STUDIES OF PNEUMONIA IN CHILDHOOD.

IV. BRONCHIECTASIS AND FIBROSIS OF THE LUNG.

BY

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It is stated that Laennec was the first to describe the condition of bronchiectasis, although fibroid conditions of the lung were described by earlier morbid anatomists.

In "De L'Auscultation Mediate" (1826) Laennec¹ has a short chapter entitled 'Dilatation of Bronchi,' in which he gives the history, the clinical condition and the morbid anatomy of four cases. In three of these the origin of the condition was apparently in childhood. One was a child of three years who died three months after whooping cough. Another was a man in middle life, who 'from infancy was subject to a cough attended by an expectoration of yellowish or greyish colour: this had not in any way prevented him from following his occupation.' The third was an old piano teacher, 'aged seventy-two years, affected upwards of fifty years with habitual cough, expectoration of opaque yellow sputa, and short oppressed breathing. However, she was always able to attend to her affairs, and indeed never considered herself as sick.' Laennec goes on to describe minutely the bronchial dilatations, and the dense contracted condition of the lung substance which he refers to as 'a cartilaginous production extending from the bronchial walls into the substance of the lungs'. His account of the subject is not only important historically: it is still useful, sound and accurate. Later reports of bronchiectasis confirm his findings of a condition dating back to childhood in a majority of cases; compatible not only with long life but even with moderate health and capacity for work; and dependent on bronchial dilatation associated with pulmonary fibrosis. His theory of aetiology is also worth quoting: it is 'a temporary dilatation produced by a voluminous sputum, and is rendered permanent by the constantly successive secretion of similar ones'.

Corrigan's² paper on 'Cirrhosis of the Lung' in 1838 is the next important contribution to the subject. He reported four cases. As his title indicates, Corrigan regarded the fibrous change in the lung as the primary condition, which produces by traction the dilatation of the bronchial passages. This explanation of bronchiectasis obtained and still obtains much support.

For a long period, there was confusion between cases of true bronchiectasis and of tuberculous cavitation: and until the demonstration of tubercle bacilli in sputum was possible, the separation of the two conditions was difficult. But in 1891 Clark, Hadley and Chaplin³ reported 45 cases of bronchiectasis under the descriptive term 'fibroid lung': and in all these a tuberculous condition was excluded by repeated examination of the sputum. In contrast to the small series of Laennec and Corrigan, the majority of these 45 patients were alive and 'in the enjoyment of excellent health'. Another important feature of the series was that, although only eight of the cases were under ten years of age, in the great majority the originating illness had occurred before the age of five years. In 33 the condition had followed measles or whooping cough or both.

In 1905 Clive Riviere⁴ published an analysis of 33 cases, all in children, with 3 autopsies. In 23, the original illness occurred under 5 years of age: in nearly all it was of the nature of bronchitis or broncho-pneumonia, and was especially associated with measles and whooping

cough. The title of his paper was 'Pulmonary Fibrosis in Childhood', but he declared that bronchiectasis was an invariable accompaniment. In 4 cases he believed the cause to have been an unresolved apical lobar pneumonia.

In 1927 Findlay and Graham⁵ reported 23 cases of definite bronchiectasis in childhood. This paper was particularly valuable in giving a number of lipiodol radiographs of the lungs, showing accurately the extent and character of the bronchial dilatations. Again in a majority of these cases, the original illness was bronchitis or broncho-pneumonia, often associated with measles and whooping cough: although in two cases the primary condition was pleurisy, and in three no originating acute respiratory illness could be traced.

This brief historical survey brings out several interesting points. Bronchiectasis was first discovered and described in the post-mortem room, many years after the process had begun: it was next studied during life, but still at an advanced stage. Also the great majority of the reported cases indicated as the original cause an acute respiratory illness in early childhood. Since 1900 careful studies of cases in children have been made, but it is uncommon to find reports of cases where the condition had been observed from its beginning, although Findlay and Graham were able to observe three 'almost from the beginning', following respectively double pleurisy, broncho-pneumonia and lobar pneumonia. Lastly, bronchiectasis was so commonly associated with fibrosis of the lung that the latter condition received an important place in the terminology, as shown by the terms 'cirrhosis of the lung', 'fibroid lung', and 'pulmonary fibrosis'.

In the first paper of these 'Studies of Pneumonia'⁶, we referred to a group of 33 cases of 'bronchiectasis' following pneumonia and bronchitis, which have been under our observation. This group was a composite one, including definite cases of bronchiectasis with or without fibrosis of the lung, and an indefinite group where physical and X-ray examination was inconclusive of either bronchiectasis or fibrosis. Yet in this indefinite group, the chronic and special character of the bronchitis and the history of an originating pneumonia or bronchitis seem to justify the diagnosis of some fibrous change in the bronchi and the interstitial stroma of the lung. Some years ago, before the introduction of lipiodol, one of us (C. McN.) reported 18 cases of 'fibrosis of the lungs and bronchi, following broncho-pneumonia', of which only 6 were of definite or massive fibrosis; while in the remainder the fibrosis was indefinite, although the clinical character of the cases in both groups was similar. The subsequent use of lipiodol in some cases of the indefinite group has demonstrated in them bronchial dilatation, and it is possible that this method may reveal some degree of bronchiectasis in many cases of chronic cough and spit following broncho-pneumonia. Certainly the use of lipiodol has shown beyond doubt that definite bronchiectasis may exist without producing either the classical physical signs or evidence in an ordinary radiograph.

From all these data, it would seem that the majority (probably the great majority) of cases of bronchiectasis date back to early childhood and originate in broncho-pneumonia or bronchitis. It might be hoped, therefore, that microscopic study of the bronchial changes in acute and chronic cases of broncho-pneumonia would throw light on the origin of bronchiectasis. The main

purpose of the present paper is to present such a microscopic study of a series of cases of broncho-pneumonia, and of early and advanced bronchiectasis.

As an introduction to this study, it may be of interest to give a short clinical record, with lipiodol X-ray photographs, of two cases of bronchiectasis, in both of which the condition is definite, has existed for some years and has permitted fairly good general health.

Clinical Case A. John M., present age 7 years. Admitted to hospital in the fifth week of double broncho-pneumonia following measles, at the age of $2\frac{1}{2}$ years. The boy was wasted very weak and pale, and in an extremely grave condition. His lips, tongue and mouth were covered with numerous dirty ulcers; these involved the larynx also, as shown by his complete

FIG. 1.

aphonia. There was irregular and patchy consolidation of both lower lobes; radiographs confirmed the pneumonic condition of the lungs. He slowly improved, and remained in hospital for twenty weeks. His recovery was marked by persistent and paroxysmal cough, which had not entirely left him on his discharge. His general health was then excellent. His cough became worse again in the following winter, and was of the typical paroxysmal "morning cough" type, with the expectoration of a moderate amount of purulent but not offensive spit. It remained, with exacerbations and improvement, until his re-admission at the age of $5\frac{1}{2}$ years. His general health had kept fairly good: he was never in bed, and he had gone to school. On re-admission, his colour was good, his nutrition fairly good: there was very slight clubbing of the fingers. His lungs showed no percussion dulness: but there were numerous hollow-crackling rales at both bases, with broncho-vesicular breathing at these areas. The ordinary radiograph of the lungs showed luminous fields: but the cardiac shadow was overlaid with an indistinct tracery which suggested thickened bronchi. The lipiodol-radiograph showed a definite bronchiectasis

at both bases close to the spinal column : and on the left side one or two slightly widened bronchial tubes could be seen passing across to the periphery above the dome of the diaphragm. (Fig. 1.) He is again under observation, æt. 7 years, four and a half years after his original pneumonia : the condition of bronchiectasis has not apparently progressed : cough and spit remain as before : the general condition is fairly good : the boy is able to attend school, and to play.

Commentary. A case of limited bilateral bronchiectasis, without massive fibrosis of the lungs, following measles and broncho-pneumonia. General health fairly good. Duration, 4½ years.

Clinical Case B. Jessie W., present age 14 years. She had measles and pneumonia at the age of 3 years, and was said to be seriously, but not dangerously, ill for several weeks. She was not under our observation during this illness. Since this time, she has never been free from cough : she has bouts of cough every morning on waking : and brings up some thick greenish spit. Her general health has been good, although she has always been a little thin : but she is

FIG. 2.

full of energy and high spirits, and takes her full share in games. Came under observation, aged 8 years, and has been watched closely until now. The general and local condition has not appreciably changed since then. Obvious physical signs of extensive fibroid change and catarrh in the lower half of the left lung, with flattening and deficient movement on this side : outward displacement of the heart, the apex beat being in mid-axilla in the 5th interspace. Slight cyanosis of the lips, cheeks and fingers, but little or no clubbing of the fingers. Lipiodol-radiograph (Fig 2) confirms the massive fibrosis in the left lower lobe, and shows extensive bronchiectasis of the terminal air tubes on this side, and widening of the main bronchi, displacement of the trachea and heart to the left side. The bronchial tree of the right lung shows normal tapering of its twigs, some of which can be seen passing across the middle line to the left side, indicating that part of the right lung has passed across the mediastinum.

Commentary. A case of extensive unilateral bronchiectasis, with massive fibrosis of the left lung, and displacement of mediastinal structures : following measles and pneumonia. General health fairly good. Duration, 11 years.

In our last paper particular stress was laid upon one feature of the pathological process in acute broncho-pneumonia. That feature was the presence, and often great severity, of acute interstitial inflammation of the bronchial walls, alveolar septa and general stroma of the lungs. It was pointed out that this condition favours a prolonged persistence of the inflammation, hinders rapid and perfect resolution, and in a proportion of cases brings about chronic pathological changes in the lungs. Two of the most important of these chronic changes, bronchiectasis and fibrosis of the lungs, are the subject of the present study. These two conditions are intimately bound up one with the other and cannot be considered entirely apart.

BRONCHIECTASIS.

Acute bronchiectasis. A very common post-mortem finding in the lungs of children who die of acute broncho-pneumonia is widening of the lumina of small bronchi, especially those in the centres of consolidated patches. The term acute bronchiectasis or bronchiolectasis is frequently used to designate this. But there are two entirely distinct types of change which may produce this widening of the tubes. In severe cases of broncho-pneumonia it is sometimes due to a destructive change in the walls of the bronchi (ulcerative bronchitis) which is described in detail below, and which, in the event of the patient's survival, necessarily leads to permanent changes in the lungs. In many cases, however, the widening of the bronchial lumen is due to pure dilatation, with acute overstretching of the wall, unaccompanied by any important structural change. This latter condition, very common in acute broncho-pneumonia, affects small bronchi in the consolidated areas and also those in unconsolidated parts. It is analogous to acute emphysema of the alveoli, which often accompanies it; it is probably due to the same causes, and is doubtless capable of complete recovery without permanent damage. It is probably this condition which Rilliet and Barthez* described as 'acute bronchial dilatation' occurring occasionally in acute broncho-pneumonia.

In descriptions of acute bronchiectasis it is not always clear which of these two entirely different conditions is intended; and indeed, without microscopic examination, it may not be possible to distinguish them. In order to avoid confusion it seems advisable to restrict the application of the term acute bronchiectasis or bronchiolectasis (for it is almost exclusively the small tubes which show the change) to the condition of true dilatation.

It is not, however, with acute bronchiectasis that the present study is principally concerned, but with the sequence of changes which, originating in acute respiratory disease, especially broncho-pneumonia, may lead to the development of chronic bronchiectasis.

Chronic bronchiectasis. The mode of development of chronic bronchiectasis is a problem which cannot be said to have been satisfactorily solved. Modern standard text-books of pathology advance various suggestions, none of which seems entirely adequate.

According to Muir⁹ 'bronchiectasis may be ascribed to certain mechanical factors acting on a weakened bronchial wall, and . . . fibrosis of the lungs plays a very important part. . . The chief mechanical factor is forced inspiration, especially that which follows the act of coughing . . . This will be specially effective when the lung beyond is not free to expand . . . as in permanent collapse or in interstitial pneumonia . . . 'The actual contraction of the connective tissue also may play a part, as was maintained by Corrigan.' The association of bronchiectasis with acute respiratory disease in childhood is referred to by Muir, who states that 'it is likely that in many cases of cylindrical bronchiectasis the lesion is started in early life by whooping-cough, the bronchitis of measles or of other diseases . . . In these (cases) the supporting muscular tissue of the bronchi has apparently suffered, though we cannot say why this should be brought about.'

Karsner¹⁰ states that 'the more acute forms of bronchiectasis are due to destructive disease of the wall . . . Such dilatations are due almost entirely to the disease of the wall and not contributed to in any large measure by increased intrabronchial air pressure'. He appears, however, to regard the chronic form as having a different explanation and mentions the factors of weakening of the wall by chronic inflammation, and the dilating effects of cough, accumulation of secretion, and fibrosis of the lung substance between the bronchi.

Kaufmann,¹¹ who recapitulates the same views, suggests that 'there is a possibility of congenital weakness of the bronchial walls in the bronchiectases of childhood'.

MacCallum¹² favours the view that a partial obstruction of a bronchus, such as can be overcome by the active inspiratory effort, but prevents the egress of air during expiration, leads to 'continuous distension of the obstructed bronchus, which finally widens it and is a prominent cause of the condition known as bronchiectasis'. He admits that 'there are many (cases) where obstruction is not . . . obvious, and these offer difficulties'; and quotes Dr. Crowe as stating 'that in dogs in which he has produced stricture of a bronchus, easily seen through the bronchoscope as an extreme narrowing of the lumen, there is no dilatation of the distal part as long as the bronchus remains uninfected'. He affirms that the only point on which there is agreement is 'that the infection and inflammation which weakens the bronchial wall and destroys its elasticity is a necessary factor.'

It is therefore abundantly clear that agreement has not been reached on the problem of how the cavities are produced, and that, as MacCallum truly states, the question needs further study.

During the course of our study of broncho-pneumonia we met with a series of seven cases in which a succession of changes was traceable which seems to us to throw some light on this problem. The observations recorded in this paper, on which certain conclusions are based, were made during the course of a very full examination of these seven cases, with the help of whole-lung sections. Details of some of the cases are given at the end of the paper.

The first stage of the process which leads to the formation of bronchiectatic cavities was found in a case of prolonged broncho-pneumonia, in which a very severe purulent bronchitis was an outstanding feature and acute interstitial inflammation of the bronchial walls was of more than usually intense degree. At the stage represented by this case the condition of the affected bronchi is as follows :—

The lumen is enlarged and filled with pus; the epithelial lining is completely destroyed; all trace of muscle in the wall has vanished; in some instances every vestige of the original wall, including the cartilage, has disappeared and the bronchus is represented by a space bounded directly by consolidated alveoli (Fig. 9). Bronchi may be found whose walls are in process of being destroyed. Sometimes only a part of the wall is affected (Fig. 10). At one side of the bronchus it may be intact while at the

FIG. 4.

FIG. 3.

FIG. 5.

FIG. 6.

FIG. 7.

FIG. 8.

(For Description of Figures, see page 189).

FIG. 9.

FIG. 10.

FIG. 11.

FIG. 12.

FIG. 13.

FIG. 14.

FIG. 15.

FIG. 16.

FIG. 17.

FIG. 18.

FIG. 19.

other it is necrotic or has disappeared. The process of necrosis and suppuration which destroys the bronchus wall may involve adjacent alveolar tissue to a variable extent, or may be confined to the bronchus. In some instances the great enlargement of the lumen at the part where the wall is destroyed makes it obvious that a certain amount of alveolar tissue also has perished. In this way there are formed cylindrical or saccular expansions of the bronchi, which are clearly not due to dilatation properly so called, but to a process of excavation, with loss of tissue from the bronchus wall and sometimes also from the surrounding lung substance, as a result of necrosis accompanying suppuration (Fig. 5 or 6). The cavities are often very sharply defined. This is the destructive change in the wall to which Karsner ascribes 'the more acute forms of bronchiectasis'. We suggest that, at least in certain cases, it is responsible for the development of the chronic form also, and is the fundamental change underlying that condition.

At a slightly later stage (represented by Case II) the early beginnings of repair are apparent. The cavities heal by granulation. From the wall of the cavity (usually formed at first by consolidated alveoli) there springs a growth of young fibroblasts and capillaries which forms a granulation-tissue membrane around the space. Fig. 12 and 13 show the earliest stage of this healing process at one side of a bronchus whose wall has been completely destroyed.

The growth of this granulation tissue continues until a definite fibrous layer, at first extremely vascular, bounds the cavity. After a time epithelium, surviving in neighbouring parts of the bronchus which have not suffered destruction, grows over the surface of the new granulation-tissue wall and gives the cavity an epithelial lining continuous with that of the bronchus. This relining process begins even while there is ample evidence of the persistence of active inflammation. Healing of the cavities in this way is represented at various stages, in Cases I, IV and V in our series. It is illustrated in Fig. 11, 14 and 15. The bronchus wall shown in Fig. 14 has remained intact at one side, while destruction at the other side has produced a saccular expansion of the lumen. The destroyed part has been replaced by a new wall composed of young and very vascular fibrous tissue, among which no trace of muscle or cartilage is to be found (Fig. 15). Over a part of this new wall a layer of epithelial cells has spread, the covering being not yet quite complete. The epithelium is of a cubical type and not ciliated.

The beginning of fibrosis of the lung substance between the ectatic bronchi may be found at this stage, but is only of slight degree. In our cases it was confined to alveoli immediately related to affected bronchi, and took the form of proliferation of fibroblasts in the alveolar walls which caused considerable thickening, and in two cases an exudate in the alveolar spaces was in process of organization by means of leashes of young fibroblasts and capillaries which sprang from adjacent alveolar septa (Fig. 18). Nowhere, at this stage, was dense contracting fibrous tissue found; nor were fibrous pleural adhesions present.

Later on the granulation-tissue wall of the cavity becomes thicker and more definitely fibrous. There is no regeneration of muscle or cartilage, and little or no new elastic tissue appears to be formed. The new wall may be as thick as, or thicker than, the original one, and may have a complete epithelial lining, but it is a purely fibrous structure, lacking in all those elements which endow the normal bronchial wall with strength and elasticity (Fig. 16).

The absence of muscle, cartilage and elastic tissue, and loss of characteristic structure in the walls of ectatic bronchi have been repeatedly described. This change is usually ascribed to 'atrophy' of these essential elements as a result of chronic inflammation or strain. To our mind, the fibrous membrane which lines these cavities is often not the original wall at all, but a new structure formed from granulation tissue around a space produced by an active process of destruction.

The true chronic stage of bronchiectasis is represented in our series by Cases VI and VII. In Case VI (Fig. 4) the amount of bronchial dilatation was not very great. In the lower lobe some of the bronchi showed a cylindrical expansion of the lumen but there were no large cavities. The walls of these bronchi presented exactly the changes which have been described. One is illustrated in Fig. 16. This wall is composed of a considerable thickness of vascular fibrous tissue covered with epithelium; muscle and cartilage are absent. Case VII (Fig. 3) was one of typical, very severe chronic bronchiectasis. The whole left lung was occupied by cavities of various sizes, mostly large. In the walls of the cavities there was no muscle, no cartilage, virtually no elastic tissue. Most of them had an epithelial lining, the cells being of a small debased cubical type.

At this stage the lung substance between the cavities shows advanced chronic interstitial pneumonia, being occupied by dense fibrous tissue, among which may be detected the remains of obliterated alveoli and small bronchi. This was the state of affairs in both of our chronic cases. In Case VII, dense fibrous pleural adhesions were present. The condition of the lung substance in the lower lobe of Case VI is shown in Fig. 19. The part illustrated is typical of practically the whole lobe. Yet there was no evidence that the contraction of this very dense fibrous tissue had stretched the bronchial walls. On the contrary, it seemed rather to have had the opposite effect, for in places the walls of the dilated bronchi were thrown into folds, showing that they were certainly not expanded to their full capacity. This is illustrated in Fig. 16.

In Case VII (Fig. 3), the cavities were so numerous and of such a size that the lung substance between them was represented by little more than broad fibrous septa, in some of which remains of alveoli, more or less completely obliterated, were demonstrable. The smaller bronchi in communication with those from which the cavities were formed, had also suffered obliteration.

From the observations which have been recorded the following conclusions have been drawn, offering an explanation of those cases of chronic bronchiectasis

which follow acute respiratory diseases in children, especially broncho-pneumonia. The initial change which underlies the whole process occurs during the acute phase of the disease, and takes the form of severe acute interstitial inflammation of the bronchial wall, going on to necrosis and suppuration. This causes the formation of a cavity by loss of tissue from the bronchus wall, and excavation of a certain amount of adjacent alveolar substance in most instances. The cavity may be cylindrical or saccular in shape according to the extent of the excavation and whether it affects the whole circumference of the bronchus equally or is more extensive at one side. Subsequently the cavity is lined by granulation tissue, becoming fibrous, and finally may be covered by bronchial epithelium, usually of a modified type. Thus a new wall is constituted round a bronchial lumen which has been enlarged to a greater or less degree according to the extent of the initial destructive process.

According to this view, a bronchiectatic cavity is not a dilated bronchus, but an excavation in the lung substance, starting in a bronchus, and is strictly analogous to a tuberculous vomica. It is not necessary, in order to explain the existence of the cavities, to postulate the operation of any of the factors usually credited with dilating effects. Destruction of tissue, and not dilatation, is the essence of the process. Nevertheless those factors may be instrumental in enlarging the cavities after they are formed. It may readily be assumed that anything which might tend to dilate a bronchus would be doubly effective in stretching the relatively weak fibrous walls of the cavities. Secretion and inflammatory products are bound to accumulate in the cavities, especially as the absence of muscle and ciliated epithelium deprives the altered bronchi of the principal means by which a healthy bronchus rids itself of secretion. This accumulation makes probable the occurrence of that partial obstruction to which MacCallum attaches importance as a dilating factor. Infection flourishes in the stagnant contents and causes enlargement of the cavities by further ulceration and excavation. Fibrosis of the lung substance, especially close to bronchi, accompanies the process of healing of the cavities and is probably constant in chronic cases. It may, in some instances, by contraction tend to dilate the cavities further, as Corrigan believed, but this can be only after the bronchiectasis is well established, and we have found no direct evidence that it has this effect.

In putting forward this view of the mode of formation of bronchiectatic cavities, we do not claim that it explains all cases. Our studies have been confined to cases in children, in whom the disease could be clearly traced to its origin in broncho-pneumonia. Certain cases which develop without any evidence of antecedent acute respiratory disease may demand some other explanation. We are, however, of opinion that very many cases of chronic bronchiectasis (many even of those which manifest themselves only in adult life) owe their origin to broncho-pneumonia or bronchitis in childhood; and there is a considerable body of evidence to support this view. Where bronchiectasis is due to foreign bodies in the lungs, the presence of infection is probably an essential factor, and the process by which the cavities are formed may well be similar to that which we have described. We have not, however, any observations of our own to record with regard to this.

PATHOLOGY OF FIBROSIS OF THE LUNGS.

Non-tuberculous chronic fibrosis of the lungs is usually associated either with gross fibrous thickening of the pleura such as results from long-standing empyema, or with chronic changes in the bronchial walls, with or without definite bronchiectasis. It is with the latter type that the present study is concerned.

It may be stated that the chronic form of bronchiectasis is always accompanied by some degree of fibrosis of the lungs, but that fibrosis may occur without gross enlargement of bronchial lumen such as could be detected clinically as bronchiectasis. As has been described in the foregoing study, in cases of bronchiectasis where cavities are formed by active destruction, fibrosis of the adjacent lung substance accompanies the process of reconstruction of the wall of the cavities. It begins in the immediate vicinity of the damaged bronchi, but may ultimately lead to an almost complete fibrous replacement of the alveolar tissue throughout the affected portion of the lung. The fibrosis is brought about in various ways.

(a) There may be proliferation of fibroblasts, with laying down of new fibrous tissue in the inflamed walls of alveoli adjacent to the damaged bronchi. This leads to great thickening of the alveolar septa and a corresponding reduction in the size of the spaces. Accompanying this change in the wall, there is usually an alteration in the character of the lining epithelium of the alveoli, which becomes cubical instead of flattened, and very much more conspicuous than it ought to be. Fibrous tissue proliferation may affect also the coarse stroma of the lungs, increasing the width of the interlobular septa and the amount of perivascular and peribronchial fibrous tissue. It may be regarded as the result of long continued interstitial inflammation of the lung framework, which in its acute form is so constant a feature of broncho-pneumonia.

(b) In certain cases organization of an exudate in the alveolar spaces takes place. The alveoli come to be occupied by strands or leashes of young fibroblasts and their fibres, which pass from alveolus to alveolus, and the origin of which from the alveolar wall at some point may be demonstrable. This remarkable appearance is illustrated in Fig. 18, which shows the process at an early stage. Its end result, if the patient survive, must be obliteration of the alveolar spaces by fibrous tissue and massive fibrosis of the affected part. This is what is known as 'organizing pneumonia.' Sometimes it occurs throughout a large area of lung as a direct result of pneumonia in which the exudate does not resolve, but becomes organized. During the course of our present investigation, we have seen two cases of this kind, in neither of which was any bronchial dilatation present. The same process, but limited to alveoli adjacent to the damaged bronchi, was observed in Case IV of our bronchiectasis series, in which it contributed materially to the early fibrosis of the lungs noted in those cases. At a later stage, when many alveolar spaces have been obliterated and the new fibrous tissue has become dense, it would be difficult, if not impossible, to distinguish fibrosis due to this process from that produced in other ways.

(c) In bronchiectatic lungs, many small bronchi communicating with those from which the cavities are formed become obliterated. We were able to observe the process of obliteration at various stages in our series of cases. During the initial stage of ulcerative bronchitis, the smaller bronchi may suffer in exactly the same way as the larger, and have their walls completely destroyed. The healing process which follows, with growth of granulation tissue forming a new wall around the cavities may, in the case of small bronchi, lead to obliteration, the whole lumen being filled with proliferating fibroblasts and new capillaries. An example of this obliterative bronchiolitis, taken from Case II, is shown in Fig. 15. In this way many small bronchi may be completely obliterated. In some instances the new granulation tissue does not occupy quite the whole lumen; spaces are left which may ultimately be lined with bronchial epithelium. This produces the curious effect of a bronchus divided into a number of minute epithelial-lined spaces separated by masses of fibrous tissue. This obliterative bronchiolitis contributes to fibrosis of the lungs not only by the formation of fibrous tissue in the small bronchi themselves, but also by producing in the alveoli communicating with them a permanent condition of collapse, which must result in further fibrosis.

In conclusion it may be stated that the pathological processes underlying bronchiectasis and pulmonary fibrosis are intimately connected. Destructive changes in the bronchial walls, the processes of healing which follow these, and the persistence of infection in and around the damaged bronchi, are together responsible for the fibrosis which accompanies bronchiectasis. Apart from those cases where fibrosis is of pleural origin, and occasional rare cases of organizing pneumonia, it would seem doubtful whether massive fibrosis of the lungs takes place in the absence of severe bronchial damage, although it is evident that the degree of bronchial damage need not be such as to produce bronchiectasis clinically obvious. Case VI of our series (Fig. 4) is an instructive example of this, where, with massive fibrosis of a lobe, only very slight bronchial dilatation was present. Yet the bronchial walls were profoundly altered, and the pathological changes which they showed were precisely the same as those in Case VII (Fig. 3) except in respect of the size of the cavities. For this reason cases of frank bronchiectasis, and cases of fibrosis of the lungs without obvious bronchiectasis (if not of pleural origin), may be reasonably regarded as belonging to the same pathological group; and the extended use of lipiodol in radiography of the chest will probably reveal bronchial enlargement in many cases of 'fibroid lung' previously believed to be free from bronchiectasis.

ABSTRACTS OF FATAL CASES.

(The case numbers are those used in the "Pathological Study").

Case I. Broncho-pneumonia of seven weeks' duration, with ulcerative bronchitis. (Fig. 5, 9 and 10).

Male, aged 6 months. Eighth child. Four others had died in infancy, 2 shortly after birth and 2 of broncho-pneumonia following measles and whooping-cough. House of 2 small rooms, with leaking roof. Breast-fed for 2 months and thereafter on cow's milk under direction of child welfare clinic. Turned ill 2 days before admission in February, 1926, with fever, heavy

breathing and cough. Died 7 weeks after admission. While under observation, there was a remittent temperature, a steady loss of flesh, a troublesome cough, considerable dyspnoea, generalized bronchitis, and, after about a week, evidence of consolidation in the right upper lobe, followed by consolidation in both lower lobes.

Post-mortem examination. Body very emaciated. Much purulent secretion in main air-passages. Pleural sacs healthy. Right lung—anterior portions of upper and lower lobes and most of middle lobe very emphysematous (vesicular and interstitial); posterior part of upper lobe, most of lower lobe, and middle lobe near root consolidated as a result of patchy pneumonia and collapse; bronchi greatly inflamed, filled with pus, and slightly dilated. Left lung—whole upper lobe and anterior part of lower lobe emphysematous; posterior portion of lower consolidated; bronchi as above but not so severely affected. Mediastinal glands much enlarged. Heart and other organs atrophied. Little or no obvious toxic change.

Microscopic examination. In general the condition is one of purulent bronchitis with both discrete patches and extensive areas of confluent broncho-pneumonia. Changes are most advanced in the right upper lobe, where clinically consolidation was first noted. Here the bronchitis has been intense and the walls have undergone complete disintegration, with very considerable erosion and excavation. In this case the process of destruction was still active at the time of death, unchecked by any effort at repair.

Case II. Broncho-pneumonia of several weeks' duration, following measles, with severe bronchial damage. (Fig. 6, 12, 13 and 17.)

Female, aged 2 years. This case was reported (Case VI, p. 123) and illustrated (Fig. 11) in the third paper of this series¹³, but it is thought desirable to amplify the description of the bronchial changes. These are widespread and are most advanced in the smaller bronchi. All the latter are plugged with thick pus, and show some degree of distension or excavation; in some, no vestige of the original wall remains and the lumen is surrounded merely by consolidated alveolar tissue. While the inflammatory process was thus intensely active at the time of death, in a few instances there has been an attempt at repair. Here and there in the walls of the cavities, very young granulation tissue is visible and a beginning has been made of the reconstitution of the wall. Efforts at repair are also seen in several of the capillary bronchioles, and here the effect has been different; organization is leading to obliteration. These bronchioles are represented by small circular patches of fibro blasts and delicate connective tissue fibrils surrounding a clump of degenerated polymorphonuclear cells. There is therefore an obliterative bronchiolitis in progress.

Case IV. Broncho-pneumonia of nine weeks' duration, with early bronchiectasis. (Fig. 7 and 11.)

Female, aged 15 months. Four other children, one in hospital with tuberculosis. Breast-fed for 11 months. First tooth at 7 months. No previous illness, but for 2 weeks before admission had a cough. Admitted in September, 1926, at age of 12 months, having been acutely ill with fever, cough and grunting breathing for 24 hours. Diagnosed as severe acute bronchitis, possibly broncho-pneumonia. Marked constitutional disturbance but no definite consolidation. After a week, improvement occurred and temperature came down by lysis. On 14th day, temperature rose to 101.4° and a rash developed. Scarlet fever suspected but not confirmed at the fever hospital, child being sent home after 3 days. Progress at home unsatisfactory; continued to cough; appetite poor; no energy or inclination to move about; weight lost. Re-admitted in November, 8 weeks after the onset of the acute respiratory illness. No rise of temperature, but child pale and listless. Weight 12½ lb. "Chesty" cough. Moist sounds in both lungs, with a suspicion of dullness at the left base. Four days after admission, temperature rose for first time to 101°; pulse uncountable; respiration 56. Unpleasant odour noticed in neighbourhood of patient at this date. Fifteen c.c. of thick foul-smelling pus removed through 9th left interspace. Death occurred 5 days after admission. Whole illness lasted therefore for about 9 weeks.

Post-mortem examination. Body that of a small and poorly nourished child. About 1 oz. of thick yellow pus with a very foul odour in left pleural sac, with much fibrino-purulent exudate in relation to it. Right pleura healthy. Left lung—mixture of collapse and patchy pneumonia; numerous bronchiectatic cavities with a smooth greenish lining in lower lobe. Right lung—more

extensively consolidated, again in a patchy fashion; innumerable small bronchiectatic cavities with a yellowish lining membrane in pneumonic areas. Mediastinal glands much enlarged. Heart atrophied. No toxic changes in spleen, but liver fatty.

Microscopic examination. There is some discrete broncho-pneumonia in the upper and more extensive consolidation in the other lobes. The bronchi are all pathological, but those in the apical regions show overstretching rather than serious destructive change. Bronchiectatic cavities are most numerous in the lower lobes and some are of considerable size. There the bronchial inflammation has been of great severity. In many cases, the original wall has completely disappeared; in others, part of the circumference is more or less intact, while the remainder is destroyed. The process is still active, but in all there has been some attempt at repair and reconstitution of the wall by granulation tissue. There is early fibrosis of the lung in the affected parts; alveolar walls are thickened and very cellular; in places the lining alveolar cells tend to be cubical; there is broadening of the septa.

Case V. Early chronic bronchiectasis, with terminal acute broncho-pneumonia. (Fig. 8, 14 and 15.)

Female, aged 16 months. Indefinite history of epilepsy on the mother's side. One other child, aged 12, healthy. Artificially fed from birth. Cut first tooth just before admission. Mentally defective. Had had one severe and numerous minor fits. Several indefinite illnesses, some of which were evidently respiratory. Admitted in February, 1926, having been ill for 4 days with gastro-intestinal symptoms, cough and grunting respiration. Ill-nourished but not obviously rachitic. All the signs of early broncho-pneumonia on admission. Died 11 days later, consolidation having become progressively more marked in both lungs.

Post-mortem examination. Right pleural sac moist. Some loose fibrous adhesions over left lung. Extensive consolidation along posterior borders of both lungs. Consolidated parts dark red on section, with yellow mottling round bronchi. Mediastinal glands greatly swollen. Heart not greatly altered. Little toxic change in organs.

Microscopic examination. Chief interest centres in the condition of the bronchi in the right lung. They are all acutely inflamed but many show in addition changes of a more chronic nature. In general, there is quite considerable dilatation. In the more dilated of the larger bronchi, in which the chronic changes can be studied best, there is profound alteration of the walls. The epithelium may be entirely absent or modified to a low cubical type. The sub-epithelial tissue is greatly increased in amount, and appears as very vascular granulation tissue thickly infiltrated with polymorphonuclear cells. In some instances practically the whole thickness of the wall is composed of tissue of this type, muscular structure being unrecognizable. Some of the large bronchi near the root show these changes only in certain parts of their walls, while other parts appear almost healthy. The picture is one of recent acute inflammation arising in bronchi which were previously the seat of chronic changes associated with bronchiectasis. In the lung substance itself, there is no general fibrosis, but there are areas, closely related to diseased bronchi, where there is diffuse overgrowth of connective tissue varying from slight increase in the thickness of the alveolar walls to the production of a structure resembling granulation rather than lung tissue. Careful examination reveals that the fibrosis is in large part the result of organization of an exudate in the alveolar spaces.

Case VI. Chronic fibrosis of the lung, with slight bronchiectasis; terminal acute broncho-pneumonia. (Fig. 4, 16 and 19.)

Female, aged 6 years. Mother died in childbirth 6 months before patient's fatal illness. Five other children alive; 2 died in infancy. Home conditions bad. Past history unreliable. Said to have been always delicate and subject to bronchitis, and about a year before admission to have suffered from a respiratory illness, the details of which were not known. Was "always coughing." Admitted in March, 1926, having been taken suddenly ill about 30 hours previously. Was fevered and had vomited repeatedly. On admission, temperature 104.8°; pulse 160; respiration 32. Semi-comatose and toxic. Throat inflamed; swab negative for diphtheria. Cerebro-spinal fluid normal. Blood culture sterile. Leucocytes 6,200. Death occurred 7 days after admission. Two days before death, the lungs "showed signs of broncho-pneumonia."

Post-mortem examination. Large quantity of turbid fluid in left pleura, with masses of thick loosely-attached fibrin on serous surface. Right pleural sac healthy. Left lung—acute broncho-pneumonia in upper lobe; slight dilatation of bronchi and fibrosis, in addition to pneumonia

with areas of suppuration, in lower lobe. Right lung—commencing broncho-pneumonia, with purulent bronchitis and some bronchial dilatation. Marked enlargement of mediastinal glands. Early fatty change in liver and kidneys.

Microscopic examination of left lung. The lymphatic vessels at the root are greatly dilated and full of pus. The upper lobe is in great part air-containing, but shows bronchitis and small patches of broncho-pneumonia. The lower lobe similarly shows evidence of acute inflammation, with suppuration in several places, but there are also very striking chronic changes. The size of the lobe is below normal, owing partly to collapse consequent on pleural effusion and partly to fibrosis. The larger bronchi are dilated, but there are no big bronchiectatic cavities. Their walls are much altered. In most an epithelial lining is present, but seldom of normal character. Muscle fibres are hardly discernible; the walls are composed of very vascular granulation tissue, densely infiltrated with lymphoid and other mononuclear cells. In some instances, the appearance of reduced alveolar spaces lined with cuboidal cells among this tissue shows that most of the original bronchus wall has been destroyed. A striking feature is the lymphocytic infiltration of peribronchial tissue.

The smaller bronchi are not dilated; many indeed are reduced in size. Each is surrounded by a dense collection of small mononuclear cells. In some places no true lumen can be distinguished, but, in the midst of vascular connective tissue and lymphocytes, merely a few small spaces lined by low columnar epithelium. In addition to these widespread chronic bronchial changes there is very extensive fibrosis in this lobe, which would appear to have resulted both from the obliteration of bronchi and from proliferative changes in alveolar walls; organization of exudate in alveolar spaces is not demonstrable. What little lung tissue in this lobe is not affected by interstitial pneumonia is collapsed.

Case VII. Advanced unilateral bronchiectasis, with terminal acute broncho-pneumonia. (Fig. 3).

Male, aged 6 years. Fairly healthy in infancy, though rather late in cutting teeth and walking. Subject to "eczema" from an early age. Measles at 2 years; no complication. Admitted to Royal Infirmary, Edinburgh, in October, 1927, at age of $4\frac{1}{2}$ years for treatment of infantile dermatitis. Ten days later developed pneumonia, which dragged on for many months and passed directly into a condition of bronchiectasis. Was in hospital for more than 8 months on end and was treated latterly by repeated bronchoscopic lavage. First admitted to the R.H.S.C. in July, 1928, i.e., 10 months after the onset of the respiratory illness. At that date, was coughing up two or three cupfuls of thick offensive sputum each day. General development quite good, but nutrition poor. Fingers clubbed. Physical signs confined to left lung. Mediastinal structures slightly drawn over to left side. Remained in hospital till January, 1929, i.e. for 6 months. On discharge, was coughing up $\frac{1}{2}$ to 3 ozs. of pus each morning. Re-admitted in February, 1929, having been fairly well in interval and having gained 2 lb. Began to have a slight evening rise of temperature and on tenth day to have all the signs of acute broncho-pneumonia. Died 14 days after re-admission, i.e. about 18 months after the onset of the original pneumonia.

Post-mortem examination. Left pleural sac completely obliterated by dense fibrous adhesions. Right pleura acutely inflamed. Left lung smaller than right and occupied throughout by a large number of bronchiectatic cavities, the walls of which were fairly smooth and of a deep red colour, and the contents of which consisted of very foul pus. Cavities separated by septa of completely fibrosed lung substance. Right lung voluminous and the seat of widespread acute broncho-pneumonia. No chronic changes. Tracheo-bronchial and broncho-pulmonary glands enormously enlarged. Heart dilated and right ventricle possibly slightly hypertrophied.

Microscopic examination of left lung. Most of the cavities have an incomplete lining of small epithelial cells, beneath which is a layer of vascular connective tissue thickly infiltrated with lymphocytes. This layer varies greatly in thickness and in places its free edge is necrotic. It merges into denser fibrous tissue, amongst which are to be found alveolar spaces lined by altered epithelium and small bronchi more or less completely obliterated. The whole of the septa between the cavities is composed of this fibrosed and obliterated lung substance. The medial part of the lower lobe shows extensive fibrosis without cavities. The absence of bronchi of any size in this area, and the presence (where bronchi apparently ought to be) of small spaces lined

by cubical epithelium, surrounded by aggregations of lymphocytes, suggests that obliterative bronchitis was a marked feature of the process in this part of the lung. Cartilage is present only in the main bronchus. Elastic tissue can be demonstrated by special staining in the walls of the blood vessels, in the main bronchus, and in the walls of such alveoli as remain, but is completely absent in the walls of the cavities.

SUMMARY.

1. A brief historical survey of bronchiectasis and fibrosis of the lung in childhood is given, followed by clinical records of two cases.

2. The genesis of these two conditions is traced in a series of seven fatal cases.

3. The conclusion is reached that many cases have an origin in an acute respiratory illness.

4. Bronchiectasis ensues when inflammation is of such severity as to disorganize the bronchial wall. The cavities so formed are subsequently lined by a new wall of granulation tissue.

5. Fibrosis of the lung necessarily accompanies established bronchiectasis.

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DESCRIPTIONS OF FIGURES.

- Fig. 1. Lipiodol-radiogram of Clinical Case A.
 Fig. 2. Lipiodol-radiogram of Clinical Case B.
 Fig. 3. (Case VII. Male, aged 6 years). Advanced unilateral bronchiectasis in left lung. Acute broncho-pneumonia in right lung. Great enlargement of root glands.
 Fig. 4. (Case VI. Female, aged 6 years.) Chronic fibrosis, with slight bronchiectasis, in lower lobe of left lung. Marked glandular enlargement.
 Fig. 5 ($\times 2$.) (Case I. Male, aged 6 months.) Ulcerative bronchitis and confluent broncho-pneumonia in right upper lobe. Bronchi distinctly enlarged; majority filled with pus. B=bronchus illustrated in Fig. 7.
 Fig. 6 ($\times 2\frac{1}{2}$.) (Case II. Female, aged 2 years.) Ulcerative bronchitis and acute broncho-pneumonia in right upper lobe. Plugs of pus in excavated bronchi. Considerable collapse between pneumonic patches.
 Fig. 7 ($\times 2\frac{1}{2}$.) (Case IV. Female, aged 15 months.) Early bronchiectasis in right lung. One cavity of considerable size towards pleural surface. Several other bronchi enlarged. Confluent broncho-pneumonia in relation to affected bronchi. Obliteration of interlobar fissure. B=portion of bronchiectatic cavity illustrated in Fig. 9.
 Fig. 8 ($\times 2$.) (Case V. Female, aged 16 months.) Early chronic bronchiectasis with terminal acute pneumonia in left lung. B=bronchus illustrated in Figs. 12 and 13.
 Fig. 9 ($\times 60$.) (Same case as Fig. 3). Ulcerative bronchitis. Bronchial wall completely destroyed and margin of cavity formed by consolidated alveoli. Plug of pus in lumen.
 Fig. 10 ($\times 60$.) (Same case as Figs. 3 and 7). Ulcerative bronchitis. Bronchial wall completely destroyed at one side (A) and relatively healthy at the other.
 Fig. 11 ($\times 110$.) (Same case as Fig. 5). Early bronchiectasis. Diverticulum of large cavity. Reconstitution of wall by granulation tissue.
 Fig. 12 ($\times 110$.) (Case II.) Ulcerative bronchitis with beginning of healing. A=young granulation tissue.
 Fig. 13 ($\times 300$.) Magnification of area A in previous photograph. Young fibroblasts sprouting out and replacing acute inflammatory products. Clump of polymorphonuclear cells to left of field.
 Fig. 14 ($\times 60$.) (Same case as Fig. 6). Bronchus in which disintegration and erosion of half of the circumference had occurred and in which repair was in process. Intact wall on the left; denuded and excavated wall on the right of the field. A=portion of wall shown in Fig. 13.
 Fig. 15 ($\times 120$.) Magnification of above. Vascular granulation tissue in wall, in which a few modified alveolar spaces (A) are visible. Extension of epithelium to form a new lining for eroded portion. New epithelial cells, seen on right, of a lower grade than original epithelium. Purulent exudate in lumen.
 Fig. 16 ($\times 120$.) (Same case as Fig. 2). Wall of damaged, slightly dilated, bronchus. Whole thickness of wall composed of very vascular fibrous tissue, infiltrated with inflammatory cells; muscle absent. Epithelial lining formed of several layers of small cuboidal cells.
 Fig. 17 ($\times 300$.) (Same case as Fig. 4). Obliterative bronchiolitis. Original wall of bronchus destroyed. Organization of exudate in lumen by young fibroblasts in process and leading to obliteration. Small amount of pus still present in centre.
 Fig. 18 ($\times 300$.) (Same case as Figs. 6, 12 and 13). Organizing pneumonia. Alveolar space seen, partly occupied by a mass of proliferating fibroblasts and young connective tissue fibres attached to the wall at one point. A few inflammatory cells, remnants of exudate, present.
 Fig. 19 ($\times 120$.) (Same case as Figs. 2 and 14). Chronic fibrosis of lung, with obliteration of alveoli. A few remnants of alveoli represented by small epithelial lined spaces. Dense aggregation of lymphocytes marks site of obliterated bronchus.