EPITUBERCULOSIS

BY

M. DE BRUIN, M.D.

(From the Department of Paediatrics, University of Amsterdam.)

In 1921 Eliasberg and Neuland¹ suggested the new clinical conception termed epituberculosis. In young children with a positive tuberculin test extensive physical changes were found in the chest, consisting of an impaired percussion note with diminished or tubular breathing, mostly localized in the upper lobe, especially on the right side. Râles were only rarely heard. The general condition was comparatively good, the temperature was normal or slightly raised, the most striking feature being that in the majority of cases the physical signs, after remaining unchanged for some months, completely disappeared. This latter fact was not in accordance with the current opinion on the course and prognosis of extensive tuberculosis in young children. A progressive destructive process was expected. On account of this Eliasberg and Neuland concluded that the extensive physical changes appearing on the skiagram as a dense diffuse shadow were not due to specific tuberculous tissue changes. They suggested that these pathological alterations were a reaction in the adjacent lung tissue to toxins produced by a tuberculous focus. If the activity of the focus ceased these alterations might completely disappear. The infiltration should be put on the same level with the perifocal inflammation (Tendeloo) which may occur in the proximity of any inflammatory focus (e.g. the inflammatory swelling round a boil).

The clinical syndrome of epituberculosis soon found its way into the literature on tuberculosis in childhood. It served to give a better insight into the activity of the tuberculous process. This holds true especially since the conception of epituberculosis is used not only for the massive infiltration of a whole lobe but also for all kinds of diffuse shadows appearing suddenly in young children and disappearing again completely after a varying period. Epituberculosis as a clinical hypothesis is used to explain the existence of extensive tuberculous changes which cause no permanent damage in contrast with the hitherto-accepted bad prognosis of extensive tuberculosis in childhood.

The necessity of confirming this clinical hypothesis by morbid anatomical data has been urgently felt. It is obvious, however, that an occasion for post-mortem examination can seldom arise, as the most essential feature of these infiltrated areas is their complete restitution to normal. Publications on post-mortem findings are rare, none offering a convincing solution of the problem (Eliasberg and Neuland, Rubinstein², Grävingshoff³,

Harms and Klinckmann⁴, Pagel⁵). Many authors do not report on the anatomical structure, others mention serous, lymphocytic infiltration of the involved lung tissue.

In a child with a marked extensive tuberculous infiltration Spence⁶ punctured the lung in two different places twice in a month. The material obtained contained caseous tissue. Microscopically tubercle bacilli were found and on injection into a guinea-pig gave a positive result. Spence believes that the whole epituberculous infiltration consists of caseous tissue. Reichle⁷ assumes that epituberculosis is in many cases merely an extensive tuberculous pneumonia, differing from the ordinary type by undergoing complete reabsorption.

The rôle of atelectasis.

In the course of a study on the rôle of atelectasis in tuberculosis in childhood another explanation of the pathogenesis of the so-called epituberculous infiltrations seemed to suggest itself. In the author's opinion epituberculosis should be considered in many cases as atelectasis caused by occlusion of a main bronchus. In a former paper⁸ attention has been called to the occurrence of occlusion of a main bronchus during chronic lung disease in childhood. Especially in tuberculosis, which is characterized by swollen glands in the hilus, changing repeatedly in extent, occlusion of a bronchus may take place.

Atelectasis offers great difficulties in respect to its recognition by means of x-rays. Roentgenological evidence is clear in those forms of atelectasis in which a hitherto normal lung is suddenly occluded, for example, by the entrance of a foreign body. The air in the lung is quickly absorbed, so that a marked diminution of volume occurs (collapse of the lung). The diagnosis is more difficult if atelectasis takes place in the course of lung disease. In these cases the typical forms of collapse of part of the lung are not evident on the skiagram on account of the pre-existing shadows. Even so, if there is enough diminution of volume, it is possible to make a correct diagnosis, which may be confirmed by further skiagrams taken after reventilation has occurred. The diagnosis, however, is impossible if the occlusion takes place progressively. In these cases the lung gets filled with pathological material (drowned lung), so that atelectasis is not accompanied by diminution of volume of the lung. Moreover pleural adhesions may hamper the displacement of the mediastinum.

X-ray evidence.

It is not possible to give a description of all the x-ray evidence tending to confirm the hypothesis that epituberculosis should be considered in many cases as atelectatic in origin. It may be divided into the following five groups:—

(1) Skiagrams of epituberculosis showing the same picture as found in atelectasis. (2) Skiagrams showing a diffuse shadow in the lung field

together with displacement of the heart towards the involved side. (3) Series of skiagrams showing displacement of the heart occurring after increase of x-ray and physical findings. (4) Series of skiagrams showing decrease of physical and x-ray findings with simultaneous return of the displaced heart to its normal position. (5) Skiagrams of a case in which the shadow disappeared and returned again. At post-mortem examination the clinical diagnosis of atelectasis was confirmed.

Of each group a typical example will be given. The case mentioned in group 5 is more extensively reported as it seems to offer convincing proof for the thesis here put forward.

Case records.

Group 1. Patient A was aged one-and-a-half years at the time he was thought to be presenting a clear case of epituberculosis. The skiagram (fig. 1) showed a mottled shadow in the right hilus and

FIG. 1.—For full description of this and other illustrations see text.

the right middle field, with a homogeneous shadow of the right upper lobe. This shadow is clearly defined at the base by a line from the hilus laterally upward. This type of shadow is repeatedly observed if the bronchus of the right upper lobe is occluded by a foreign body (a similar case has been observed, in which the diagnosis was confirmed at autopsy). It may be surmised that in this very young child the tuberculous focus in the right middle field has caused a marked swelling of the glands in the hilum, which has brought about occlusion of the bronchus of the right upper lobe.

Group 2. Patient B, a boy aged two years, showed the clinical picture of epituberculosis of the right upper lobe. On x-ray examination (fig. 2) the heart was seen in the middle of the chest. The right border of the heart extended rather far to the right.

FIG. 2.

FIG. 3.

Caution is advisable in the interpretation of the position of the heart in young children as it is very variable. However under normal conditions the heart rarely extends so far to the right as in the case reported; in epituberculosis on the right side a similar displacement is repeatedly observed. Displacement of the mediastinum towards the involved side is generally either caused by collapse of the lung or by shrinking of the lung tissue.

As the latter condition is rare in the type of tuberculosis in which epituberculosis occurs, the conclusion seems justified that the x-ray evidence of displacement of the heart to the involved side must be accounted for by collapse of the lung. Increased translucency is shown at the base of the right lung as is often seen in the adjacent tissue in atelectasis.

Group 3. Patient C, a boy came to the hospital when two-and-a-half years of age. Physical examination revealed an area of slight dullness with diminished breath sounds between the scapula and the spine over the right lung. The first skiagram showed a homogeneous shadow on the right side with normal position of the heart (fig. 3). Some weeks later on physical examination displacement of the heart was found. The area of dullness had increased. The skiagram (fig. 4) confirmed the clinical diagnosis.

FIG. 4.

The trachea, which in the first skiagram was visible in the mid-line was now displaced to the right. The border of the heart extended further to the right. The size of the shadow had increased. The simultaneous incidence of increase of physical and x-ray findings in the lung with displacement of the heart makes it probable that this was a case of atelectasis with collapse.

Group 4. Patient D, an infant, was brought to the hospital when four months of age. The tuberculin test was positive. In the first skiagram taken on 26.iv.1934 (fig. 5) the left border of the heart was not visible and only a mottled density was seen. In the left upper lobe, close to the spine, a convex, dense diffuse shadow was seen. The right upper and middle field were entirely

opaque. This is one of the typical x-ray pictures of collapse of the right lung in which the heart is so much displaced to the right side that dextrocardia has developed. The next skiagram,

FIG. 5.

FIG. 6.

four weeks later (fig. 6), shows that the shadow on the right side had nearly disappeared. The remaining part of it was accounted for by an infiltration of the hilum accompanied by swollen glands. These pathological alterations had caused the collapse. The left border of the heart had returned to its normal position. The

convex defined shadow which was noticeable in the first skiagram was now overshadowed by the mediastinum. In this case the collapse made it possible to discern the shadow of a swollen gland, otherwise not visible on an antero-posterior skiagram. The child died (14.vi.1934) and at autopsy no remains of atelectasis were

FIG. 7.

FIG. 8.

found. However this is no argument against the clinical diagnosis as the atelectasis had disappeared some time before death occurred.

Group 5. Patient E, a boy aged three months was admitted to the hospital on 20.ix.1934 suffering from tuberculosis. The first skiagram on 24.ix. (fig. 7) showed a homogeneous shadow in the

left upper lobe. This shadow gradually disappeared and a swollen paratracheal gland became visible on the left (fig. 8). The child contracted chickenpox, which activated the tuberculous process. The next skiagram (fig. 9) showed bilaterally swollen glands and again a homogeneous shadow in the left upper field. This shadow increased during the following days. The child became rapidly worse, clinical signs of tuberculous meningitis developed and death occurred on 9.iii.1935.

The x-ray findings in this case may be considered typical for epituberculosis. A homogeneous shadow in the upper lobe, disappeared and later reappeared when the tuberculous process was activated by a non-specific infectious disease.

From the findings at autopsy, kindly furnished by Dr. M. Straub, may be quoted the following essential facts:—

FIG. 9.

On section of the lower lobe of the left lung, below the centre of the posterior aspect of this lobe a subpleural yellow caseous focus was found, 1.5 cm. in diameter communicating freely with a bronchial branch and liquified in its centre (tuberculous primary focus). Round this focus the lung tissue showed a grey pattern of septa, and moreover a wedge-shaped portion was found here of a dark violet colour, extending up to 2 cm. from the pleural surface (atelectasis). The cranial third of the left upper lobe was relatively diminished in size, and on section showed a picture widely different from the adjacent lung tissue. It was of a greyish pink and showed a grey pattern of interlobular septa, which were widened. The lobules were small, and often showed a yellowish-brown, clover-leaf design, 1 to 2 mm. in diameter, and a minute grey reticular pattern. The bronchi in this portion was somewhat dilated. This abnormal lung portion was clearly demarcated from the normal tissue, the limit coinciding with a notch in the upper lobe surface (chronic atelectasis).

The broncho-pulmonary glands in the left hilum with the adjacent glands along the aortic arch and trachea were 0.75 to 1.5 cm. in diameter and completely caseous. A group of similar glands enclosed the bronchus that lead to the left upper lobe; one of these had perforated into the lumen of the bronchus, with an opening of 2 mm. (glandular component of tuberculous primary complex).

Of the microscopical picture the left upper lobe is of interest. Here the interlobular septa were found to be considerably widened by a loose connective tissue, with scanty cells. The lobules were small, as are the alveoli, the bronchi and bronchioles rather dilated and consequently salient in the picture. Round the bronchi and between the alveoli likewise an increase of connective tissue was found here and there. The alveoli contained numerous large vesicular cells, some of them with clear-cut vacuoles, some of the alveoli being crowded with them, locally mixed up with polymorphonuclear leucocytes. In some places the greatly narrowed alveoli had a lining of cubical epithelium. The bronchi and bronchioles were filled with a stringy mucus, containing shed epithelial cells and sometimes numerous polymorphonuclear leucocytes. The lining epithelial cells were normal in size and well preserved. Here and there some very small tubercles were found, composed of epithelioid and giant cells. The microscopical picture thus confirms the macroscopic aspect, namely, collapse of the lung tissue with indurative changes and indications of inveterate oedema. Acute pneumonic changes and tuberculous lesions remain in the background.

This autopsy record thus showed:—

1. The primary focus had grown into the bronchus, causing its obstruction and consequently atelectasis of the corresponding lung tissue. This proves that the clinical and x-ray changes which may be found round a primary focus, and often explained as a perifocal inflammation, must in some cases be ascribed to atelectasis.
2. The changes in the left upper lobe, which on valid considerations had been designed clinically as epituberculosis, proved to consist of atelectasis, caused by pressure of tuberculous glands on the bronchus.
3. The bronchi and bronchioles in the collapsed area were dilated. In anatomical sense bronchiectasis could be said to have already developed.

Discussion.

That the epituberculous infiltration is in some cases nothing else but atelectasis, is no new hypothesis. A search of the literature reveals many data pointing in this direction (Wallgren⁹, Kleinschmidt¹⁰, Engel and Segall, Beitzke, Duken). This applies equally to the massive extensive shadows, as to the small diffuse ones, which are at the present also considered to be indicative of epituberculosis. Some of these facts may be summarized here.

After the disappearance of the extensive epituberculous infiltration as a rule swollen glands remain in existence in the hilum on the involved side.

It is obvious that pressure of swollen glands on the main bronchus and lung tissue will occur in these cases. Wallgren states that in epituberculosis symptoms of stenosis of a bronchus are often present, the Jacobson phenomenon repeatedly being positive. On close examination of the skiagrams in some publications on epituberculosis (Langer, Kleinschmidt) a displacement of the mediastinum to the involved side is found. In the case described by Langer¹¹ the heart returned to its normal position after disappearance of the shadow. Cameron¹² reports that the shadow disappeared in a very short time. The same was observed in one of the patients under the author's care.

In a case of epituberculosis in an infant Fischl¹³ found atelectasis at autopsy. Further proof is offered by Morlock and Pinchin¹⁴. In their patient suffering from a typical form of epituberculosis of the right upper lobe, bronchoscopy was performed. In the right main bronchus, close to the bronchus of the upper lobe a tumour was protruding. By excision tuberculous glandular tissue was found. From the skiagram taken after bronchoscopy it appeared that the right upper field had become nearly clear. Only the lower branches of the bronchus of the upper lobe were still occluded. After two weeks the whole upper lobe was again opaque. After a week re-inflation had again taken place.

The question arises whether the clinical conception of epituberculosis can be dispensed with. Eliasberg and Neuland suggested it mainly because the good general condition and complete recovery were not in accordance with the prevailing opinion on the prognosis of tuberculosis in childhood. It has been repeatedly observed, that atelectasis complicating a chronic lung disease often does not affect the general condition in a marked degree. Moreover opinion on the prognosis of tuberculosis in childhood has much changed, especially in recent years. Complete recovery from extensive pathological alterations is no longer considered to be a great exception. On the other hand, a typical progressive destructive tuberculous process is sometimes seen developing in the same part of the lung as that in which formerly epituberculosis was diagnosed. In view of these facts there is less need for a specific explanation of cases like those described by Eliasberg and Neuland. Also from another point of view objections may be raised against the entity of epituberculosis. Post-mortem examination of children having died from extensive pulmonary tuberculosis never reveals a pronounced perifocal reaction, although in these cases large amounts of toxin are produced. Goldberg and Gasul¹⁵ have followed ten patients suffering from epituberculosis for more than two years. They leave the question open whether these pathological alterations should be considered as a perifocal reaction, or as caused by atelectasis or finally as not differing from other forms of tuberculosis.

It cannot be denied that the way in which the shadows in epituberculosis extend and disappear (for example, the phase of bipolarity) is not always identical with what has been observed in atelectasis. However, present knowledge of the clinical manifestations and x-ray findings in

atelectasis is limited. It has been obtained by studying cases of occlusion of a main bronchus, which is only a special form of this condition. Probably the clinical and x-ray findings will be different if a tuberculosis process is complicated by pressure of swollen glands on main and small bronchi and by direct pressure on lung-tissue.

Prosoroff¹⁶ has compared the shadows in epituberculosis with those in atelectasis in adults, suffering from tumours in the chest. He found a striking resemblance. Versé¹⁷ recently reported a case in which the shadows in the hilum, which were attributed to tuberculous foci proved at necropsy to be caused by atelectasis.

Occasional development of bronchiectasis in the atelectatic tissue is to be expected. Of this various cases are reported (Wallgren, Engel¹⁸, Rubinstein, case E in this paper). Children having recovered from epituberculosis should be followed during a long time as the clinical symptoms of bronchiectasis after atelectasis may reveal themselves sometimes after years (Anspach¹⁹).

Finally, it is possible that specific tuberculous tissue is present as well as atelectasis. A similar case was observed by Epstein²⁰. At the autopsy (performed by Ghon) the shadow proved to be caused by a primary focus with many tubercles in the proximity and atelectasis in the remaining part of the upper lobe.

Conclusions.

The clinical and x-ray findings in epituberculosis are often due to atelectasis. In other cases the infiltration consists of specific tuberculous tissue, resolving in course of time. A number of cases remain in which the pathological changes should be considered as a perifocal reaction around a tuberculous focus. Only clinical observation continued for a long time and post-mortem examination will reveal in what mutual relation these three conditions are occurring.

REFERENCES.

1. Eliasberg, H., & Neuland, W., *Jahrb. f. Kinderh.*, Berlin, 1921, XCIII, 88; *ibid.*, 1921, XCIV, 102.
2. Rubenstein, H., *Beitr. z. Klin. d. Tuberk.*, Berlin, 1928, LXX, 773.
3. Grävinghoff, *Monatschr. f. Kinderh.*, Berlin, 1921, XXI, 447.
4. Harms, & Klinckmann, *Tuberkulose*, Munich, 1926, VI, 340.
5. Pagel, W., see Engel, S., and Pirquet, C., *Handb. d. Kindertuberk.*, Leipzig, 1930, 241.
6. Spence, J. C., *Arch. Dis. of Childh.*, London, 1932, VII, 1.
7. Reichle, H. S., *Am. J. Dis. Child.*, Chicago, 1933, XLVI, 969.
8. De Bruin, M., *Nederl. tijdschr. v. geneesk.*, Amsterdam, 1935, LXXIX, 2902.
9. Wallgren, A., *Acta radiol.*, Stockholm, 1926, VII, 595.
10. Kleinschmidt, H., see Engel, S., & Pirquet, C., *loc. cit.*, 502.
11. Langer, H., *Ztschr. f. Kinderh.*, Berlin, 1923, XXXIV, 142.
12. Cameron, H. C., *Guy's Hosp. Rep.*, London, 1932, LXXXII, 290.

13. Fischl, R., *Arch. f. Kinderh.*, Berlin, 1922, LXXI, 17.
14. Morlock, H. V., & Pinchin, A. J. S., *Lancet*, London, 1933, i, 1114.
15. Goldberg, B., & Gasul, B., *Am. J. Med. Sc.*, Philadelphia, 1930, CLXXX, 824.
16. Prosoroff, A., *Beitr. z. Klin. d. Tuberk.*, Berlin, 1929, LXXII, 566.
17. Versé, M., *Röntgenbefund u. pathologisch-anatomischer Befund bei Lungenkrankheiten*, Berlin, 1935.
18. Engel, S., *Klin. Wchnschr.*, Berlin, 1921, LVIII, 877.
19. Anspach, W. E., *Am. J. Dis. Child.*, Chicago, 1934, XLVII, 1011.
20. Epstein, A., *Jahrb. f. Kinderh.*, Berlin, 1922, XCIX, 59.