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LUNG ALVEOLAR TUMOURS: A REPORT OF TWO CASES

BY

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Alveolar tumours of the lung, as the name implies, show proliferation of cells within the alveoli, and within the lungs the growth is confined to these spaces. Growths in which there has been an alveolar spread from an evident bronchial carcinoma, however minute, have always been excluded from this group of tumours, and equal care has been exercised to eliminate any possible extra-thoracic primary growth. The proliferating cells, which are non-ciliated and either cuboidal or columnar, closely line the alveolar walls in one or more layers. They are always extremely regular in form, but sometimes show free secretion of mucus (Case 1). As a rule they show remarkably little local "malignant" tendency, and the alveolar septa are only rarely broken down; involvement of the pleura is uncommon; and invasion even of thoracic lymph glands is often absent. But in occasional cases there are quite widespread metastases to the bones, brain, and other viscera: this variation in malignancy has led some to regard the tumours as adenomata, others to regard them as carcinomata, and yet a third group to apply non-committal titles (e.g. "carcinosis").

The tumour may involve the lungs widely, as though from many quite separate centres, or it may be confined, at any rate for a time, to one lobe through which it appears to spread in a continuous expanse; these two forms may be seen together in one subject. As a general rule dyspnoea and cyanosis with heart failure are more prominent symptoms at death than wasting and cachexia.

Neuberger and Geever (1942) have estimated that alveolar cell tumours do not comprise more than one-twentieth of all lung tumours. The two cases described below were characteristic of tumours of this kind.

Case Reports

Case 1.—A mechanic, aged 58 years, had right-sided dry pleurisy in February, 1947; subsequently he never felt really well and was troubled by frequent coughs and by gradually increasing dyspnoea, which was troublesome even at rest during the last six weeks before his admission to Redhill County Hospital on Sept. 17. During this time the dyspnoea was associated with pain in the back, pleuritic pain over both costal margins, a cough productive of much purulent sputum, and a loss of ten pounds in weight. Before 1947 he had always been quite well.

On admission.—On admission he was a dyspnoeic, thin, plethoric patient with coated tongue and a frequent cough productive of much purulent sputum and of pleuritic pain below the right costal margin. He was afebrile. There was no clubbing of the fingers; the trachea and mediastinum were central; and there were no enlarged glands.

Chest.—Both lungs expanded poorly and showed dullness at the bases. Breath sounds were generally poorly heard and were absent at the bases, but there was pectoriloquy at the right base Moist rales were scattered over both lungs and were especially numerous in the axillae and at the bases.

Heart, blood pressure, pulse rate, and all other systems were normal.

Radiographs of the chest on Sept. 18 and Oct. 2, 1947 (Plate XIII*a*), showed coarse mottling in both upper zones and opacities at the bases of both lungs, with a lateral fading. In the middle zones the right lung showed a patchy density and the left a coarse mottling. The appearances in the lower parts of the lungs resembled those of confluent bronchopneumonia.

Sputum on three occasions was found to contain neither tubercle bacilli nor other pathogenic organisms.

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Blood count.—The blood count on Sept. 19, 1947, showed 110 per cent haemoglobin and 8,000 leucocytes per c.mm. of blood, with a normal differential count.

Course.—No fever developed, but neither the general condition nor the chest signs and symptoms improved, in spite of courses of sulphathiazole and systemic penicillin begun eight days after admission. For the next three weeks the patient suffered from persistent headaches and a tendency to vomit.

Cerebrospinal fluid.—On Sept. 20, 1947, cerebrospinal fluid was found to be normal.

Blood count.—On Oct. 15, 1947, a blood count showed 132 per cent haemoglobin; the leucocyte count remained normal.

The chest signs and general condition changed little during October, but haemoptysis occurred for the first time on Oct. 22. In November rapid deterioration began, with increased dyspnoea and cyanosis. Sputum was still purulent but more frothy and profuse. There were moist rales all over the lungs, and a radiograph on Nov. 4, 1947, revealed an extension of shadowing in all zones with possible early cavitation in the right mid-zone (Plate XIII*b*). On Nov. 9 the patient became comatose, intensely cyanosed, and dyspnoeic with rapid, bubbling respirations, feeble rapid and irregular pulse, and unrecordable blood pressure. He died on Nov. 11, 1947.

Post-mortem findings (Dr. J. L. Hamilton Paterson)

Lungs.—The lungs were voluminous, heavy, and nodular to feel. The left lung weighed 1,500 g. and the right 1,700 g. On section all lobes showed a diffuse and patchy white infiltration, confluent in some places, with one or two broken-down areas. A careful search of the bronchial tree revealed no carcinoma within its lumen. The trachea, larynx, and pleura were all normal; the hilar and tracheobronchial lymph nodes did not appear involved.

Other systems.—There were no abnormalities; brain and meninges were clear.

Histology (Dr. H. C. Moore)

Lungs.—The lungs (Plate XIV*a* and *b*) and lymph glands both showed "alveolar carcinoma." The component cells were tall, columnar, and mucus-secreting. These cells lined the alveoli faithfully, evoking no stroma response and causing a minimal distortion of alveolar pattern. Mucus secretion was variable, but in large areas was very considerable. In some areas all traces of growth were lost, and instead the alveoli were filled with mucus and a large number of "foamy" histiocytes. Apart from these areas, where no absolutely intact alveolus was seen, the alveolar pattern was preserved. There was some emphysema and purulent bronchitis.

Lymph-nodes.—Two glands showed invasion by cells similar to those in the lung, and these cells retained an acinar pattern. In one gland the metastatic cells were becoming necrotic. The appearances in a mediastinal lymph-node are shown in Plate XIV*c*.

CASE 2.—A stevedore, aged 56 years, had had a chronic cough, productive of scanty sputum, ever since measles in infancy. He had no great disability, although the cough showed seasonal variations, until early July, 1946, when he had increased cough and sputum, occasional slight haemoptysis, and left-sided pleurisy. Chest radiographs in early and late July, 1946 (Plate XV*a* and *b*) showed increasing consolidation and possibly some collapse in the left lower lobe. Soon afterwards, he lost the chest pain, and the sputum diminished in amount, but dyspnoea and cough persisted, and when he returned to work in October he could only manage sedentary duties. He lost twenty pounds in weight in the eleven months before his admission to Redhill Hospital on June 22, 1947. On the day before admission he was working in his garden when he felt suddenly unwell, shivery, and more short of breath. He went to bed and soon afterwards experienced a return of the left-sided chest pain, which on the day of admission had extended to the left mammary and scapular regions.

On admission he showed dyspnoea, severe wasting, moderate dehydration and cyanosis, and clubbing of the fingers.. Temperature was 99° F. and pulse rate 110 per minute. The chest was emphysematous, with generally poor movements. The trachea and mediastinum were central. The whole left lower lobe was dull to percussion and in it the breath sounds were bronchial and distant; vocal resonance diminished and vocal fremitus was absent. At the lowest part of the left lower lobe the breath sounds were absent, and at the right base there was a small patch of bronchial breath sounds.

The other systems appeared normal, but blood pressure was only 65/50 mm. Hg.

Sputum was scanty, mucopurulent, and blood-stained; culture produced mixed organisms including haemolytic streptococci; no carcinoma cells were seen.

Blood count.—A leucocyte count on June 24, 1947, showed a total of 15,400 per c.mm. of blood (polymorph neutrophils 86 per cent, lymphocytes 10 per cent, monocytes 4 per cent).

Radiograph.—A chest radiograph on June 24, 1947 (Plate XV*c*), showed coarse patchy mottling in all zones of the right lung, with increased vascular pattern. In the left lung the upper zone was clear, but there was a hilar enlargement in the middle zone, and medial density; the lower zone was opaque (Dr. E. J. E. Topham's report).

Further course.—The patient was given a five-day course of sulphamezathine followed by a fifteen-day course of penicillin (750,000 units daily), but his sputum increased to 150 ml. daily and became frankly purulent with frequent blood-staining. At same time numerous rales appeared all over the right lower chest. Blood pressure was now 90/60 mm. Hg. A chest radiograph taken on July 11, 1947 (Plate XV*d*), was reported by Dr. Topham to show coarse mottling in all zones of the right lung, rather more

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extensive than on June 24. The upper zone of the left lung was clear, the middle and lower zones opaque. This lesion had also extended.

A leucocyte count on July 10, 1947, showed no significant change.

During the first eleven days the evening temperatures rose to between 90° and 100.2° F. Subsequently there was no pyrexia, and little change in the general condition until four weeks after admission, when a brief bout of diarrhoea led to rapid weakening and signs of cardiac failure such as pale cyanosis, bubbling lungs, and engorged neck veins (July 19, 1947). In spite of digitalis and oxygen-tent therapy, these signs increased, and oedema appeared in the legs and sacral region, but there was no fever. The patient died on July 22, 1947, almost exactly one year after the first onset of symptoms

Post-mortem findings (Dr. H. C. Moore)

The body was that of a middle-aged man with oedema of legs and sacrum.

Heart.—This was slightly larger than normal, with marked myocardial friability. There was sclerosis of the aortic valves, severe in the anterior cusp, and moderate atherosclerosis of the aorta and coronary arteries.

Lungs.—The right pleural cavity contained about 500 ml. of clear, straw-coloured fluid. The right lung was voluminous (weight 2,100 g.), and all the lobes showed gross oedema. The right lower lobe also had a patchy bronchopneumonia.

The left lung weighed 1,450 g. and its lower lobe was small and wholly consolidated, apparently at a late stage of grey hepatization. The parenchyma near the fissure was necrotic, and the inferior border of the left upper lobe contained an old abscess with inspissated pus.

The urinary bladder contained a papilloma. No metastases were seen.

Histology

In the lower lobes of both lungs there was an alveolar carcinoma (Plate XVI) somewhat similar to that found in Case 1. As may be seen on comparison of the plates, the cells in Case 2 showed much less mucus production than those in Case 1. As in Case 1, there was no increase in the tissue of the alveolar septa, though in some parts these septa were somewhat widened by congestion and oedema.

The myocardium showed fatty degeneration.

Discussion

Growths of the lungs confined to the alveoli are not often described, but they have an interest out of all proportion to their number. Some of the points of disagreement which have arisen in past discussion of these tumours are: (1) whether an alveolar origin of lung tumours is possible; (2) the nature of the parent cells, whether mesenchymal or epithelial; (3) whether the tumours are benign or malignant; (4) the possibility of an infective aetiology for them.

1. *Possibility of alveolar origin.*—Probably the strongest evidence in favour of an alveolar-cell origin for these tumours is to be found in animal pathology, where a disease of sheep (and rarely of horses) known as jaagsiekte (Cowdry, 1925) produces tumours almost identical in appearance with those found in alveolar growths of human lungs. This disease of sheep, which from its epidemic nature is evidently infective (Dungal, 1938), is found in such distant areas as South Africa (Cowdry and Marsh, 1927), Iceland (Dungal, 1938), Switzerland, Germany, and England. Evidence points to a virus aetiology, and the columnar and cuboidal epithelium, which lines many alveoli in infected animals, appears in each case to arise simultaneously in many centres in each lung. In spite of the vast extent of the disease no metastases, such as are found in bronchial carcinoma, occur in the infected sheep, who are killed by a "suffocating" illness. The alveolar growths seen in man (Gordon, 1920; Richardson, 1940; Neuberger and Geever, 1942) as a general rule have behaved in a similar way, preserving the alveolar septa and lining them with cubical or columnar cells; but metastases may occur in the human disease.

Despite the strong histological similarity of this ovine disease to "alveolar-cell" lung tumours in man, it has been stated that the latter tumours are not an entity and that all lung tumours are bronchogenic and arise from the basal-cell layers of the bronchial or bronchiolar epithelium (Arkin and Wagner, 1936; Frissell and Knox, 1937; Herbut, 1944). Herbut goes on to say that if cells arising from such a site are anaplastic or squamous they will destroy the alveolar septa and entirely permeate the alveolar spaces; but that if they are cuboidal or columnar they may line the alveolar septa. He points to the similarity between this cell arrangement in bronchial carcinomata and that seen in "alveolar carcinomata," and considers that in all cases there is one originating centre for the growths.

This view does not easily explain the almost entire lack of septal destruction seen in the two cases here reported and in many of those reported in the literature, nor does it account for similarity between human alveolar tumours and jaagsiekte. But disconnected nodules seen in many human cases may sometimes be explained by lymphatic or bronchial dissemination, and, as Frissell and Knox (1937) have pointed out, the intra-alveolar arrangement of columnar cells, whether from bronchial

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growths or from lung metastases, may in places simulate jaagsiekte.

Most important are the modern views of tumour formation recently expressed by Willis (1948), who states that tumours may arise from large as well as from small fields of tissue and may "enlarge not only by cellular proliferation, but also by progressive neoplastic conversion of tissue within those fields." He considers that an extensive origin is particularly apparent in diffuse, sometimes bilateral, lung cancers. This type of origin certainly appears to occur both in jaagsiekte and in the multicentric "alveolar" lung adenomata produced in mice by subcutaneous injection of dibenzanthracene (Grady and Stewart, 1940).

2. *The nature of the parent cell.*—Among those who hold that an alveolar origin of these human tumours is possible, there are two conflicting views as to the nature of the parent cell. The older view, which is still widely held, is that the cells lining the alveoli in these growths are epithelial, and arise from the alveolar walls (Bonne, 1939; Richardson, 1940; Dacie and Hoyle, 1942; Sims, 1943; Taft and Nickerson, 1944; Wood and Pierson, 1945; Ikeda, 1945). The opposed view is that there are no epithelial cells in the alveolar walls and that these carcinoma-like tumours arise from mesenchymal cells (Frissell and Knox, 1937). Neuberger and Geever (1942) quote Oppenheimer's observation that germ-layers are not absolutely specific and that mesenchymal cells may produce carcinoma-like tumours. Various suggestions, and therefore no one fully satisfactory explanation, have been brought forward to support an epithelial origin. Some feel that under certain conditions the alveolar lining may revert to its foetal condition; others stipulate epithelial cell "rests" in the alveolar linings as the starting points for these tumours (Bell, 1943).

Willis considers that bronchial surface epithelium and glands alike participate in formation of bronchial carcinomata, and that it is impossible to deduce the different specific origins from the structural variants of the growths. He refers to Richardson's case of multifocal "adenomatosis" of the lungs without attempting to ascribe it either to widespread neoplastic conversion of alveolar tissue or to relatively benign bronchial new growth extending into the alveoli. It is probably wiser to consider that the tissues of both of the terminal bronchioles and of the alveoli contribute to these diffuse neoplasms. A unifocal bronchiolar site of origin (Herbut, 1944) is not easy to fit in with growths having the structure and extent of these alveolar tumours, nor is it very helpful to consider with Sweany (1935) that they originate from "between the lower respiratory bronchi and the alveoli."

3. *The malignancy of the tumours.*—This appears to be very variable and has given rise to such terms as "carcinosis" (Bonne, 1939) and "multiple adenomatosis" (Sims, 1943) for alveolar tumours which do not produce metastases. This apparent lack of malignancy in about half the described cases (Neuberger and Geever, 1942) gives support to the view that they are a true entity. Writers quoting many cases (Neuberger and Geever, 1942; Ikeda, 1945) agree that of the 50 per cent of patients who do show metastases, only about a fifth show a distant dissemination of growth to such places as the brain (Geever and others, 1945); to kidneys, spleen, and liver (Hedinger, 1923); to ribs (Fried, 1925); to the pericardium; and to extrathoracic lymph glands. Possible confusion with bronchial carcinomata with a very minute primary might be responsible even for some of this small group. The majority of the metastases are into intrathoracic lymph nodes.

In connexion with metastases there are three special points of interest:

1. They occur from primary growths in which the cells line, but do not destroy the alveolar septa.

2. They show a histology identical with that of the parent growths.

3. They are often very limited and local, and occur late in the disease, whose course they do not noticeably influence; for example, small pleural metastases after twenty-one months in the case of Dacie and Hoyle (1942).

This last observation conflicts with the views of Frissell and Knox (1937), who regarded alveolar tumours as identical with bronchial adenocarcinomata, which they found consistently to be "among the most widely metastasizing of the lung tumours."

One case of alveolar tumour has been described (Uspensky, 1937) with a possible duration of eight years, and cases dying after two and a half years without metastases have been described (Bell, 1943; Wood and Pierson, 1945). In the case reported by Fishman and others (1945), the tumour was extensive in the lungs of a patient who survived so long (3 years) that it caused pulmonary atherosclerosis, chronic cor pulmonale, and right-sided heart failure; and yet there was no bronchial involvement and no metastasis.

4. *Possibility of infective origin.*—The strong similarity of the more "benign" types of alveolar

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tumour to the infective jaagsiekte prompts the suggestion that in man, also, the condition may be due to infection, a factor which in the past has been blamed for other types of neoplasm. Many writers have emphasized also the similarity to the alveolar-cell layers seen in association with virus pneumonias, bronchiectasis, chronic pulmonary tuberculosis, atelectasis, and chronic pleurisy (Dacie and Hoyle, 1942 ; Bell, 1943 ; Ikeda, 1945 ; Geever and others, 1943). But chronic congestion of the lungs, the action of certain salts (Young, 1928), and irritation by dusts (Davson, 1939), oils, and gases may lead to a similar cell proliferation, so that it is difficult to regard infection as the sole aetiological factor.

Some of the lungs containing tumour have been reported to show evidence of chronic inflammation in the alveolar septa, and also large areas of fibrosis, which appear to result from previous inflammation quite distinct from the terminal pneumonia which may occur in these cases (Taft and Nickerson, 1944). Cowdry (1925) considered that an inflammatory thickening of the alveolar septa always preceded the alveolar epithelialization in jaagsiekte, but this is not a constant finding in man (Bonne, 1939 ; Richardson, 1940).

Diagnosis

The diagnosis of alveolar tumours during life is difficult, since the clinical features and the radiographic appearances, while often unusual, are neither uniform nor truly distinctive ; and although the histological features are quite characteristic, and although they proved the nature of the condition in one lobe removed at operation six months before death (Wood and Pierson, 1945), they cannot be a diagnostic aid during life in the great majority of cases. The problem of diagnosis will be considered from clinical, radiological and pathological aspects.

Clinical features.—Neuberger and Geever (1942) have pointed out that in general behaviour many of these tumours have little to distinguish them from other lung growths. Most commonly the illness lasts less than a year and is marked by cough, haemoptyses, chest pain, increasing cyanosis, and dyspnoea. Pleural effusion often develops in association with alveolar growths, which also occasionally show predominant symptoms from metastases, such as those in the brain. Other cases may show a prolonged course (see the discussion of their malignancy above), and these tend to simulate chronic infective conditions as phthisis or unresolved pneumonia. At the other end of the scale are patients surviving only a few weeks (Hedinger, 1923) ; these often appear to die as a result of acute pneumonia.

In general the condition causes death by its "sheer extent" within the alveoli and not by its malignancy, as in the case of Dacie and Hoyle (1942) ; but it is evident that some cases grow much more rapidly than others. Metastasis may occur in either rapid- or slow-growing tumours, but must be more likely to occur in the former. The occurrence is equal in males and females ; the ages of the reported cases range from 17 to 89 years, but the majority are between 40 and 60.

Radiological appearances.—There are two morphological types of alveolar tumour ; one diffuse, causing a large homogeneous opacity, and the other multiple and nodular, with a varying number of well-defined nodules varying from miliary to cherry size. A combination of the two forms may be seen (Schuster, 1929), but the multiple, nodular type is most frequent. In any type the picture may be masked to some extent by the development of a pleural effusion or by concurrent pneumonia. The radiological findings, in consequence, may be as diverse and confusing as the clinical picture, simulating in different cases lobar pneumonia, bronchopneumonia, pulmonary metastases, pulmonary tuberculosis, and various kinds of pleural effusion. In six cases, with ages ranging from 17 to 76 years, Geever and others (1945) found that the radiographs suggested multiple metastases of malignant disease in two, pneumonia in two, phthisis in one, and bronchial carcinoma in one. One of the seeming pneumonias was rendered even more obscure by the development of atelectasis, bronchiectasis, and pleural effusion.

In conclusion it may be said that, while the radiographs may add false scents to the diagnostic trail, in a case in which they show many nodules of varied size in both lungs of a patient in whom no primary cancer can be found elsewhere, an alveolar growth should be considered. This diagnosis is made more likely if the case resembles intractable pneumonia or phthisis. If a lobar pneumonia-like shadow accompanies the nodular ones, then the possibility of an alveolar tumour becomes even stronger.

Pathological findings.—These may be divided into macroscopic and microscopic, and while the former may continue to deceive, the latter are always characteristic.

First and most important, the bronchial tree should be entirely free from tumour. The tumour tissue is firm, but may show areas of friability, necrosis, and even cavitation. It is yellow, pinkish, or grey, and in a number of cases is abundantly

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mucus-secreting. It is not surprising that ever since the first diffuse or "lobar" case was described by Musser in 1903 many of these cases have been thought at autopsy to have died in the "grey hepatization" stage of lobar pneumonia. Such was the first main appearance of our Case 2. Others have been thought to show "caseous pneumonia." In the more frequent multiple nodular type (first described in 1876 by Malassez) metastatic nodules, bronchopneumonia, or pulmonary tuberculosis may at first be suspected. Mucus secretion from the tumours is prominent in a number of the cases, computed by Ikeda (1945) at one third of all those described.

Microscopic examination in all cases shows the alveolar framework in an involved area to be generally preserved and fully lined by layers of cuboidal or columnar cells. These cells may be closely applied to the alveolar walls or the cell layer may be detached. As the cells multiply, papillary-like folds may project into the centres of the alveoli. Elsewhere individual cells may become shed off into the alveoli; in other cases the cells may lie more than one layer deep around the alveoli. The cells are not ciliated; they have, usually, pale, oval nuclei, and hyperchromatic and giant forms may also be seen. Mitotic figures naturally vary in number according to the degree of malignancy, from very few to fairly numerous. Mucus secreting cells may be present. Tumour cells are occasionally seen in the lung lymphatics, but the bronchial tree is not involved by growth. The alveolar walls often show chronic inflammatory thickenings, but in places may be broken down to a very limited extent. Necrotic areas may occur. The sputum may be sparse till near the end of the illness, when it often becomes purulent, but without the appearance in it of significant organisms. In the multiple nodular cases there is often no evident connexion between the growths in the clearly demarcated nodules, but all show the same histology. This uniformity, as has already been mentioned, extends to metastases when they occur.

SUMMARY

Two cases of alveolar lung tumour, in men aged 58 and 56 years, are described. One ran a course of nine months and showed a multiple nodular lesion in the lungs and small metastases in the hilar lymph glands. The other lived a year after initial pleuritic symptoms, and for a time showed a diffuse lobar lesion, with later a nodular lesion in the other lung. In this case a complicating right-sided bronchopneumonia made the diagnosis more difficult both during life and at necropsy; and at necropsy even the main alveolar growth was thought to be a lobar pneumonia in the stage of grey hepatization, a similarity which has been recorded in almost all the "diffuse" cases of alveolar tumour.

In neither case were the radiographic findings helpful; in the first they suggested a condition of confluent bronchopneumonia, and in the second they were at first those of partial lobar consolidation.

In both cases cough, purulent sputum, and leucocytosis suggested a diagnosis of lung inflammation, but in neither case was fever either an early or a prominent feature. Weakness, loss of weight, haemoptyses, and gradually progressive dyspnoea and cyanosis were features of both cases, and both died in cardiac failure with pulmonary oedema and venous congestion.

Some of the features were suggestive of new growth, but in spite of the long history in each case metastases could not be found during life, and only microscopic hilar-gland metastases were seen in one of the cases after death.

The growth does not involve the bronchi; and its histology, which shows the alveoli lined, but not destroyed, by layers of non-ciliated columnar cells, is characteristic. In some cases the condition appears to remain static for many months before it becomes malignant and then it may be only locally invasive, as in Case 1; in others (for example, Case 2) it may always remain non-invasive ("adenomatosis"), and these resemble the infective disease, jaagsiekte, seen in sheep.

The cause of alveolar tumours is unknown. It is known that not only in sheep but also in man certain infections and irritations will cause affected alveoli to become lined with cubical epithelium; but the alveolar tumours of man cannot be clearly separated, except in degree of their malignancy, from other lung carcinomata.

I am indebted to my colleague, Dr. L. I. M. Castleden, for notes on the first case which was under his care; also to Dr. J. Hamilton Paterson and Dr. H. C. Moore, who carried out the pathological investigations on these two cases. I am very grateful to Miss M. H. Shaw, who has prepared the photographs.

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(a) (b)

PLATE XIII.—(*a*). Case 1: radiograph of chest, Oct. 2, 1947. (*b*). Case 1: radiograph of chest, Nov. 4, 1947.

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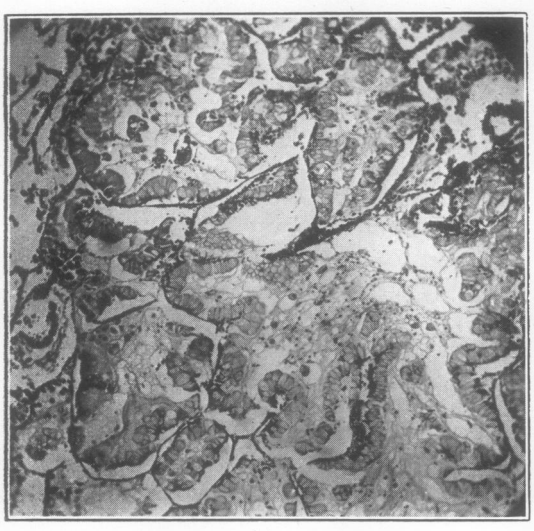
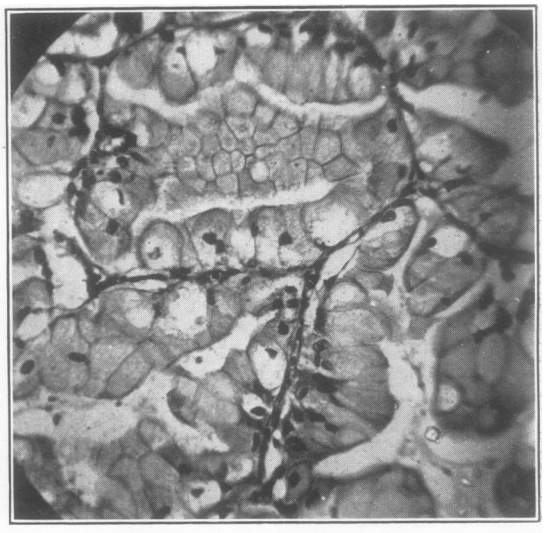
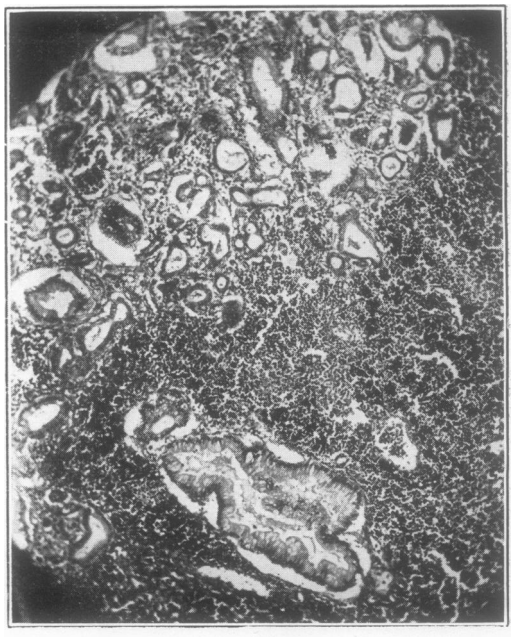


(a)



(b)



(c)

PLATE XIV.—Case 1. (*a*) Lung (x 120), showing the acinar arrangement of tall columnar mucus-secreting cells within the alveola. (*b*) The same (x 450). (*c*) Metastases in hilar lymph node (x 120).

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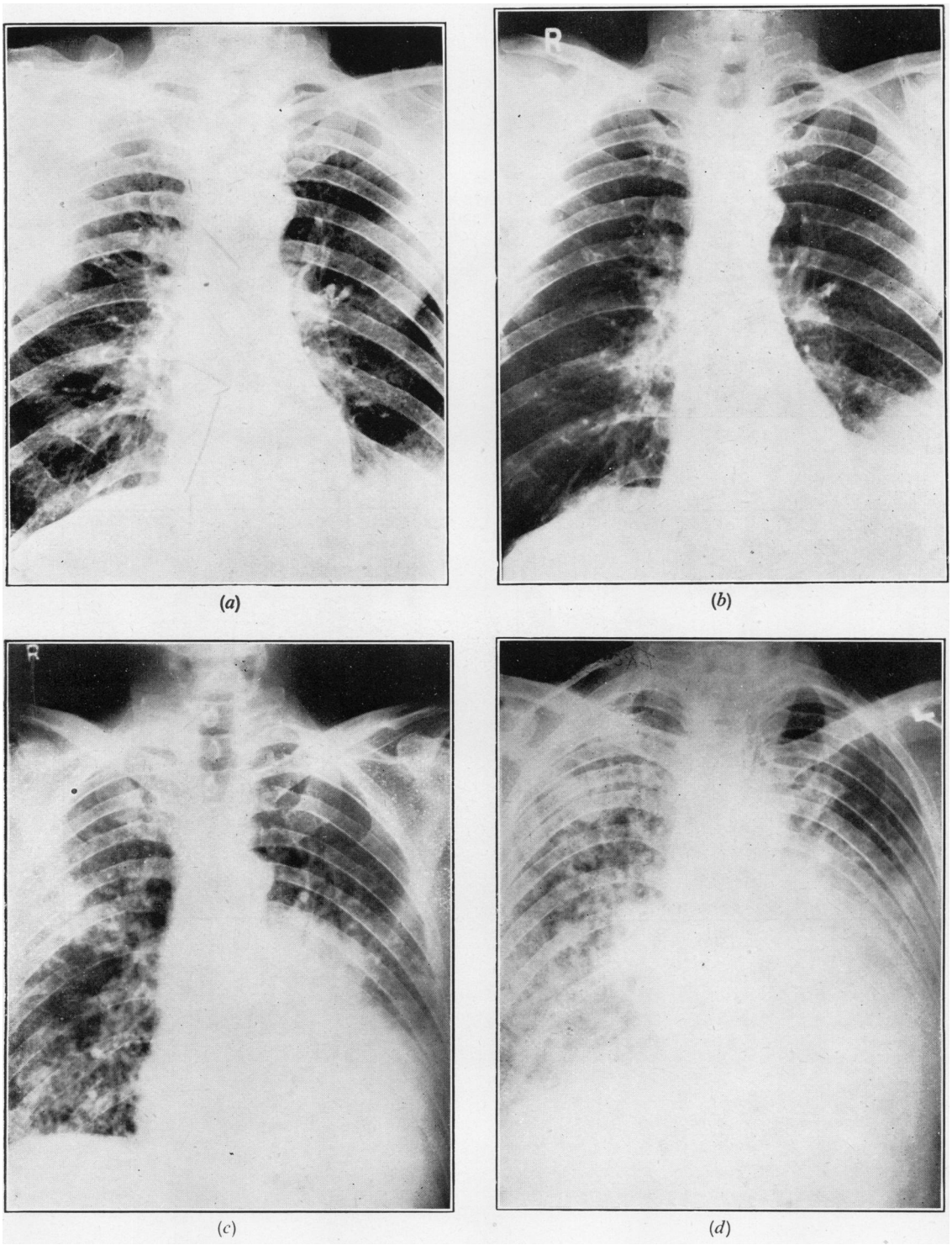

PLATE XV.—Case 2. (*a*) Radiograph of chest, July 6, 1946. (*b*) Radiograph of chest, July 30, 1946. (*c*) Radiograph of chest, June 23, 1947. (*d*) Radiograph of chest, July 10, 1947.

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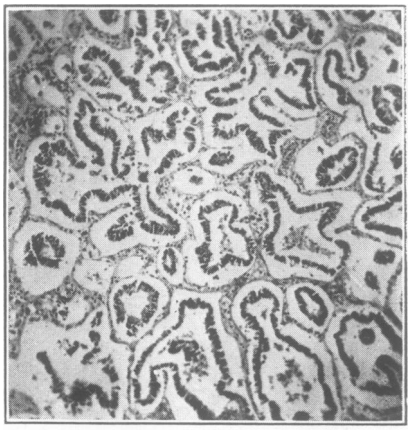
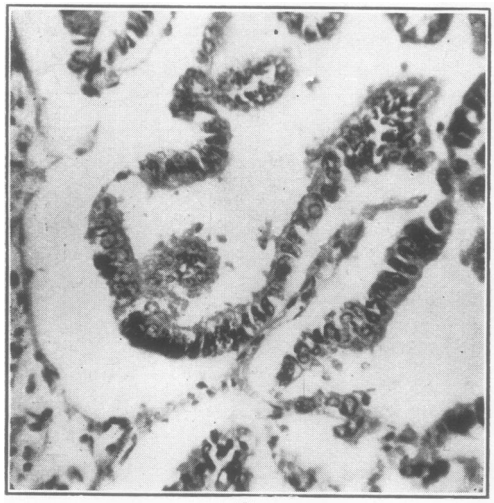
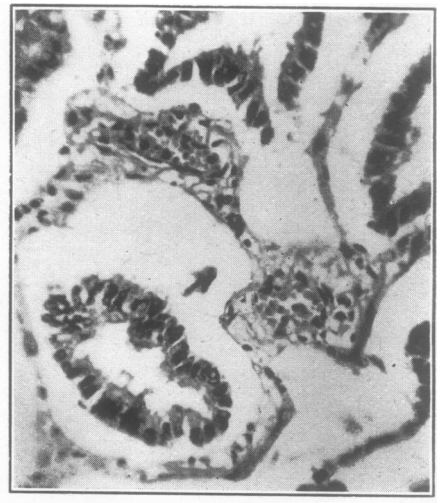


(a)

PLATE XVI.—Case 2. (*a*) Lung (x 120). (*b*) The same, showing the regular arrangement of the lining columnar cells and the large, pale, oval nuclei (x 450). (*c*) The same (x 450), showing the slightly congested and oedematous alveolar septa.



(b)



(c)

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