a shadow extending over an entire lobe. The condition remained virtually unaltered for a period of weeks or months, then there was a gradual clearing of physical signs and a diminution in the shadow seen in the x-ray picture, the shadow disappearing from the periphery towards the hilum and leaving a central shadow which was compatible with enlarged hilar glands. Because of the benign course of the condition, it was not possible to obtain any pathological material. The term epituberculosis has since been applied to conditions which do not always conform to the original description, thus leading to some confusion, especially when epituberculosis has been applied to radiographic appearances without reference to the clinical picture. Further studies of tuberculosis in children since the time of Eliasberg and Neuland show that the condition they described is probably usually the result of glandular erosion into a bronchus causing either collapse of part of the lung or a spread of tuberculous material, by aspiration, giving rise to non-caseating tissue reaction in the lung (Pagel, 1938).

MANAGEMENT OF CASES OF PRIMARY TUBERCULOSIS

Prevention

It is advisable to prevent primary pulmonary lesions during infancy and during adolescence and early adult life since it appears that, at these ages, primary lesions are liable to have serious effects. At any age, lowered resistance and a heavy and repeated infection may give rise to complications developing from primary lesions. During infancy it should be possible in most cases to protect the child from exposure to known cases of open tuberculosis. After this age, protection from infection is more difficult but no uninfected child or young person should be knowingly allowed to be exposed to large and repeated doses of infection without proper precautions.

The spread of infection can be greatly diminished by making a correct diagnosis of the tuberculous condition early, and by removal of infected persons to hospital

or sanatorium where, not only are they isolated from their households but they are taught good hygiene and are given treatment which aims at eliminating tubercle bacilli from the sputum. Early diagnosis has been improved by the more widespread recognition of early symptoms by the medical and lay populations and by improved facilities for x-ray examination, including mass radiography. Unfortunately, however, it is often the chronic elderly case with heavily infected sputum which is not included in these examinations. The ideal procedure of removing the acute tuberculous patient to hospital or sanatorium is often impracticable at the present time owing to shortage of institutional facilities. It is then advisable to remove a young child from the home if possible or to keep it strictly isolated from the tuberculous patient. Sensible nygiene and good housing with ample living space then become important factors in preventing infection. Ample living space is another ideal which is far from being realized today and this deficiency together with lack of institutional accommodation often force on the child the dangers of repeated tuberculous infection. In this case a B.C.G. inoculation is of value and should be advocated.

Treatment of primary tuberculosis

In childhood

In the majority of cases in Great Britain, by the time the child is known to be in contact with an active case of tuberculosis, infection has taken place and the primary lesion has already developed. When the primary lesion is the typical small lesion, undetectable apart from a positive tuberculin test, no treatment is required. Mention has already been made of the latent period between the primary infection and the appearance of enlarged hilar glands in radiographs. Because of this, it is advisable to have a further x-ray taken, even if the first one shows no abnormality, after a period of three months.

If there is radiological evidence of a small primary lesion and a moderate degree of enlargement of the glands, it is not usual to give any special treatment apart from taking steps to maintain general resistance and to avoid as far as possible exposure to other infections, especially measles and whooping-cough. Regular observation with repetition of x-ray examination at least every three months is advisable until there are signs of disappearance of the lesion with or without deposition of calcium in the primary complex.

When the primary lesion is more extensive and accompanied by gross hilar enlargement, opinions vary about treatment. Each case has to be considered on its own merits and the home circumstances and family history of resistance to tuberculous infection must be taken into account. There is little doubt that rest in bed in suitable surroundings increases the rate at which caseating lesions heal, consequently, in most cases, bed rest is recommended in the open air, out of direct sunlight, or in a fresh and airy room. It may be necessary to remove the child to an institution where it is easier to carry out rest in bed, where there is trained supervision and facilites for x-ray examinations. There are certain disadvantages in having the child in hospital, chief of which is the risk of developing infections from other children. The period of observation and treatment, to be of any value, may have to be one of six months or more and there are obvious disadvantages in a young child being removed from its home atmosphere for so long a period.