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DIFFUSE CYSTIC LUNGS OF GRANULOMATOUS ORIGIN

A HISTOLOGICAL STUDY OF SIX CASES

BY

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The term cystic disease of the lung embraces a number of conditions aetiologically and morphologically distinct. Although pulmonary cysts may be developmental in origin, there is considerable evidence that the cystic disease is often acquired during childhood or adult life. In a recent paper, Oswald and Parkinson (1949) described 16 cases in which there were small air-containing cystic spaces scattered through both lungs, a condition referred to as honeycomb lungs. In six cases the pulmonary changes were associated with other disorders, namely, xanthomatosis, tuberous sclerosis, hepatic disease, and pituitary disease. In the remaining 10 cases there was no definite extra-pulmonary disease and no conclusive histological evidence as to the cause of the cyst formation. Some cases, however, showed an extreme degree of fibrosis around the pulmonary cysts, and it was suggested that this might have resulted from the healing of a disease process similar to the ones producing the associated disorders already mentioned. With a view to examining this suggestion more fully, histological sections from nine cases of honeycomb lungs were examined in detail, and, as a result, six cases are now reported because they appeared to have distinct histological features, suggesting that they were all different stages of a granulomatous process ending in extensive pulmonary fibrosis. These histological characteristics were not present in the sections from the other cases of honeycomb lung that were examined, confirming that this type of cystic disease arises from a number of different causes.

Many previous case reports of polycystic disease of the lungs make reference to the finding of granulomatous changes, giant cell formation, and interstitial fibrosis. In some cases the appearances are similar to those found in the present series, and various explanations have been put forward to explain the presence of the granulomatous tissue. Bernstein (1905), whose case has been included in the present paper, described giant-cell formation in the walls of the pulmonary cysts, which were surrounded by closely packed round or oval cells, thought to be inflammatory in origin. The liver in this case showed pericholangitis. Buchmann (1911) reported the case of a woman with polycystic lungs who died at the age of 55 years. Here the cyst walls were formed by granulation tissue, and there was much interstitial fibrous tissue. Giant cells were found in both the interstitial tissue and the cyst walls. Buchmann thought that these changes were secondary to foetal atelectasis, and did not clearly separate the case from the cases of bronchiectasis described in the same paper.

Kerley, Shore, and Young (1927) described a patient who died from right heart failure due to polycystic lungs. Histologically the lungs showed interstitial fibrosis with granulomatous areas containing fibroblasts, endothelial and mononuclear cells, eosinophils, and occasional giant cells. The authors postulated that the pulmonary changes were akin to those found in fibrocystic disease of the breast. Collins (1933) reported a child aged 15 months with polycystic lungs, lymphadenopathy, and hepatomegaly. The lungs, liver, and lymph nodes showed " epithelioid " cell proliferation and giant cell formation. In the lungs these changes were most marked beneath the pleura and in the fibrous septa between the cysts. Collins regarded the pulmonary cysts as congenital in origin and not caused by the giant-cell hyperplasia. Cole and Nalls (1938) described a boy aged 17 who had bilateral spontaneous pneumothorax and later died from right heart failure secondary to honeycomb lungs. The lungs showed an increase in the interstitial connective tissue and focal collections of lymphoid tissue. Calma (1941) recorded a case of polycystic lungs in which there was a large amount of collagen between the cysts, and also collections of lymphoid and reticulo-endothelial cells. He thought that the fibrous overgrowth was compensatory and protective to the weakened lung parenchyma. In reporting a similar case, Eha (1944) considered that the cysts were derived from lymphatics, a view first held by Grawitz (1880). In addition to these cases, a number of others are on record which showed dense interstitial sclerosis between the pulmonary cysts, but in which the granulation tissue is not described in detail (Oeschli and Miles, 1934 ; Weiss, 1936 ; Nolte, 1937 ; Bruce, 1939).

It has generally been assumed that the interstitial changes have been produced by added infection in lungs in which the cystic changes were congenital in origin, or that the fibrosis resulted from diffuse interstitial pneumonia (Peirce and Dirkse, 1937). The similarity of the changes described in the literature to some of the cases included in the present paper, and the complete absence of such changes in other examples of cystic disease of the lung, led to a reconsideration of this relationship of cause and effect.

MATERIAL

Full clinical and radiological details of these cases have been published elsewhere (Fletcher, 1901 ; Bernstein, 1905 ; Oswald and Parkinson, 1949). The main clinical features are given briefly here, and the significant data summarized in Table I.

TABLE I

SUMMARY OF CASES

Case	Sex	Age at Onset	Spontaneous Pneumothorax	Right Heart Failure	Other Data
1	M	3	—	D	Hepatomegaly; pericholangitis
2	F	3	Right	D	Pericholangitis
3	M	12	Right and left	—	Transient polyuria. Died from tuberculosis
4	M	23	Right and left	D	Previous malaria
5	M	27	—	D	
6	M	57	—	D	

D = Cause of death

CASE 1 (Fletcher, 1901 ; Oswald and Parkinson, 1949).—A boy aged 3 years was admitted to St. Bartholomew's Hospital in April, 1900. For two weeks he had suffered from abdominal pain, breathlessness, and cough. Examination showed a raised respiratory rate, dyspnoea, and added sounds over the chest. The liver was enlarged, but not the spleen. The child died with extreme dyspnoea five days after admission.

Necropsy.—The lungs were voluminous and the pleural surfaces studded with bullae. The cut surface was reddish-grey and riddled with small spherical air-containing spaces, giving a honeycomb appearance. The liver weighed 600 g. and contained a large number of cyst-like spaces surrounded by thick white walls, representing cystic dilatation of the bile ducts. All the other organs were normal.

CASE 2 (Bernstein, 1905).—A girl aged 3 years was admitted to Westminster Hospital with a history of pain in the back and cough for one month. She was cyanosed, febrile, and severely breathless, and she died very soon after admission.

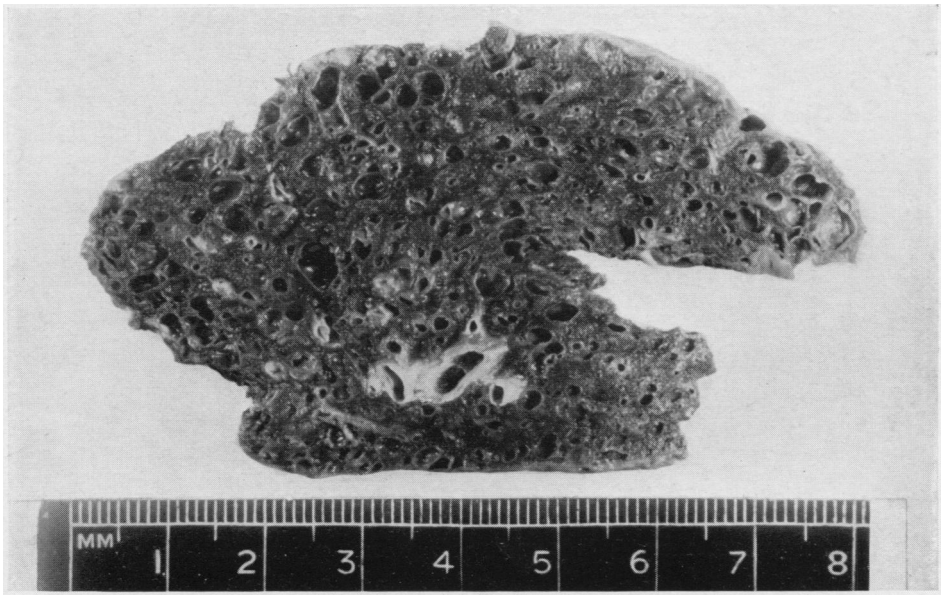

FIG. 1.—Section of whole lung (Case 2).

Necropsy.—There was a tension pneumothorax on the right side. Both lungs contained a honeycombed system of cavities throughout (Fig. 1). The liver weighed 500 g. and, on section, showed yellow nodules the size of a pin's head. Microscopy of the liver showed small round and oval cells surrounding the bile ducts.

CASE 3 (Oswald and Parkinson, 1949, Case 8).—A boy aged 12 years was admitted to the Brompton Hospital in May, 1941, with increasing shortness of breath for two weeks. He was found to have a spontaneous pneumothorax on the right side, and this was treated by intrapleural suction. Next day he developed a spontaneous pneumothorax on the left side and this was also treated by continuous suction. During the next two months he had repeated attacks of spontaneous pneumothorax affecting both lungs. In July and August, 1941, pleural adhesions were induced with 10% silver nitrate.

He left hospital in April, 1942, at which time there was no radiological abnormality of the lungs. The patient also complained that he had been passing excessive amounts of urine during the three months before admission, and during the first two weeks in hospital his average daily urinary output was 4.9 litres. The specific gravity of the urine was 1.001. The polyuria was controlled by pituitrin injections, but full details of the dosage and duration of this treatment are not available. After discharge he remained well until April, 1943, when he was readmitted with tuberculous pneumonia of the right lower lobe, from which he died in May, 1943.

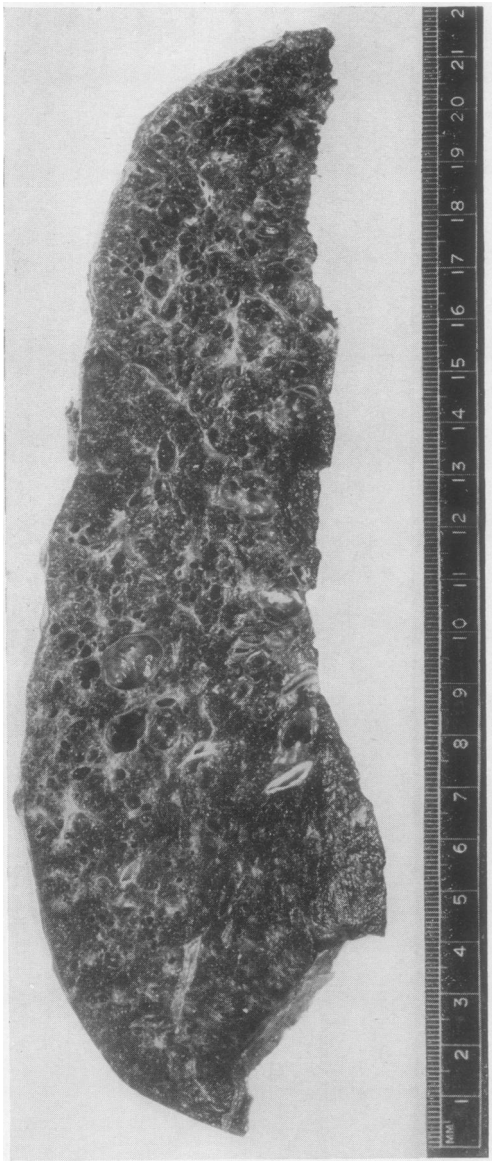

FIG. 2.—Section of whole lung (Case 4) showing cystic changes.

Necropsy.—There were diffuse cystic changes throughout both lungs, and caseous tuberculosis of the right lower lobe. The abdominal organs were normal. The brain was not examined.

CASE 4 (Oswald and Parkinson, 1949, Case 11).—An Indian, resident in England, in 1939, when he was aged 23, had a sudden onset of severe pain in the left side of the chest whilst lifting a weight. During the next six months he had five similar attacks. In 1940 a right-sided pneumothorax was diagnosed, and he was admitted to the Brompton Hospital. Radiographs of the chest showed a diffuse reticular pattern throughout both lung fields. In view of the history of recurrent pneumothorax, a right-sided pleurodesis was carried out, using 1% "gomenol" in olive oil. On the following day he developed a tension pneumothorax on the left. This was treated by continuous suction, and later a pleurodesis was done on this side. The patient left hospital in July, 1940, at which time the left pneumothorax had almost re-expanded. He remained fairly well until early in 1949, when he was admitted to the London Hospital with increasing shortness of breath. He died from right heart failure shortly after admission.

Necropsy.—Both lungs showed diffuse cystic changes (Fig. 2). There was right-sided cardiac hypertrophy and congestive changes in the liver and spleen. Other organs appeared normal.

CASE 5 (Oswald and Parkinson, 1949, Case 14).—A man, an instrument maker by trade, aged 27 years, was admitted to the North Middlesex Hospital in November, 1944. One sister had died from pulmonary tuberculosis. The patient had been subject to winter coughs since childhood. In January, 1943, he began to suffer from progressive breathlessness and cough. On examination he was cyanosed and dyspnoeic. There was no clubbing of the fingers. Râles and rhonchi were heard over the chest. There was no oedema and no hepatomegaly. A month later he suddenly became more cyanosed and died, from acute right heart failure, within an hour.

Necropsy.—The lungs were firm and elastic; there were numerous bullae on the surface. Sections of the lung showed air-containing cysts throughout their substance. The hilar lymph-nodes were enlarged. The abdominal organs showed chronic venous congestion but no other abnormality.

CASE 6 (Oswald and Parkinson, 1949, Case 16).—A labourer, aged 57 years, was admitted to the Prince of Wales Hospital, Tottenham, in November, 1947. He complained of increasing breathlessness for the previous two years. He was cyanosed and dyspnoeic. There were râles over the chest, but no other abnormal signs. Radiographs of the chest showed coarse reticulation through the lung fields. Other investigations were negative. He was discharged from hospital in December, 1947. A few days later he died suddenly in the street.

Necropsy.—The lungs were firm and rubbery and showed diffuse cystic changes. On the cut surface the cysts were larger and more numerous in the peripheral portions of the lung.

HISTOLOGICAL FINDINGS

Technique.—In five of the six cases large slices of lung were cut on the sledge microtome and mounted on lantern slides. In the sixth (Case 3) only ordinary-sized sections were available. The large sections proved to be of great value in giving a more complete picture of the disease process. Sections were stained by the following methods: (*a*) Haematoxylin and eosin; (*b*) haematoxylin, Verhoff's elastin, and van Gieson; (*c*) Picro-Mallory method; and (*d*) Sudan black (paraffin sections).

Case 1.—The cystic spaces were seen evenly distributed throughout the lung substance. The majority of the cysts were without epithelial lining; a few were lined by a simple cubical epithelium. The cysts were surrounded by a cellular exudate which, in many cases, formed the walls of the cysts (Fig. 6). The cellular tissue was largely composed of histiocytic cells, though some lymphocytes and eosinophils were present. Multinucleate giant cells of the foreign-body type were seen both in the cystic spaces and in the interstitial tissue (Figs. 8 and 9). The giant cells appeared to be formed in the cyst walls by a process of desquamation and coalescence of the simple cubical epithelium (Fig. 8). Normal alveoli were occasionally seen between the cysts (Fig. 3). In some areas enlargement of the cyst spaces appeared to cause compression of neighbouring bronchioles with the production of local emphysema (Fig. 7). The interstitial tissue showed little fibrosis, and the blood vessels appeared normal.

Case 2.—Although the general structure of the lung was well seen, this tissue could not be made to take up the nuclear stain satisfactorily. This may have been due to the age of the tissue, or to the effects of the fluid in which it had been stored for many years. Much normal lung tissue was present in addition to a number of cystic spaces. The cysts were mostly devoid of epithelial lining; they were surrounded by large numbers of histiocytes. When a fragment of lining epithelium was identified it was simple cubical in type.

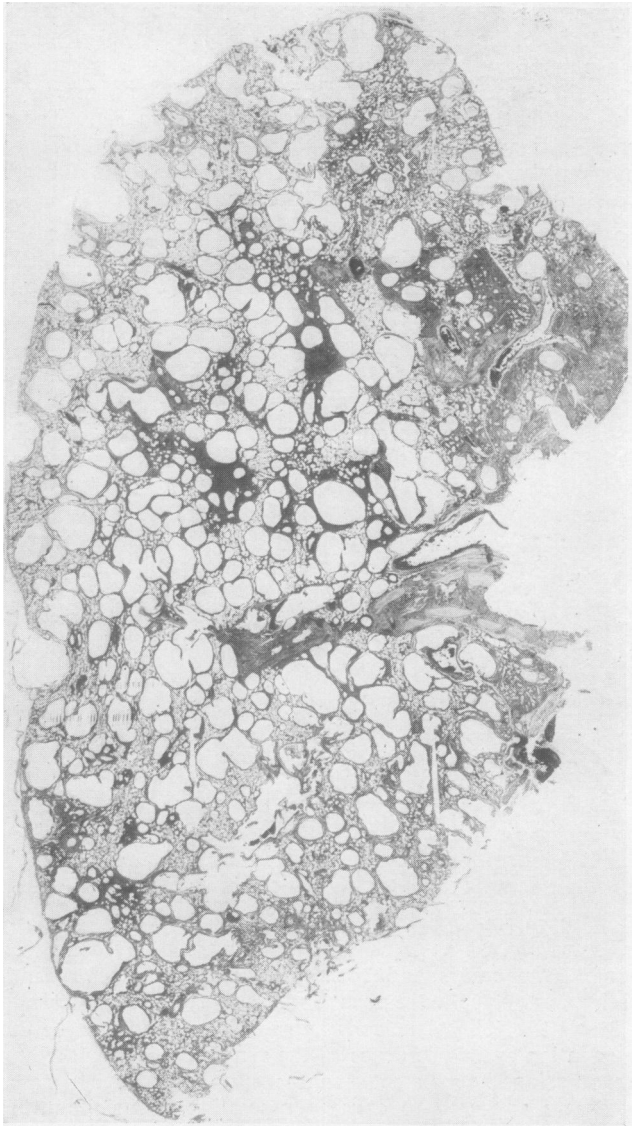

FIG. 3.—Generalized cystic changes (Case 1) with little increase in fibrous stroma. Areas of normal lung tissue present. × 2.

Case 3.—Sections of the left lung showed thickening of the pleura with diffuse cystic changes of the underlying lung. No normal lung tissue was found. The cellular exudate in the interstitial tissue was essentially similar to that seen in Case 1, except that no eosinophils were found. Many histiocytes were large and had a foamy appearance. The giant cells were of the foreign-body type. Amongst the cellular exudate the remains of alveoli could be made out; histiocytes were present in the lumina of these alveolar remains.

Sections of the right lung showed a similar appearance, though in places the picture was complicated by tuberculosis.

Case 4.—The lung tissue was congested. In addition to the cystic spaces, emphysematous areas and a remarkable amount of normal lung were seen. The cystic spaces varied in appearance, some being lined by a flattened epithelium whilst others were lined by masses of histiocytes. Most of the cysts were surrounded by a granulomatous exudate of histiocytes, lymphocytes, plasma cells, and eosinophils resembling that described in the other cases (Figs. 12 and 15). No giant cells were found. Areas of alveolar destruction were present, and groups of cubical cells, presumably representing alveolar lining, were seen.

Case 5.—The lungs were deeply congested; red cells and oedema fluid were found in the cyst spaces. A granulomatous exudate containing histiocytes, eosinophils, and giant

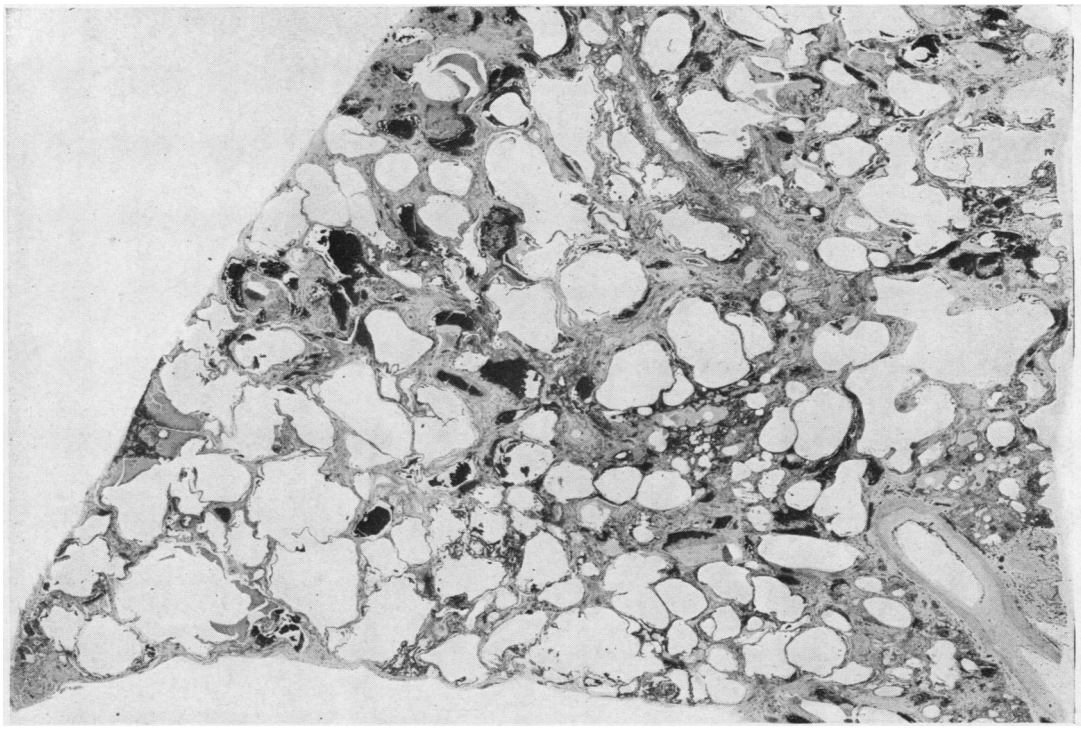

FIG. 4.—Intermediate stage (Case 5) with moderate increase in fibrous stroma. × 2.

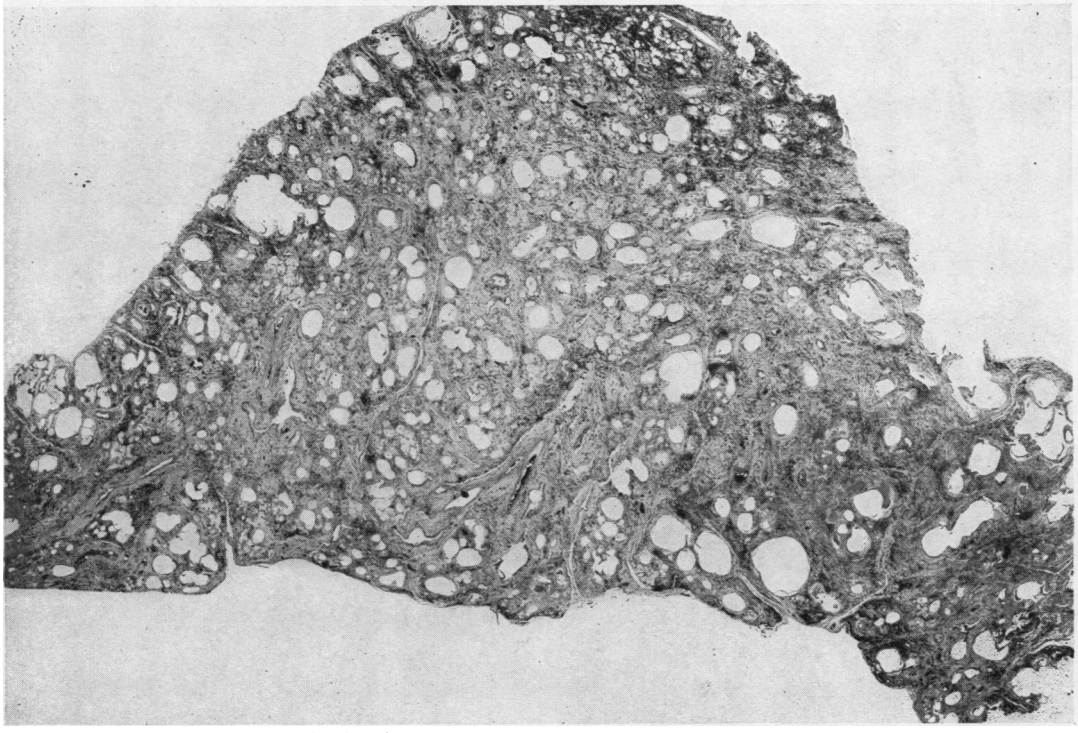

FIG. 5.—Late stage (Case 6) showing coarse generalized fibrosis and no normal lung tissue. ×2.

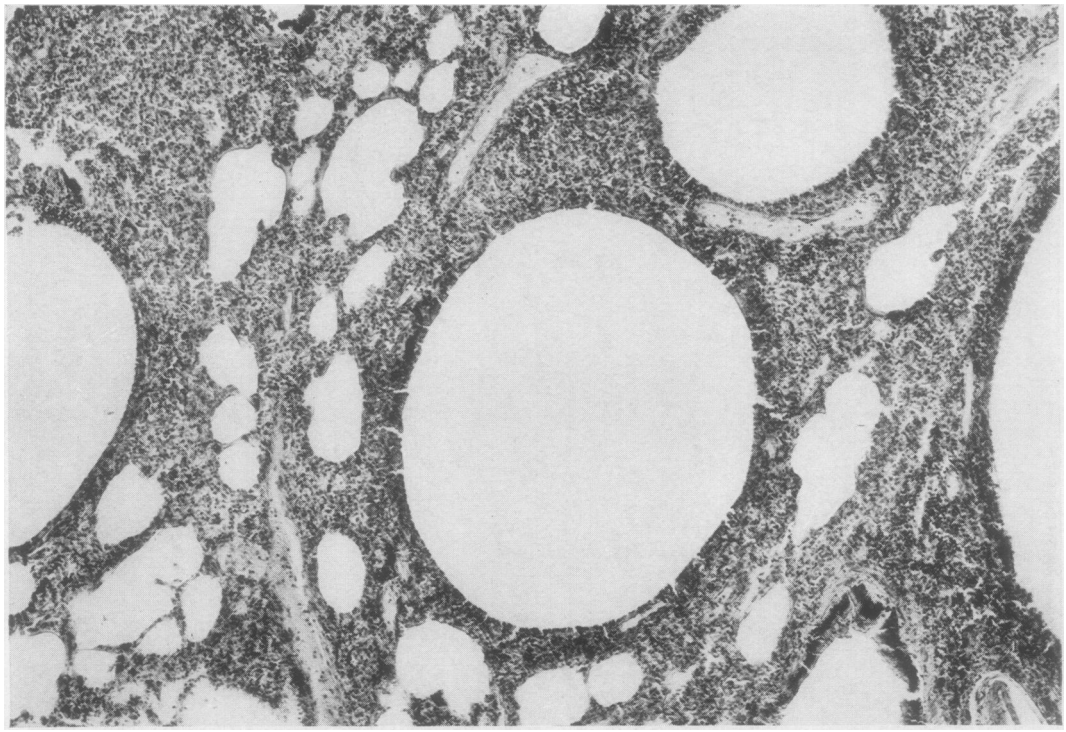

FIG. 6.—Cystic spaces (Case 1) with no epithelial lining and surrounded by granulomatous deposit. × 70.

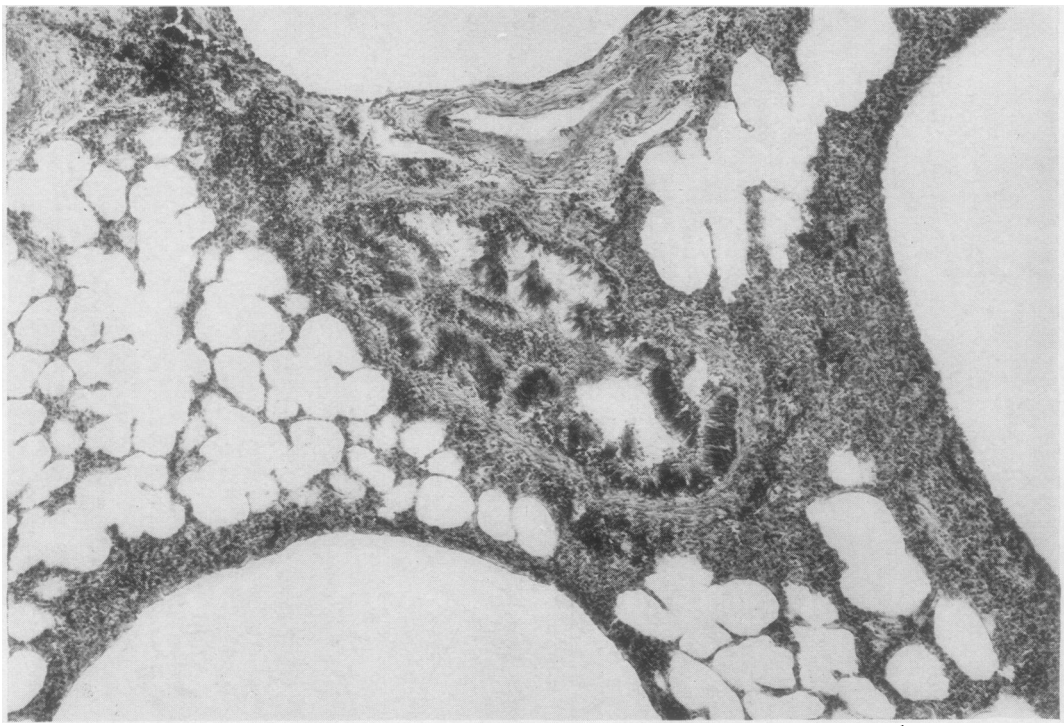

FIG. 7.—Three cystic spaces (Case 1) causing compression of bronchiole and local emphysema. × 70.

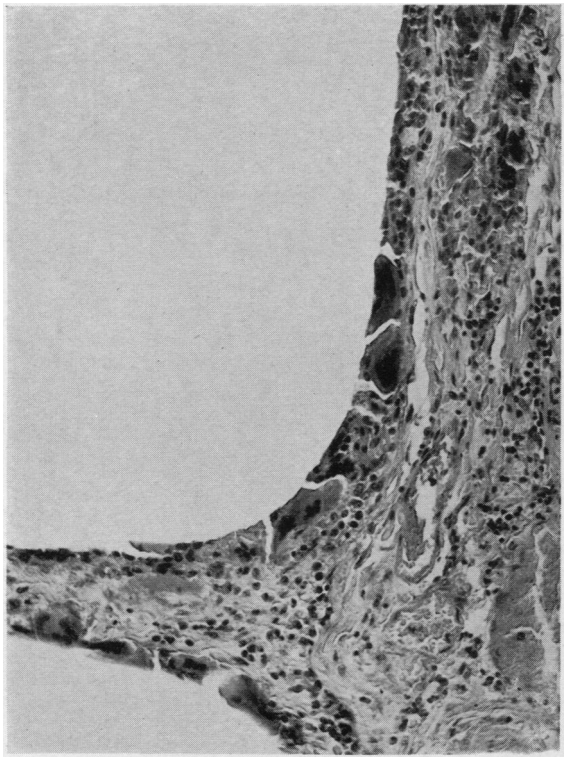

FIG. 8.—Giant cell formation from cyst lining (Case 1). × 150.

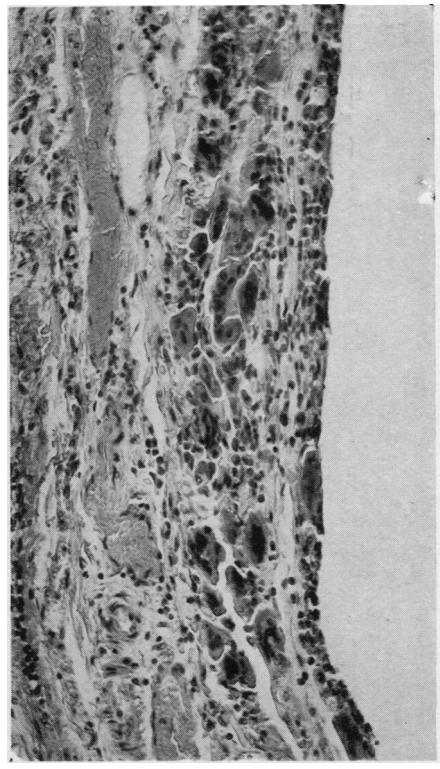

FIG. 9.—Giant cells in the interstitial tissue (Case 1). × 150.

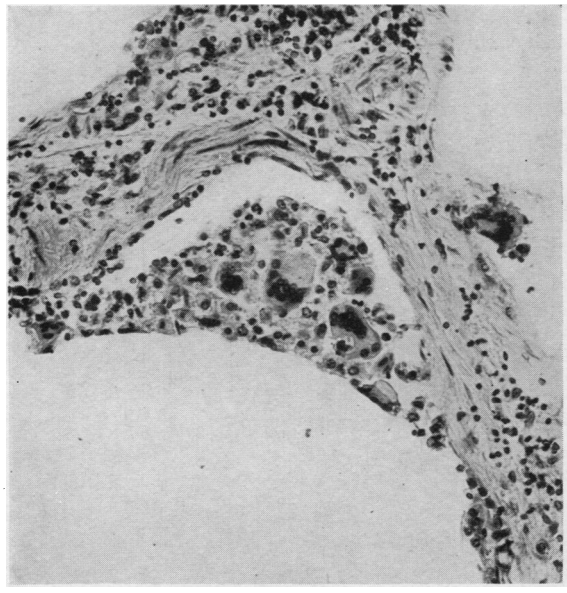

FIG. 10.—Desquamated giant cells in lumen of cyst (Case 6). × 180.

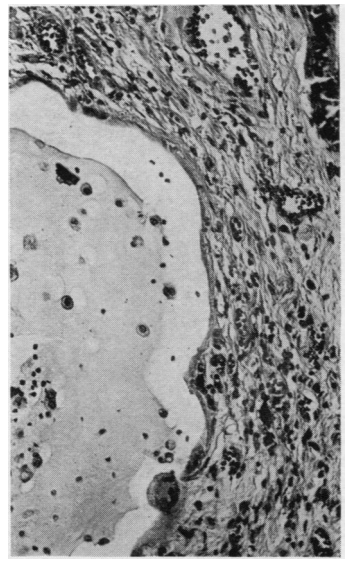

FIG. 11.—Giant cell attached to cyst wall (Case 6). × 135.

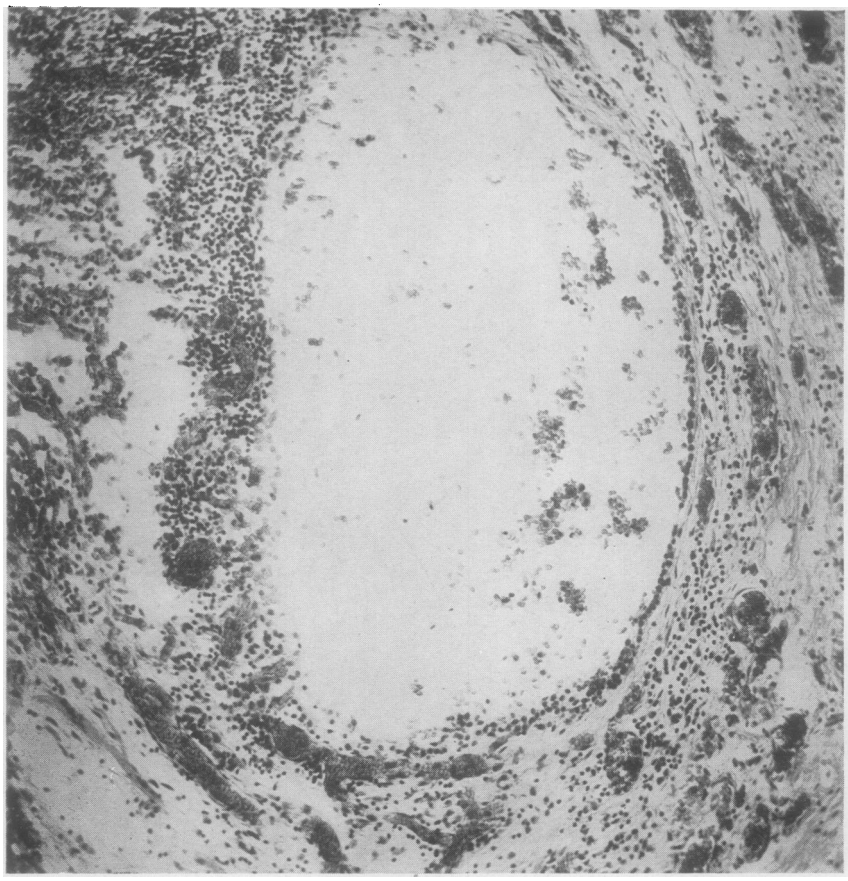

FIG. 12.—Cyst (Case 4) partially lined by cubical cells. Cellular infiltration of surrounding tissue. × 135.

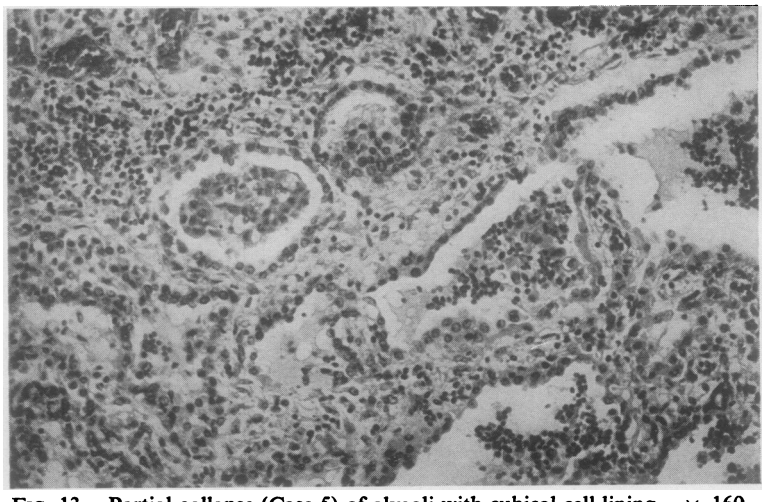

FIG. 13.—Partial collapse (Case 5) of alveoli with cubical cell lining. × 160.

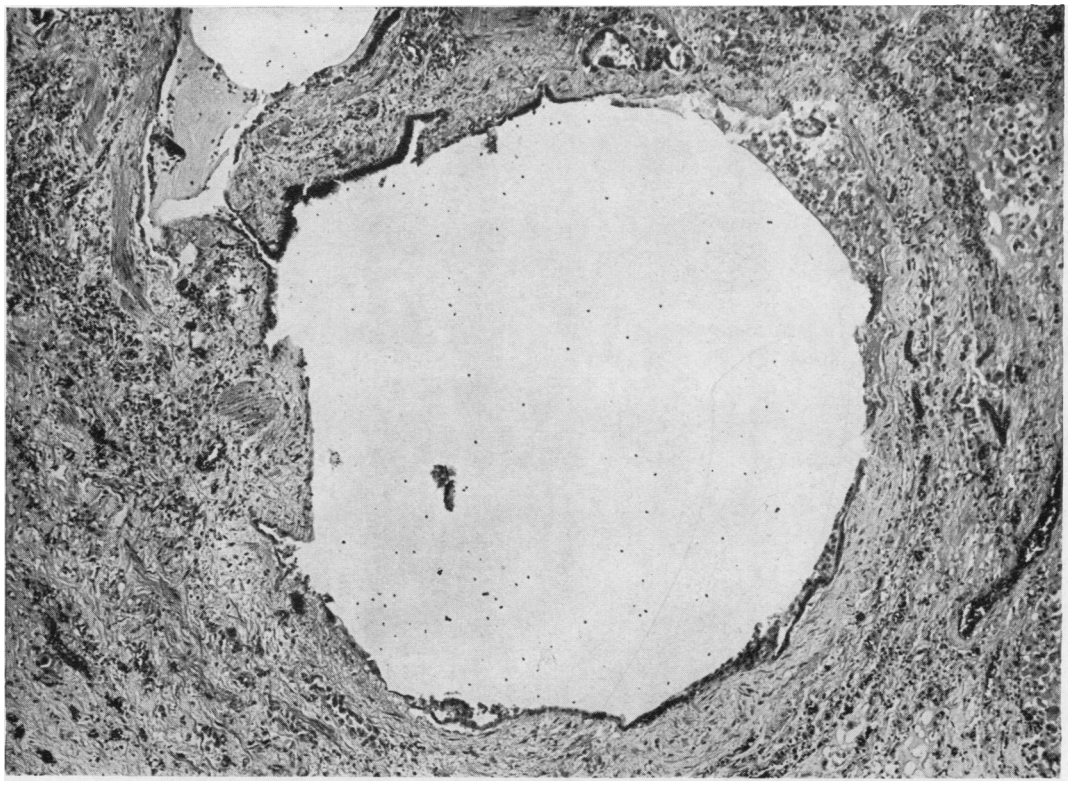

FIG. 14.—Variation in cellular lining of cyst (Case 6). Surrounding fibrosis with absence of alveoli. × 70.

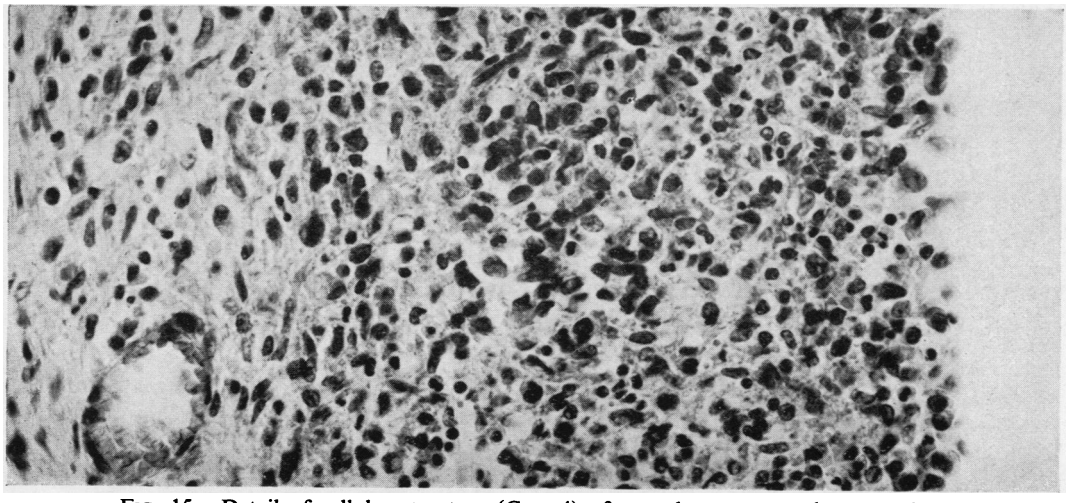

FIG. 15.—Detail of cellular structure (Case 4) of granulomatous exudate. × 370.

cells was present. Many of the histiocytes had a foamy appearance. The giant cells, which occasionally contained small globules, had a peripheral arrangement of the nuclei. Transition of the cubical epithelium to a more flattened type was seen in some spaces. In the fibrous tissue between the cysts partially collapsed alveoli could be seen (Fig. 13). The increase in fibrous tissue in the sections was marked (Fig. 4), and some arteries showed narrowing of their lumina from sub-intimal fibrosis. Little normal lung tissue was seen.

Case 6.—The lung tissue was greatly reduced in bulk as a result of diffuse fibrosis. Most of the fibrous material was well formed, relatively acellular, and contained numerous fragmented elastic fibres (Fig. 14). The cystic spaces had thick fibrous walls, relatively few having a cubical epithelial lining (Fig. 14). Muscle fibres were present in some of the cyst walls, suggesting that the cysts had originated from larger bronchioles. In spite of the similarity of the picture to that of burnt-out inflammation, there were still indications of a granulomatous process. Amongst the fibrous tissue there were remnants of alveoli, and, in addition, collections of foamy histiocytes, lymphocytes, eosinophils, and giant cells. Some giant cells were also seen in the cystic spaces (Figs. 10 and 11). There was some thickening of the overlying pleura.

DISCUSSION

At the beginning of this study sections from nine cases of honeycomb lungs were examined to see if there was a common histological lesion, and, as a result, six cases were chosen for further examination and three rejected. Each of the sections from these six cases was subsequently found to contain histological evidence of a chronic inflammatory lesion. In spite of some variations, the basic similarity enabled us to postulate that they represented different stages in the evolution of a single pathological process. Case 1 was by far the most cellular, and indeed the most striking, and this picture with its relative absence of fibrosis suggested an earlier phase of the disease. By contrast, Case 6 showed the maximal amount of fibrosis, whilst Case 5 occupied an intermediate position. It was notable that these three cases showed a diffuse lesion, particularly Cases 5 and 6 where little normal lung tissue could be found. On the other hand the affected areas were rather patchy in Cases 2, 3, and 4, and both early and late lesions were found in Case 4.

The granulomatous exudate seen in each of the sections from these cases was remarkably similar. Moreover, its constant relationship to the dilated cystic spaces at once suggested its essential importance in the pathogenesis of the condition. Whilst many of the cellular constituents, such as lymphocytes, plasma cells, giant cells, and eosinophils, could in no way be regarded as specific, the large numbers of histiocytes gave this lesion a characteristic appearance. These histiocytic cells were never arranged focally as in tuberculosis, and did not closely resemble the endothelial cells seen in that disease. In some sections they had a foamy appearance, but staining with Sudan black did not confirm the presence of lipoid material within these cells. Unfortunately no fresh tissue was available for the examination of frozen sections, so the presence or absence of lipoid could not be definitely decided.

In an attempt to identify the site of origin of the cystic spaces the lining epithelium and the structural constituents of the walls were studied. Some of the cysts had no

epithelial lining at all, their walls being formed by solid columns of tightly packed histiocytic cells. Many others, however, were lined by simple cubical epithelium. In the older cases the walls of the cysts were more fibrous and less cellular, and those cysts which had no epithelial lining were now lined by a layer of collagenous tissue. In some cysts epithelial desquamation was taking place. This process is of great importance, as it appears to throw light on the mode of formation of the giant cells. Giant cells were present in the cystic spaces as well as in the interstitial tissue. This finding has also been reported by previous workers, most of whom suggested that the giant cells were of the foreign-body type. In our sections the cubical epithelial cells could be seen undergoing fusion during the process of desquamation, thus accounting for their appearance in the cystic spaces. Their presence in the neighbouring interstitial tissue suggested that they might either be absorbed from a cystic space, or find their way to a normal bronchiole from which absorption could take place. Except in Case 6, supporting elements in the cyst walls, such as plain muscle fibres, were difficult to find. It was therefore considered that the granuloma affected the finer parts of the bronchial tree where the delicate supporting structures had been completely destroyed in the inflammatory process. Some workers have separated cysts of the lung into those of alveolar and bronchiolar origin, a distinction which was impossible in our cases. It is known that as the bronchioles pursue their course peripherally the lining membrane changes from compound ciliated columnar successively to ciliated cubical and simple cubical before giving place to the flattened cells lining the alveoli. Furthermore, under conditions of disuse the alveolar lining may become cubical, and the ciliated cubical epithelium of the bronchioles may change into a simple cubical type. The frequent finding of cysts with cubical epithelial lining, together with a relative absence of supporting structures in the walls, suggested that the cysts in our cases were derived from the smallest bronchioles, the respiratory bronchioles, or the alveolar spaces. We considered that further division of the cysts into those of alveolar or bronchiolar origin was pointless, artificial, and probably incorrect.

The mechanism of destruction of lung tissue was of interest, since it has already been mentioned that some sections showed no normal lung tissue at all. In some sections the cystic spaces appeared to be causing pressure on neighbouring bronchioli as they expanded, a finding which suggested that bronchiolar compression with local alveolar collapse occurred. This view was supported by the observation of collapsed and inactive alveoli in many of the sections, and by the presence of emphysematous bullae which were easily distinguished from the cystic spaces by the absence of a surrounding granulomatous exudate. Once collapsed the alveoli probably underwent atrophy from pressure by the neighbouring expanding cysts. In view of the constant occurrence of granulomatous material in the walls of the cystic spaces it is difficult to escape the conclusion that the disease process weakens the walls of the bronchioles, and that this is the direct cause of the cyst formation. Partial bronchiolar obstruction may be a secondary cause, but in Case 1 bronchiolar compression appeared to be the result, rather than the cause, of the cystic dilatation. To regard cases showing such changes as being examples of congenital cystic disease seems to be fundamentally wrong. The absence of normal alveoli in a given case cannot be used as evidence of a congenital origin, as our cases clearly show a progressive destruction and distortion

of normal alveoli from the acute to the chronic phases. The granulomatous process must be regarded as the cause of the cystic changes, which result from the peculiar situation and the destructive nature of the pathological process.

The underlying cause of the granulomatous process giving rise to these changes is difficult to determine. It is unlikely that it results from infection, since the appearances are not those usually associated with chronic pyogenic infections; neither is the granuloma similar to that of tuberculosis or syphilis. The interstitial changes found in our cases do not resemble those found in the virus pneumonias (Opie and others, 1921) or those in the diffuse interstitial fibrosis described by Hamman and Rich (1944).

In considering the cause of the granuloma it is important to note that three of the cases in the present series showed clinical or pathological evidence of extrapulmonary disease. Cases 1 and 2 had a similar granulomatous condition of the liver, and Case 3 had transient diabetes insipidus, suggesting that the pituitary was affected. It seems probable, therefore, that some of these cases are examples of a generalized granulomatous process with visceral localization, caused by an unknown inflammatory agent. Mallory (1948) drew attention to a progressive granulomatous pneumonitis, of obscure aetiology, which, by analogy with other cases, he regarded as being the end-result of sarcoidosis. Some of Mallory's cases showed emphysema and bronchiolectasis, and the granuloma was found to invade the bronchiolar walls. It is recognized that sarcoidosis frequently involves the liver (Scadding and Sherlock, 1948) and that pituitary disorders, especially diabetes insipidus, are not uncommon in this disease (Kraus, 1942; Leitner, 1942; Barber, 1945). For these reasons sarcoidosis was considered as a possible cause for the cases reported here, but none of the sections examined showed the focal histiocytic proliferation of sarcoidosis. In Case 6, where extensive fibrosis predominates, it is impossible to exclude late sarcoidosis as the cause, but in all the other cases the granuloma differed fundamentally from the type seen in that disease. For similar reasons, and also because there was no industrial risk in these cases, beryllium poisoning, which sometimes produces a similar granuloma (Agate, 1948; Dutra, 1948), was excluded. Polyarteritis nodosa is another generalized disease known to give rise to pulmonary granulomatosis (Sweeney and Baggenstoss, 1949), but the affection of the pulmonary arterioles so characteristic of this disease was absent in our cases.

A group of disorders worthy of fuller consideration is that which has been called eosinophilic xanthomatous granuloma. Under this heading Thannhauser (1947) included the granulomatous conditions which are separately known as the Hand-Schüller-Christian disease, the Letterer-Siwe disease, and eosinophilic granuloma of bone. It is now widely accepted that these three disorders are closely related and that they are probably phases of the same disease (Wallgren, 1940; Farber, 1941; Mallory, 1942; Jaffe and Lichtenstein, 1944). In the acute phase of eosinophilic xanthomatous granuloma there is abundant proliferation of histiocytes with eosinophilic invasion, and in the chronic phase complete fibrosis replaces this cellular exudate. The intermediate phases show a varying degree of lipoid infiltration, on occasions the lipoid-containing histiocytes being abundant enough to give the lesion its characteristic imprint. It is also known that honeycomb lungs are found in this group of disorders (Rowland, 1928; Farber, Hampton, and Mueller,

1942; Oswald and Parkinson, 1949; Parkinson, 1949; Schafer, 1949) and that pulmonary fibrosis occurs in the chronic phase (Thannhauser, 1940; Currens and Popp, 1943). Extensive pulmonary fibrosis is sometimes the predominant, and perhaps the only, manifestation of this disease (Chester, 1930; Jaffe and Lichtenstein, 1944). There is no doubt that the histological changes in our cases would fit into this wider concept of eosinophilic xanthomatous granuloma. The younger cases (Nos. 1 and 2) showed a highly cellular picture, the older cases showed mainly fibrosis, and the others occupied an intermediate position. In Case 3 there was a predominance of foamy histiocytes resembling those often seen in this disease. Also, the hepatic and pituitary abnormalities found in some of the cases are in keeping with this hypothesis. It is unfortunate that, with the exception of Cases 1 and 4, only sections of the lungs were available for study. In Case 1, sections of the liver showed a granulomatous exudate in relation to the bile ducts; the exudate was similar in all respects to that seen in the lungs. In Case 4, Professor Dorothy Russell, to whom we are indebted, kindly examined sections from other organs and found no histological evidence of a pathological process similar to that seen in the lungs.

It is, of course, possible that there is no single cause for the granulomatous condition of the lungs in these patients, and that grouping them together on histological grounds is not justifiable. It is, indeed, likely that the granuloma is a non-specific pathological response to a number of aetiological agents. A clearer concept of the cause of the pulmonary granuloma might be achieved by further search for extrapulmonary lesions in such cases. Whatever the cause of this unusual pathological process may be, there seems little doubt, from the histological findings in our cases, that the granuloma is the direct cause of the cystic changes in the lungs.

SUMMARY

Detailed histological studies on six cases of honeycomb lungs are reported, and brief clinical records of the patients are given.

All cases showed a granulomatous process in the walls of the cysts and in the inter-cystic spaces. In the acute phase this process was characterized by a highly cellular histiocytic response, and in the chronic phase by widespread fibrosis. In the intermediate stages, foamy macrophages were present in large numbers, sometimes being the predominant cell.

It is suggested that the cystic spaces are produced by weakening of the walls of the smaller bronchioles as a result of granulomatous infiltration. In the present material the distinction between cysts of alveolar and bronchiolar origin is impossible.

The nature of the granulomatous process is discussed.

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