APPLICATIONS OF ASPIRATION LUNG BIOPSY

WITH SPECIAL REFERENCE TO

THE PATHOGENESIS OF THE RESOLUTION

OF

ACUTE AND CHRONIC LOBAR PNEUMONIA.

A Thesis

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by

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INTRODUCTION.

INTRODUCTION.

Lung biopsy is neither widely known nor practiced and it was only in 1949 that I first came across a paper on this subject. The title was: "Cellular analysis of the aspiration lung biopsy from normal and some pathological conditions by Z. Godlowski" (1949). The very term "lung biopsy" conjures up the picture of a needle being introduced into an air filled, very vascular structure where the bleeding of an injured vessel cannot readily be stopped, where the stage is set for air embolism and where tension pneumothorax may occur. It was with great surprise that I found that it was not only a relatively simple but also an apparently innocuous procedure. Unfortunately, at that time, there was no opportunity to use the method.

In 1950 I became the University Assistant at the New Somerset Hospital in Cape Town. Many of the cases admitted to the wards presented with chest pathology. Patients with pneumococcal lobar pneumonia were not infrequent and occasional cases did not resolve as expected but went on to become so-called chronic pneumonia. What happened when an acute lobar pneumonia went on to the chronic stage and why did this occur? It was suggested that I investigate this problem.

It was obvious from the meagre literature on chronic pneumonia that the mere compilation of data, such as the presence of coexisting pathology, would yield nothing new.

The problem had to be investigated from a new angle. Lung biopsy appeared to be the answer. This might give information, in the living patient, as to what was happening in the area where consolidation persisted.

It is an aphorism that before one can recognise the abnormal one must know the normal. Thus it was necessary to do biopsies on normal lungs and also on the lungs of cases of "normal" acute lobar pneumonia.

Various modifications of technique were adopted so that both bacteriology and histology could be studied. Biopsies were performed on the first few cases of pneumonia shortly after admission. Their illness was in the acute stage and showed the expected pathological picture. There was some delay with one case and biopsy was performed on the fourth day in hospital after adequate sulphonamide and penicillin therapy; the physical signs were those of dullness, bronchial breathing and medium crepitations. The histology in this case was quite different from the expected grey hepatisation described in the text books. This opened up a whole new field of investigation and by means of biopsies at different stages of resolution and by serial biopsies one was able to show that the cellular changes fell into a definite pattern.

Meanwhile a few cases went on to the chronic stage and it was possible to show at which stage resolution stopped and appeared to be in a state of "suspended animation".

From this latter work there developed a method by which it was hoped that resolution might be accelerated.

During the period when these biopsies were being performed it became increasingly obvious that there were many lung lesions, other than pneumonia, where one would like to know what pathological process was actually taking place. In this way a series of cases developed where biopsy was done for diagnostic purposes. Most of these cases were unusual types of lung consolidation. In the past biopsies had been frequently performed for the diagnosis of peripheral rounded pulmonary masses but there were few reports of its use in the diagnosis of more diffuse lesions.

In this way the investigation developed from a consideration of the etiology of chronic pneumonia to embrace the resolution of the ordinary acute lobar pneumonia after treatment and also the etiology of some obscure pulmonary consolidations.

The cases are numbered according to the order in which they were done so that one can obtain an idea of whether any given case was done early or late in the series.

In all, ninety four lung biopsies were done on seventy three patients. These were divided into groups:

Group	Type of Case	No. of Patients	Total No. of Biopsies	No. of Biopsies done after Death
Group I	Normal lungs	13	13	3
Group II	Diagnostic Cases	24	29	3
Group III	Acute pneumonia with normal resolution.	21	27	0
Group IV	Chronic lobar pneumonia	13	20	0

In addition in 4 biopsies the cells were of hepatic origin, and in 1 biopsy (done after death) the cells were of splenic origin. These will be described fully under the section on complications.

In the whole series only 7 biopsies were done after death.

Table 1 and Table 2 show the sex, race and age distributions of the 73 patients.

Table 1.

Sex and Race Distribution of the Seventy Three Patients.

Race	Sex	Number of Patients
Coloured (C)	Male	37
Coloured (C)	Female	14
Native (N)	Male	11
Native (N)	Female	7
Moslem (M)	Male	2
Moslem (M)	Female	0
Indian (I)	Male	1
Indian (I)	Female	0
European (E)	Male	1
European (E)	Female	0

The term "Native" is used to denote an African usually of the Bantu race.

Table 2.

Age Distribution of the Seventy Three Patients.

Age	Number of Patients
0- 9 years.	2
10-19 years.	9
20-29 years.	23
30-39 years.	12
40-49 years.	16
50-59 years.	8
60-69 years.	1
70-79 years.	1
80-89 years.	1

The New Somerset Hospital, where most of the cases were done, is exclusively for non-Europeans. This accounts for the almost absence of European cases. It is unlikely that this selection of material will in any way prejudice against the application of the results of this investigation to Europeans as it is well known that the Cape Coloured have similar illnesses and react to disease in the same way as the Europeans.

It will be shown that, as far as pneumonia is concerned, the African appears to react in no way differently from the Cape Coloured.

The oldest living patient to be biopsied was Case 5, a coloured woman of 74 years of age (the 82 year old case was done after death). Two biopsies were performed on her without any untoward events except for slight blood streaking of the sputum for a few hours after the first biopsy. The youngest patient was Case 68, a coloured male infant of 4 months. He showed no untoward reaction to biopsy.

It will be noted that quite a wide variety of ages and races, and members of both sexes have been biopsied.

SECTION I

ASPIRATION LUNG BIOPSY.

ASPIRATION LUNG BIOPSY.

HISTORY AND A REVIEW OF THE LITERATURE.

In 1883 Leyden did the first appiration lung biopsies on three cases of pneumonia and he isolated organisms from one of these patients. In the same year Gunther did a pleural aspiration, found none of the suspected pus but punctured the lung and found diplococci in the material obtained. There seems some disagreement on the work of Talamon (also in 1883) who was quoted by Thomas and Barker (1920) as having performed postmortem lung punctures in nine cases of pneumonia finding pneumococci in smears of the exudate in eight; Smeall (1948) stated that Talamon punctured the consolidated lungs in eight cases of pneumonia during life and obtained in one case a pure culture of diplococci.

In 1886 Menetrier made a diagnosis of carcinoma of the lung by microscopic examination of tissue aspirated during the puncture of an infected pulmonary tumour.

For over 50 years these were the two main applications of aspiration lung biopsy, namely the culture of organisms directly from pneumonic lungs and the diagnosis of pulmonary tumours.

Patella (1888) did punctures before and after the crisis in lobar pneumonia. Before the crisis the exudate contained

a large number of pneumococci, after the crisis inconstant results were obtained but during the hours immediately following defervescence he was able to recover viable pneumococci.

Hellendall (1899) diagnosed two cases of sarcoma of the lung by antemortem lung biopsy. In both cases the diagnosis was confirmed at postmortem.

Fränkel (1896), Sokolowsky (1898) and Jacobson (1899) all mentioned lung puncture in discussions on tumours of the thoracic cavity.

Tchistobitch (1904) inoculated the exudate from lung puncture into rabbits and mice and was convinced that even after the crisis one could obtain viable virulent diplococci from the lung.

Horder in 1909 rediscovered lung biopsy. His indications for biopsy were: in any case yielding signs of consolidation of the lung in which careful examination of the sputum failed to reveal the nature of the disease; in abscesses to obtain a specimen of pus from the actual seat of suppuration; and in bronchiectasis for the same reason. He did 14 cases of which he quoted six case histories - an abscess of the lung following a perforated duodenal ulcer, an abscess of the lung following an incomplete abortion, a pneumonia following a generalised peritonitis, a staphylococcus aureus pneumonia, an erysipelas with bronchopneumonia, and lastly a most interesting case of chronic pneumonia which will be discussed in more detail

under the section dealing with this subject.

His work was favourably commented on in an annotation in the same issue of the Lancet.

Colby in the same year reported 12 cases of unresolved pneumonia treated by lung puncture with "good results".

Eyre in 1910 examined the "lung juice" from 164 cases of bronchopneumonia. Most of his cases were done after death although a few cases were biopsied during life by means of an aspirating needle.

Rosenow (1911) continued the work of Patella and showed that, while positive cultures were obtained from pneumonic lungs throughout the course, the percentage of positive results were much higher in the early stages in favourable cases and tended to diminish in these cases as the crisis was approached. On the other hand he found that positive cultures persisted until death in unfavourable cases.

Larger series of lung punctures done on living patients were now described. Lister (1916) reported 50 per cent of positive cultures in 200 cases of pneumonia. Many investigators were still cautious, and Abrahams in his paper on purulent bronchitis in 1917 did only one lung puncture and that was by accident during an attempted pleural aspiration. Clough (1917) obtained organisms from lung puncture and noted that in most of the cases the cultures were pure. Netter in the 1918 influenza epidemic recovered the influenza bacillus in four

out of eight lung punctures. Nuzum et al. in the same epidemic did 36 lung punctures but failed to find influenza bacilli, though pneumococci were recovered 11 times.

Thomas and Parker (1920) stated that "antemortem lung puncture is a relatively infrequent procedure". They then went on to review the literature. The technique that they used was in many ways very similar to that used today. In a series of 73 cases they showed that the death of the organisms in the lung did not occur, in every case, at the time of the crisis, but might occur several days before or after the crisis. Positive cultures were obtained on every day of the disease including the period of critical fall in temperature and twice after the temperature had reached normal. On the other hand negative cultures were obtained as long as 4 days before the crisis. Such findings, which confirmed the work of Patella and Rosenow, did much to upset the theory that there was a sudden destruction of organisms at the time of the crisis.

Ellis, of the Memorial Hospital of New York, in 1922 made an antemortem diagnosis of carcinoma of the lung from the preparation of material found clinging to an aspirating needle which had been used for a thoracentesis. This was the beginning of what was later to become one of the largest series of lung biopsies for the diagnosis of pulmonary tumours.

Lyon (1922) adopted a very conservative attitude towards lung biopsy. He inserted a needle into the chest only if

fluid was suspected; if no fluid was present, he assumed that the needle had entered the lung and he would then wash out the tip of the needle in sterile broth. In a series of 20 cases of lobar pneumonia (two done after death) he obtained a positive culture in 10 cases, and in 18 cases of bronchopneumonia again 50 per cent were positive. No mention was made of the stage of the pneumonia at which the punctures were done.

Glynn and Digby (1923) obtained 37.5 per cent positive cultures from 44 cases of lobar pneumonia during life and concluded that "the examination of the lung juice in pneumonia is a valuable but neglected aid to exact bacteriological diagnosis, especially in children".

Cecil et al. (1927) did not do lung punctures on living patients but frequently employed the procedure after death for the purpose of making a bacteriological diagnosis, or for controlling cultures previously made from the sputum.

D. Stewart (1930) obtained positive cultures in 76 per cent of 17 cases of lobar pneumonia. He concluded that the method was of value in those cases without sputum in which culture and typing was desired.

Ellis and Martin (1930) recorded a large series of 65 malignant neoplasms proved by needle puncture and aspiration. They described the technique in detail. Only two of their cases were of pulmonary carcinoma but they established aspiration biopsy as a diagnostic method. By 1934 they had collected 41 cases of aspirated pulmonary tumours.

Alston and Stewart (1930) did lung punctures to ascertain the type of pneumococcus in those cases of lobar pneumonia without sputum.

Sharp in 1931, using the method of Martin and Ellis, successfully aspirated a lung tumour and diagnosed it as a carcinoma. This case was done at the Memorial Hospital which was to become one of the centres of aspiration biopsy. Fernandez and Tobias (1931) diagnosed a case in a similar manner.

Cruickshank in the same year obtained 50 per cent of positive cultures in a series of lobar pneumonia.

Shibley and Rogers (1932) did lung punctures in clear cut cases of lobar pneumonia, and inserted the needle into the area of maximum consolidation. The material was cultured at once in glucose broth and upon blood agar plates. Smears were studied but these were only stained by Grams's method and by Hiss' capsule stain. In 10 postmortem cases all showed positive cultures; ten live patients showed six positive and four negatives and of the latter all were in crisis or lysis at the time of puncture.

F.W. Stewart in 1933 reported the results of 2500 aspiration biopsies on tumours. The method was applied to a very wide field and material was obtained from lymph nodes, antra, jaw bones, parotid glands, breast lumps, thyroid, liver, spleen, kidney region (for recurrence in nephrectomy scars), prostate, testes, bone lesions and finally there were 41 cases of suspected lung tumours. He used the method of Martin and Ellis

In 1934 Martin and Ellis published their new series of 41 lung biopsies on tumours and once more described their technique in detail.

Curphey in 1935 applied lung biopsy to a new field of investigation. Much experimental work on animals had been done and autopsy material had been examined in human cases to determine the means by which the resolution of lobar pneumonia was brought about. Curphey was the first investigator to examine biopsy material from cases of lobar pneumonia from a histological point of view. Robertson in 1938 wrote: "Curphey has bridged the gap between our experimental observations and the postmortem studies by means of biopsies performed on the lungs of patients during the course of lobar pneumonia. He showed that the celular reactions which we have observed in the resolving lung after death occur during recovery." Unfortunately an abstract of Curphey's paper, which will be quoted in full later, gave little indication of the scope of his work.

Martin and F. Stewart (1936) discussed advantages and limitations of aspiration biopsy without any special reference to the lungs.

Greenwald et al., in discussing chronic pneumonia in infants in 1936, considered that these might have been cases of lipoid pneumonia. They rather wistfully suggested that

"lung puncture might be tried but whether consistent and sufficient information could be obtained to justify its use is questionable". The answer to their query was to be given by Nathanson et al. in 1943.

Sappington and Favorite in 1936 supplied a much nedded review on lung puncture in lobar pneumonia. They were able to collect more than 2000 cases in which various investigators had performed puncture of the lung for bacteriological purposes. Most of these workers have been quoted above but in addition they referred to a personal communication from J.G.M. Bullowa who used lung puncture routinely on 1467 cases in a large pneumonia service at the Harlem Hospital and obtained positive cultures in 35 per cent. This is probably the largest series of lung biopsies ever to have been performed. It is a pity that it was never written up for publication. Sappington and Favorite did 68 punctures on 60 cases (on one case a positive culture was obtained only on the third puncture) and obtained positive cultures in 54 cases, that is in 90 per cent of the cases the organism was isolated. In every case the culture was actually or practically pure. In 25 cases in which pneumococci from both lung and sputum cultures were typed, there was 100 per cent agreement. In 22 of the cases sputum was not available and it was in these that the lung biopsy cultures were so valuable in determining the type of antiserum which should be given.

Lavalle in 1937 rpported lung punctures done in Buenos

Aires. Needle puncture was used to "cure" tuberculosis. He stated bhat needle puncture of the "nucleus" in the lung released autovaccines and haptens into the blood stream and these favoured cure of the tuberculosis. He reported 100 cases with beneficial results. No details were given and one must take his conclusions on their face value.

Lanari and Pavlovsky in the same year, and also from Buenos Aires, reported their results in the diagnosis of carcinoma of the lung. They obtained 13 positive punctures in 24 suspected cases and recommended the method.

By 1938 the Memorial Hospital records showed 130 cases of clinical primary carcinoma of the lungs of which 56 had been proved by lung aspiration biopsy. These cases were reviewed by Craver and Binkley who came to the conclusion that aspiration biopsy of selected tumours of the lung was a valuable and relatively safe diagnostic procedure. It was particularly helpful where bronchoscopy failed to yield useful information.

Reimann, in his book "The Pneumonias" (1938), stated that "material for examination was obtained directly from the involved area of the lung by German and French clinicians of the past century, but the method fell into disuse until its recent revival".

Blady in 1939 aspirated tumours of the lung in the region of the hilum, in mediastinal and juxtacardiac situations and

in the anterior and posterior mediastinum. He introduced his needle under roentgenological guidance and was able to aspirate tumours as small as 5 cm. in diameter. This was certainly refined lung biopsy.

Craver again reviewed cases aspirated in the Memorial Hospital up to 1940. Between 1935 and 1939 aspiration biopsy accounted for 51.6 per cent of all cases of carcinoma of the lung histologically proved.

Cases off the beaten track, diagnosed by van Ordstrand and Lambert in 1941 using aspiration lung biopsy were unresolved pneumonia and a fuso-spirochaetal lung abscess. They showed cases diagnosed as aneurysm, tuberculosis, interlobar empyema and interlobar effusion to be bronchogenic carcinoma and confirmed cases of secondaries from a breast carcinoma (which had been removed 6 years previously), a superior sulcus tumour and a suspected upper lobe carcinoma. One feels that they must have been very certain in the case of suppected aneurysm that the diagnosis was incorrect. No details of the cases were given but it appeared that the diagnosis of the unresolved pneumonia was made on the culture of a Type III pneumococcus, but no account of the histology was given.

Faber, Carpenter and Pellicano (1942) suspected a case to be one of lipoid pneumonia and on aspiration obtained 3 c.c. of blood tinged with an oily fluid. On standing this settled into a definite layer of oil over a layer of clotted blood. They felt that this confirmed the diagnosis.

A much more convincing series of cases of suspected lipoid pneumonia was reported by Nathanson et al. in 1943. Aspiration biopsies were done on 10 patients who had been taking liquid paraffin for long periods and in some there was a lesion involving the ninth and tenth cranial nerves. X-ray showed infiltration of the lower lobes of both lungs, and particularly the mesial portion of the right lung adjacent to the heart was the earliest site of involvement. Repeated biopsies were done to show the stages of the lesion and a positive diagnosis was made on the presence of lipoid filled macrophages which were shown to finally disintegrate releasing the oil which then became entrapped in a meshwork of fibrous tissue. Positive results were obtained in five cases. They concluded that any case taking liquid paraffin for long periods especially if there was dysphagia or dysarthria or if the case was bedridden, was a candidate for lipoid pneumonia. This was one of the few papers apart from those where carcinoma was suspected where the histology of smears of the biopsy material was examined.

Wilson (1945) reported his experience with aspiration biopsy in Australia but there was litle reference to cases of lung pathology.

Scadding in his paper on pneumonia in "The Practitioner" (1946) mentioned that lung puncture was justifiable only for special purposes.

In 1949 Gladhill, Spriggs and Binford reported 75 lung biopsies for the diagnosis of tumours of the lung.

Finally in 1949 Godlowski did 75 lung aspiration biopsies on 75 normal men and women and examined histologically the material obtained. He gave an excellent account of the morphology of the normal cells of the lung. He showed that the lung of the heavy tobacco smoker contained many more macrophages than that of the non-smoker. He also did biopsies on 10 cases with various pathological conditions but gave no details of his findings.

Thus it was possible to follow lung biopsy from the first few attempts by French, German and Italian investigators to its fairly frequent use in the diagnosis of lung tumours and in the isolation of organisms in cases of pneumonia; finally the method was used in the diagnosis of lipoid pneumonia. Godlowski supplied the histology of the normal lung biopsy and with this paper the pattern was almost complete. It was obvious how few pathologists and clinicians have made use of lung biopsy in the 70 years that it has been in existence.

This present paper contributes the histology of acute and chronic lobar pneumonia and also illustrates the use of lung biopsy in the diagnosis of many a puzzling area of consolidation in which carcinoma does not enter into the differential diagnosis. It is felt that lung biopsy is a

useful and much neglected research and diagnostic weapon.

TECHNIQUE.

The method of doing an aspiration lung biopsy has varied only in minor details from one investigator to another. In essence, a needle was inserted into the lung, suction was applied by means of a syringe and the material obtained dealt with according to the purpose of that particular biopsy.

There was little information to be obtained on the methods used by the very early investigators such as Leyden, Talamon, Menetrier, Patella, Hellendall and Tchistovitch but it would appear that they employed the same large trochars that they used for thoracentesis.

Horder in 1909 advised a "good-sized" needle attached to a syringe. The needle was inserted into the lung, the piston withdrawn about an inch so as to maintain suction, and the needle then withdrawn. As the needle point left the chest wall two or three drops of bloody material spurted into the barrel of the syringe. He made smears of the material and also inoculated an agar slope. Although, he stated that the purpose of the investigation might be the cytological rather than the bacteriological examination, there was no comment on any of the cells seen in the smear preparations.

Eyre (1910) simply stated that he used an ordinary

aspirating needle.

Thomas and Parker (1920) used a very similar technique to Horder. They produced local anaesthesia using 0.5 per cent procaine and then introduced a No. 16 needle into the lung to a depth of about an inch. Negative pressure was maintained using a 10 c.c. or 20 c.c. syringe and the needle slowly withdrawn. A few drops of bloody fluid were obtained and this material was cultured in broth and on blood agar and a film made on a slide. The direct smear was discarded as yielding little of value. This is very surprising as most of the information in the present paper depends on this smear preparation.

Lyon (1922) in cases of a "dry tap" washed out the tip of the aspirating needle in a tube of sterile broth and was gratified to find that he not infrequently "obtained a culture direct from the seat of the pathologic process".

Martin and Ellis (1930, 1934) very carefully described their technique in detail. Iodine was used as theskin antiseptic; one per cent novocaine was infiltrated into the skin and then a stab incision made with a No. 11 Bard Parker blade to facilitate the insertion of the aspirating needle. A new, sharp 18-gauge needle (5-10cm. in length) attached to a 20 c.c. syringe was inserted into the lung and into the tumour (a difference in the consistency of the tumour indicated when it had been entered). The piston of the syringe was then partly withdrawn and care being taken to maintain the

suction, the needle was inserted further then withdrawn to its original situation and inserted again in another direction and again withdrawn. The plunger was then released, the syringe detached and the needle now fully withdrawn. This was to prevent material splashing into the syringe and making collection difficult. The syringe was then filled with air, reattached to the needle and used to expel the aspirated material from the needle. The biopsy material was made into a smear preparation and stained or the small particles were collected and passed through the usual stages to the final paraffin section. A quick paraffin method of preparation was described. Sharp (1931) used the above method in the successful aspiration of a lung tumour.

Bullowa (1936), in his very large series of pneumonias, used a very fine, 22 gauge, flexible, stainless steel needle 10cm. in length with a medium point and a 35 degree bevel. In his syringe he placed 3-4 c.c. of blood broth so that the withdrawn material mixed immediately with the culture medium.

Sappington and Favorite (1936) used alcohol as the skin antiseptic. No skin anaesthetic was used and the "patients made little or no complaint". A No. 20 needle attached to a 5 c.c. syringe was inserted into the chest for 5-6 cm. and then strong suction made on withdrawal. Bloody material, varying from a drop to as much as 1 c.c. was obtained and washed onto an agar slope using plain broth.

Reimann in "The Pneumonias" (1938) recommended the use of local anaesthetic and the "suction on withdrawal method". The needle was a No. 18 or No. 20. The material was in part smeared onto a slide and the rest injected into a mouse.

Craver and Binkley working in the Memorial Hospital in 1938 naturally adopted the method of Martin ad Ellis of the same institution. Morphine sulphate (one-sixth grain) was given 30 minutes before the biopsy ; the patient was placed in the sitting position. The needle with syringe attached was inserted into the lung and intermittent suction applied. If blood or air entered the syringe, it was disconnected from the needle, emptied and the needle withdrawn slightly and moved in at a slightly different angle. If the patient coughed or complained of pain he was "reassured and quieted". Once the tumour was entered the procedure was as described by Martin and Ellis. The majority of their cases were done as outpatients who returned to their homes by taxi or by subway within an hour after aspiration.

Blady (1939) when he aspirated tumours near the heart and great vessels inserted the needle under radiological guidance. He had a special rotating stool with foot rests and hand grips so that the arms could be kept above the head. He used a needle with a stylette, and he attached the syringe when the tumour was entered.

Craver in his 1940 series used an 18 gauge needle because "a thicker one would appear to offer too much trauma to vessels

and bronchi and with a thinner one there was the danger of it breaking off".

Lambert and van Ordstrand (1941) preferred a 15 gauge needle, used sedation before aspiration, and placed their patients in the sitting postion. The material obtained was expelled into formaldehyde and then centrifuged and paraffin sectioned.

Wrenn, Feder and Anderson described a fearsome weapon for doing aspiration biopsy (1942). This instrument had a sharp serrated edge and was fitted with a stylette. It was used to obtain pieces of tissue suitable for section but was obviously not suitable for lung aspirations. A useful technical point was that there was a lock on the syringe so that it could be kept at full suction.

Faber et al. (1942) inserted a 16 gauge needle into a patient with suspected lipoid pneumonia. They obtained three cubic centimetres of oily blood, possibly a record in quantity if not in quality.

Nathanson et al. (1943) used a very peculiar method. A 20 c.c. syringe with a spinal tap type needle was employed. The plunger was withdrawn to 5 c.c. and the needle then inserted through the skin to a depth of 9-10cm. An attempt was then made to withdraw the plunger, so as to be sure that the tip of the needle was not in a vessel or bronchus, and then the 5 c.c. of air was ejected forcibly into the lung "so

as to remove any tissue that may have entered the needle in its passage through the chest wall". The position of the needle was then changed slightly either by withdrawing or altering the needle's direction and the plunger then slowly withdrawn with aspiration of as much material as possible. Finally theneedle was withdrawn and the contents smeared onto slides. This injecting of air into the lung "forcibly" simply to clear the needle seemed an unnecessary and very dangerous procedure and could have been avoided by using a stylette.

Gladhill et al. (1949) used morphine as a premedication, had the skin prepared as for a surgical operation, used local anaesthetic and then a small scalpel cut. Their needle was 18 gauge and they followed the method that Blady described in 1939.

Godlowski (1949) at first used morphine premedication but found that in some cases the morphine upset them more than the lung biopsy and he soon abandoned its use. He emphasised the importance of careful and thorough infiltration with local anaesthetic (2 per cent procaine hydrochloride) not only of the skin and chest wall but of the parietal and visceral pleura and the adjacent parts of the lung tissue itself. In this way he hoped to minimise the danger of vasovagal syncope. Five to ten minutes later the chest was screened as a control. He used the "two needle method" so as to be quite sure that only cells from the lung itself were obtained. One short needle of large calibre with stylette

in place was pushed through the whole chest wall and both pleurae, and, as soon as the needle appeared in the lung itself (the whole procedure being controlled by X-ray), the stylette was removed and a second needle much longer and thinner than the first and also with a stylette was passed through the first needle. As soon as the second needle appeared in the lung the stylette was withdrawn and a 20 c.c. syringe was attached. By making an intense, sharp aspiration the second needle was pushed into the lung at times as depp as 20cm. and moved in and out sweral times to the tip of the first needle. This was certainly a heroic procedure. The patient must stop breathing during the actual biopsy in order to avoid laceration of the lung by respiratory movements. The aspiration was stopped at the point where the second needle on the way out approached the tip of the first one; the second needle was then slowly drawn through the first one and its contents spread onto a slide. The first needle was removed and the puncture area dressed. In a few cases an incision was made in the skin and the two needle method used through the wound. After a week a routine X-ray chest was done.

Klassen et al. (1949) carried lung biopsy to its logical conclusion. Under positive pressure cyclopropane-oxygen anaesthesia, an 8cm. incision was made over the 4th inter-space lateral to the sternum. The pleura was opened and under positive pressure by the anaesthetist the junction of the upper, middle and lower lobes presented through the wound. A wedge-shaped fragment of the lobe was removed between clamps

and the area sutured. In one case that came to autopsy the biopsy site showed good repair. Fifty cases of diffuse pulmonary lesions were done by this method without serious complications. They gave as examples of their cases: Boeck's sarcoid, fibrocaseous tuberculosis, metastases from a thyroid carcinoma, an adenocarcinoma of the breast and a melanoma. No cases of chronic pneumonia were operated on! This is a far cry from the very simple aspiration lung biopsy and has been included for the sake of completeness.

TECHNIQUE USED IN THE PRESENT SERIES:

It was necessary to evolve a method which was simple, as safe as possible, and which would yield material both for histology and bacteriology. It was essential that the technique would not be such as to increase the burden of an overworked and understaffed radiology department.

No premedication was used except in Case 68, an infant of 4 months who received half a grain of nembutal thirty minutes beforehand. The situation of the biopsy depended on the site of the pathology and, as shown in Table 3, no lobe of the lung was exempt. At first the position of the patient was considered immaterial but after the death of Case 34, all patients were placed in the horizontal position. This position was adopted on the purely theoretical assumption that if air embolism did occur the air was more likely to go to limbs than to the brain. Craver (1940) after having had two

cases of possibly air embolism did all his patients in the recumbent position and had no further trouble.

The skin was cleansed with spirits and then with iodine. About 4 c.c. of 2 per cent planocaine was used to infiltrate the skin, underlying muscle, pleura and the superficial lung tissue itself. For the deep infiltration a 5 cm. No. 20 needle was used. In one case as the result of an ill fitting needle a pneumothorax occured during the infiltration and the biopsy had to be abandoned; from then onwards only B-D Lok-Syringes and B-D needles were used.

A small stab incision was made in the skin using a No 11 Bard Parker blade; this prevented contamination by skin cells and also facilitated the introduction of the needle.

At this stage the patient was warned that he was now going to be "given the injection" and that after the injection he might cough up some blood. If he did then he was not to worry as that was "a good sign"; if he did not it did not matter. This warning was necessary as patients had a great fear of coughing up blood and if a haemoptysis occurred they became very distressed. They were much less agitated if they had been warned of the possibility beforehand.

The biopsy needle (18 gauge, 9cm. in length with a short bevel and a well fitting stylette) was then introduced through the skin incision and into the lung. Very often the resistance of the visceral pleura could be felt and the needle then easily penetrated into the lung which had a soft

spongy consistency. The stylette was then removed and a 20 c.c. B-D Lok-Syringe attached. One had to take great care that the tip of the needle was actually in the lung; if the stylette was removed with the needle tip in the pleural cavity an immediate pneumothorax naturally resulted. It seemed certain that in some cases the visceral pleura "gave way" in front of the needle point and there resulted a false impression of the depth to which the needle had been inserted. Under these circumstances even though the needle may have been inserted to a depth more than could be accounted for by the thickness of the chest wall, a pneumothorax might result when the stylette was withdrawn. (See Fig. 1).

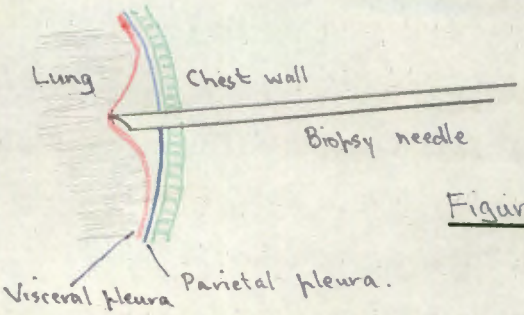


Figure 1.

After the attachment of the syringe, which was well locked in position, the plunger was withdrawn to the 20 c.c. mark. In some cases this simple procedure caused blood to apear in the syringe and in these it was best to withdraw the syringe and needleand use the material obtained. In most cases simple withdrawal of the plunger gave no obvious result. With suction maintained the needle was then inserted 2-4cm. further into the lung and then withdrawn to its original position. In the first few biopsies the needle was then inserted for a second time in another direction but this

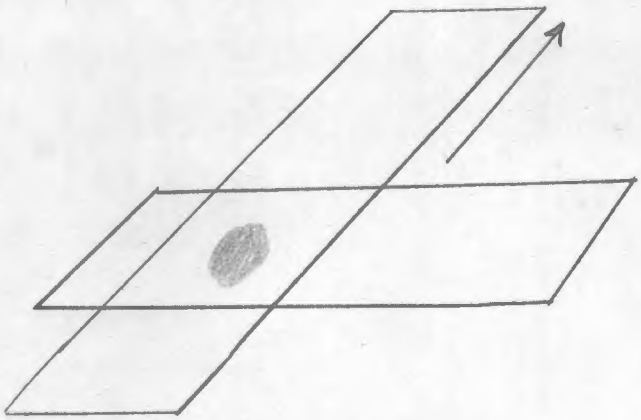
second insertion was soon abandoned as it was thought to be the probable cause of a high percentage of haemoptyses; sufficient material could be obtained from one insertion. The negative pressure was released and the needle with syringe attached withdrawn. The procedure is illustrated in Figures 2 to 7.

The actual method of doing the biopsy may be varied according to the circumstances of the particular case. In some cases where there was a little fluid present or a very shallow pneumothorax the needle was inserted deeply so as to avoid the fluid or air and then the syringe was attached, suction applied and the needle withdrawn about 2-3 cm. The suction was then released and the syringe and needle withdrawn. Probably the material obtained by this method was not as plentiful as by the method of suction and pushing the needle inwards. In the one infant in the series an intramuscular needle with a 5 c.c. syringe was used for the biopsy and good material was obtained. In one case (Case 62-1) where fluid was suspected the needle was inserted already attached to syringe and aspirations were done at deeper and deeper levels - no fluid was found but fairly numerous pulmonary cells were obtained. In these ways the method could be altered but the best results were usually obtained using the orthodox procedure.

After the syringe and needle had been withdrawn a drop of material was expelled onto a non-sterile glass slide, care being taken not to touch the slide with the needle tip. The

procedure that followed dppended on the amount of material obtained. If sufficient fluid was present in the needle a drop was placed onto a blood agar plate, a drop onto a slope of Lowenstein medium in a small capped bottle, and the rest into a small capped bottle of serum broth. Usually the best biopsy, certainly from a histological point of view, was when only a small drop of bloody material could be expelled from the needle. If blood appeared in the syringe then the lung cells were almost certainly to be much obscured by the red cells present.

The original drop of fluid on the slide was then distributed over as many slides as possible and crushed smears were made by placing a clean slide crosswise over the material on the other slide and crushing and smearing at the same time. (See Figure 8) This procedure was essential for spreading out the particles. No paraffin sections were made.



Figuve 8.

Figure 2.
Infiltration of the local anaesthetic

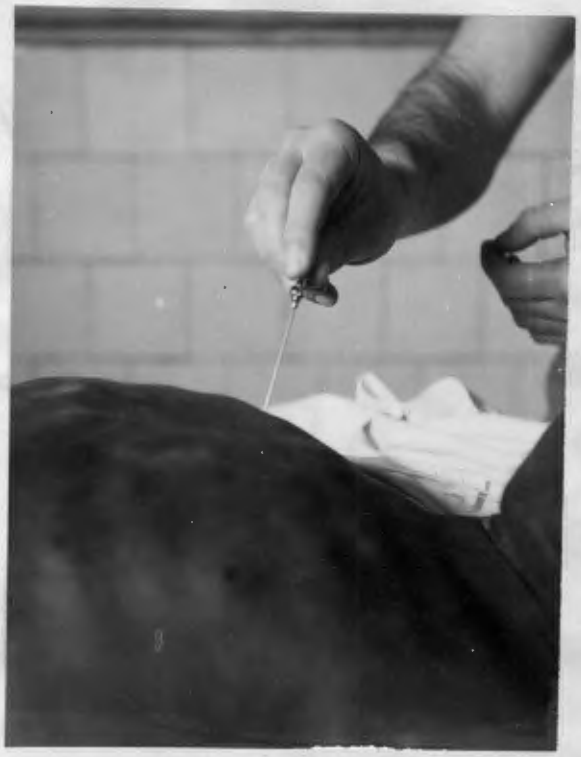


Figure 3.
Insertion of the Biopsy Needle.

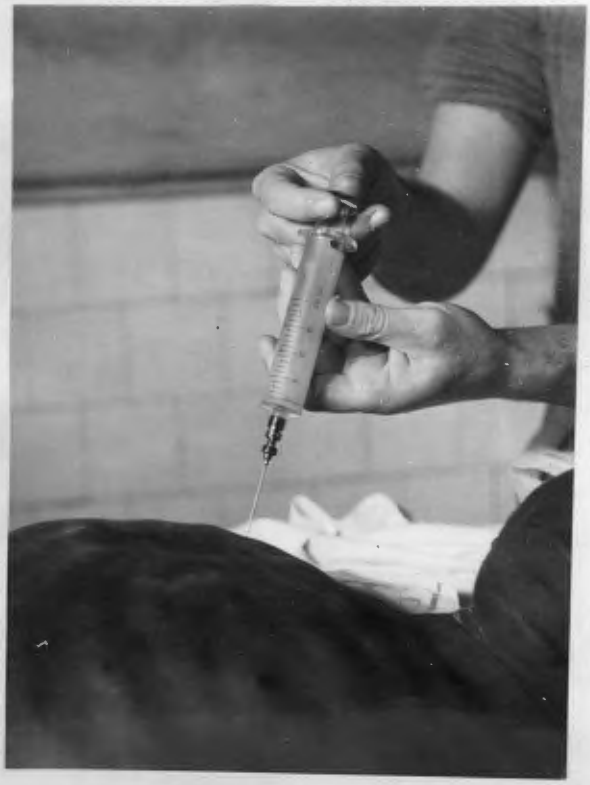


Figure 4.
The Syringe attached to the needle.

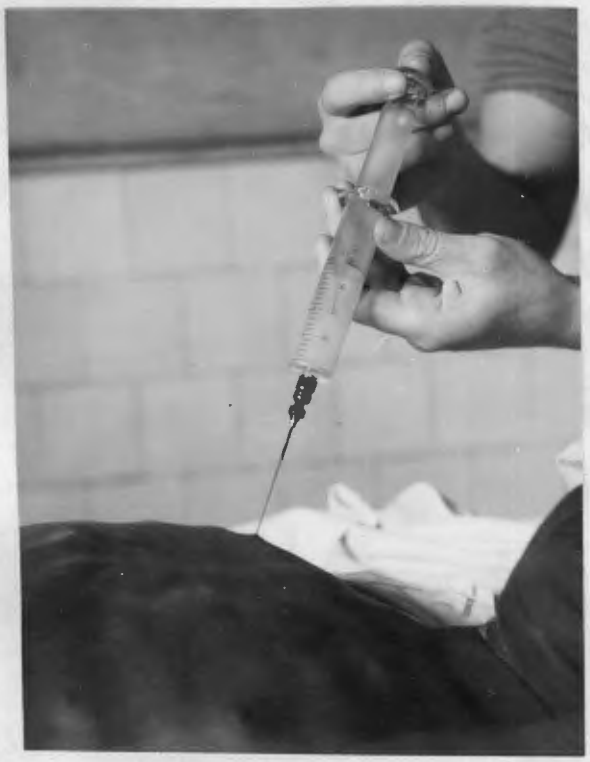


Figure 5.
Suction Applied

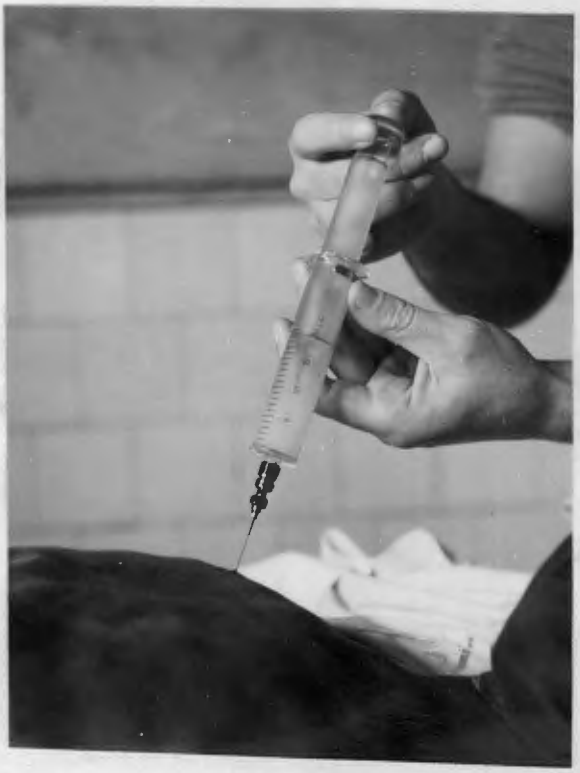


Figure 6.
With Suction Maintained the Needle is Inserted about 3-4 cm.

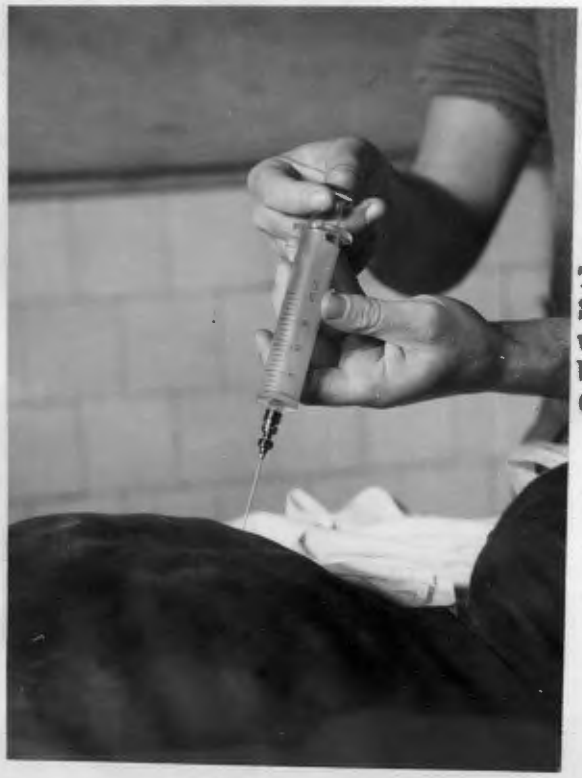


Figure 7.
The Needle is Withdrawn and Suction Released. The Syringe with Needle Attached will then be completely withdrawn from the Chest.

The drop on the blood agar was plated out with a platinum loop in the usual manner.

If only a very small amount of fluid was present in the needle this was all expelled onto the slide. Then a few drops of serum broth were aspirated into the syringe and inoculated onto the blood agar, Lowenstein medium and finally the remainder was expelled into the serum broth bottle.

The patients was kept in the recumbent position during the above procedures. A little collodium soaked cotton wool was applied to the small skin incision. The patient was then allowed to return to the sitting position.

It was considered wise to have a syringe containing 8m. of adrenaline at hand and also an oxygen cylinder connected up and ready for use. A spirit lamp was necessary for flaming the platinum loop.

Elaborate preparation of the puncture site as for a surgical operation and the use of a sterile gown, cap, mask and rubber gloves was found to be unnecessary. A simple "non-touch" technique with liberal use of iodine was sufficient; in none of the cases was there any sign of infection of the puncture site. Direct roentgenological guidence was not used.

An X-ray of the chest was done on the following day or as soon as possible thereafter to check for the presence

of a pneumothorax.

The culture media were taken immediately to the laboratory (in the present series this was unfortunately 10 miles away) and incubated. If only small quantities of fluid were obtained it was specified that the cultures be incubated for 72 hours. The Lowenstein medium was examined only after several weeks.

At the same time as the biopsy, sputum (if available) was plated out onto blood agar and incubated with the biopsy cultures. Four slides of the sputum were made for histological examination.

The biopsy and sputum slides were allowed to dry at room temperature - this took only a few minutes. One slide of each was stained with haematoxylin and eosin (as recommended by Martin and Ellis 1930, 1934), one slide with Leishman stain (as used by Godlowski 1949), one slide by Gram's method and the last slide by Ziehl-Neelsen's method for tubercle bacilli. In the last few biopsies an additional slide was stained by the method recommended by Terrell et al. (1933) by which in the same slide the cells, fibrin and pneumococci could all be clearly demonstrated.

The Gram and Ziehl-Neelsen staining methods are well known and need not be described here.

Haematoxylin-eosin stain:

1. Fix in 95 per cent alcohol for 1 minute.

2. Wash in tap water for 1 minute.

3. Place in haematoxylin for 2-3 minutes (this depends on the particular batch of haematoxylin used).

4. Wash well with tap water till the nuclei of the cells become blue.

5. Stain with alcoholic eosin for 2-3 minutes.

6. Differentiate in 95 per cent alcohol for 30 seconds.

7. Clear well in several washes of xylol, blotting the slide as necessary.

8. Mount in Canada Balsam.

The Leishman stain was done in the usual manner but the dry stained slide was mounted in Canada Balsam.

The fibrin stain was a more elaborate procedure and was unnecessary for routine work. The method used was a combination of that recommended by Terrell (1933) and that described by Clayden (1951):

1. Stain with haematoxylin as above.

2. Dip into half per cent aqueous eosin for 30 seconds.

3. Wash quickly.

4. Stain with Weigert's aniline methyl violet for 5 minutes.

5. Wash off excess stain with distilled water.

6. Wash off distilled water with Gram's iodine and then pour on fresh iodine for 5 minutes.

7. Cast off the iodine and blot thoroughly.

8. Differentiate in aniline-xylol (2 parts xylol to 1 part aniline oil) until the fibrin is sharply defined as dark

purple threads.

9. Wash well in xylol and mount in Canada Balsam.

Weigert's aniline methyl violet was made up from two solutions:

Solution 1	Absolute alcohol	33 c.c.
	Aniline oil	9 c.c.
	Methyl violet in excess.	
Solution 2	Saturated aqueous solution of methyl violet (Grubler's).	

One part of solution 1 was used with 9 parts of solution 2. The two solutions kept well separately but after mixing the stain lasted only about 10 days and the best results were obtained 3 - 8 days after preparation.

By this method fibrin and Gram positive organisms showed up a deep purple, nuclei were dark blue, the outlines of the cells were distinctly seen due to the counterstain, and the red cells were pale blue or pink.

A list of the apparatus used in the above method is given below and illustrated in Figures 9 to 15:

Spirits.

Iodine.

1 5 c.c. B-D syringe.

1 intradermal needle gauge 26.

1 intramuscular needle 5 cm. in length and 20 gauge.

1 No. 11 Bard Parker blade with handle.

1 lung biopsy needle.

1 20 c.c. B-D syringe.

Glass slides.

2 blood agar plates.

1 screw capped bottle of serum broth.

1 screw capped bottle containing a Lowenstein medium slope.

A spirit lamp.

A syringe containing 8m. of adrenaline.

An apparatus for giving emergency oxygen.

1 platinum loop.

Swabs, sterile towels, collodium.

Staining bottles and stains.

It was useful to have several biopsy needles 10 cm., 15 cm. and 20 cm. in length, the longer needles being necessary in cases where the lesion was deep in the lung or where the patient was fat. In practice, at least the first 70 biopsies of this series were done with a single simple 18 gauge lumbar puncture needle 9 cm. in length (Figure 16). Needles ordered from England arrived about a year after the order was placed.

Figure 9.
Spirit Lamp, Adrenaline, Planocaine, Spirits, Iodine and Collodium.

Figure 10.
Lung Biopsy Needle, No. 11 Bard Parker Blade and Handle, Local Anaesthetic Syringe and Needles.

Figure 11.
Biopsy 20c.c. Syringe and Biopsy Needles of Various Lengths.

Figure 12.
Lowenstein Medium, Serum Broth, Blood Agar Plates and Platinum Loop.

Figure 13.
Syringe and Needle for Adrenaline

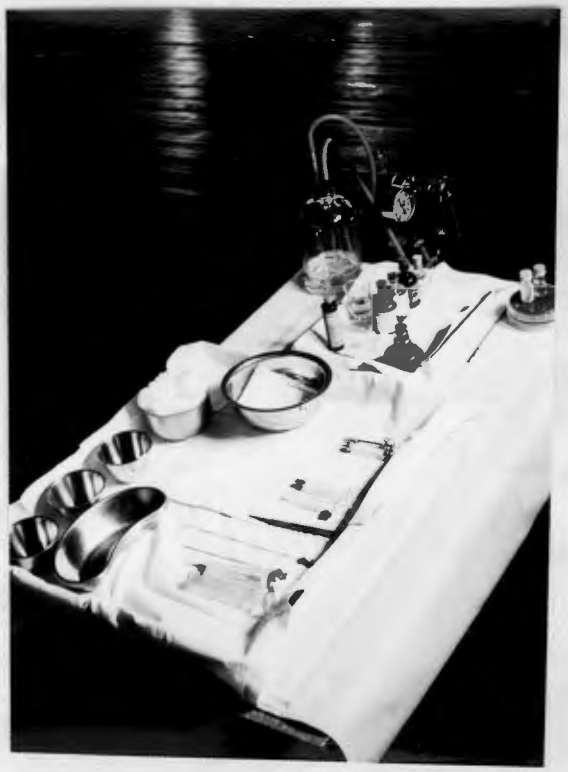


Figure 14.
The Apparatus Set Out and Ready for Use.

Figure 15.
The Apparatus Set Out and Ready for Use.

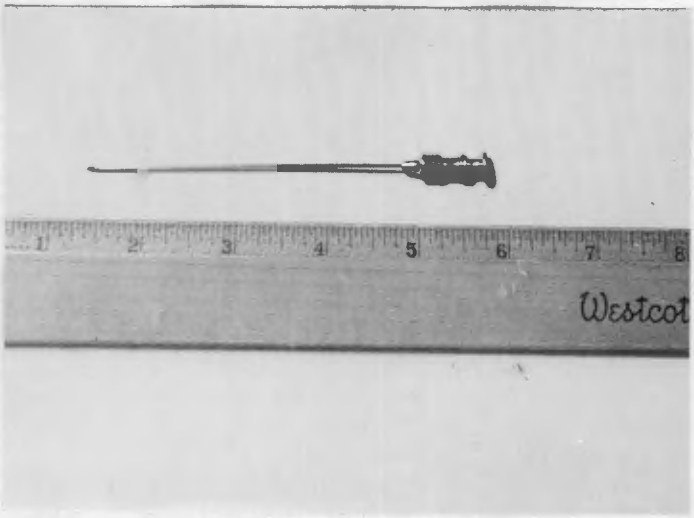


Figure 16.
The Lung Biopsy Needle which was Used for the Majority of the Cases.

Figure 17.
Laboratory with "Running Water".

The staining of the slides was done in the hospital laboratory which had a floor ppace of 10 by 15 feet and was shared by a House Physician and twenty or more students. Running water was obtained from an enema can hung on the wall as shown in Figure 17. These details illustrate that lung biopsy can be done with the very minimum of apparatus and under the most unfavourable conditbons.

By using the method outlined one was able to obtain a histological picture stained by various methods and also one was able to observe either on direct smear or culture most of the common organisms. Positive cultures of tubercle bacilli on the Lowenstein medium were obtained in several cases. This was particularly gratifying. The haematoxylin-eosin method was probably the most useful for the histology especially in showing up the cells in dense masses of poorly crushed tissues. The Leishman stain showed up the cells very well in thin smears but in the denser portions of material it was very poor indeed.

Using the method described sufficient material was obtained in all cases except two; Case 8 was one of the first cases with a normal lung to be investigated and the needle was inserted cautiously and superficially and only once; Case 58-1 had a pleural effusion and an attempt was made to push the needle very deep into the lung through the effusion; although this was successful, on withdrawing the needle much pleural fluid entered the syringe and so

diluted the biopsy material that it was useless for examination.

It was not necessary to have the patient hold his breath during the biopsy. This was discovered by necessity as a very ill dyspnoeic lobar pneumonia case cannot hold his breath except for a very short period. By using a skin incision and a needle with a well fitting stylette the amount of contamination of the biopsy smears by skin, muscle or pleural cells was negligible. At first it was thought necessary to have very fresh blood agar plates and thus agar was melted, mixed with blood and the plate poured fresh before every biopsy. This laborious procedure was unnecessary and organisms grew well on plates which have been kept as long as a week in the refrigerator.

A comparison of the histology of the sputum cells with the histology of the lung biopsy cells is beyond the scope of this thesis and will be reported in a separate communication at a later date.

COMPLICATIONS AND DANGERS OF LUNG BIOPSY.

The chief critics of lung biopsy are those who have had no experience with the method. Lung biopsy has been roundly attacked because of its possible theoretical dangers, namely air embolism, pneumothorax, uncontrollable haemorrhage, empyema, and the spreading of tumour metastases. To add

insult upon injury it has been suggested that no information is obtained that could not have been acquired by other "safer" means.

An attempt will be made to reply to these criticisms firstly by a brief survey of the complications encountered during the 70 years that lung biopsy has been in use and then by an analysis of the present series of eighty three biopsies on living patients

How many patients have died directly as the result of lung biopsy? Naunyn (1889), Waldvogel (1906), Bonniger (1907), Metzler (1915) and Stähelin (1919), all reported cases in which death occurred, generally due to perforation of intercostal arteries and atheromatous vessels within the parenchyma of the lung. With the exception of Waldvogel's case, the patients were elderly with arteriosclerosis. Rather large trocars were commonly used for thoracentesis and puncture of the lung was quite accidental in most cases. At autopsy all these patients were found to have suffered from severe diseases but death was generally due to the puncture of an atheromatous vessel with haemorrhage into the pleural cavity, into the lung, and occasionally into the bronchi and trachea. As a result of Horder's paper in 1909 a spirited correspondence took place in the Lancet. Both Dr. Fortescue-Brickdale and Dr. Russel quoted several cases dying instantaneously after lung puncture or within

hours or days. Three of these were attributed to haemorrhage and the other eight cases appeared to die of what we would today call "pleural shock". Horder replied that there was no greater risk of such unusual calamities occurring after lung puncture than after any negative pleural puncture. He pointed out that in all operations, however trivial, there was the possible contingency that the patient might die suddenly; and considering the great frequency with which a negative thoracentesis was performed "it can scarcely be said that this contingency is more than the rarest of events".

Thomas and Parker (1920) reported one case which died suddenly but this case was being tapped for suspected fluid and the lung puncture was done unintentionally. They commented that "such accidents are encountered in any large series of chest taps".

Thus it would appear that the chance of death occurring from lung biopsy is small and probably has the same incidence as deaths following chest aspiration.

Now to consider the other extreme - <u>which investigators have reported that lung biopsy was a safe procedure</u>?

Horder (1909) reported 14 cases with no ill effects. Colby (1909) biopsied 12 cases without untoward complications. Thomas and Parker (1920) stated: "There appears to be a

general impression among clinicians that lung puncture is a hazardous procedure, apt to produce such complications as empyema; in answer to such objections and to allay such fears, we can say that we never have seen any unfavourable results (in 73 cases), such as empyema, haemorrhage, etc. following lung puncture".

Lyon (1922) admitted that no untoward effects were to be anticipated from the puncture of a solid lung. He gave a very human reason for not doing punctures in the children under his care: "At best, it is a somewhat painful procedure, and often excites in the child patient a terror which for several days to come reawakens with every appearance of the physician". Glynn and Digby (1923) were content that the danger was negligible. Other investigators who have had wide experience and who pronounced the method safe were Stewart, D (1930), Stewart, F (1933), Sappington (1936), Bullowa (1936), Martin and Ellis (1934), Lavalle (1937), Craver and Binkley (1938), Reimann (1938), Nathanson (1943) and Godlowski (1949). The total experience of the investigators quoted above embraced well over two thousand cases and their combined opinions must be treated with respect. It will be noted that biopsies were not done on only one type of case - there have ben cases of pneumonia (both lobar and bronchopneumonia), lung tumours, lung abscess, tuberculosis and lipoid pneumonia; and Godlowski did 75 biopsies on normal people. Thus the safely of the procedure was not related to the obliteration of the pleural space as

was suggested by Faber (1942) and Nathanson (1943).

That empyema is a danger of biopsy was disproved by the figures of Sappington and Favorite (1936) who showed that the incidence of empyema in lobar pneumonias which had been biopsied and those not biopsied was the same. Tuberculous empyema seems an unlikely event if one accepts Lavalle's series of 100 cases of tuberculosis biopsied without complications (1937). Many other observers including Bullowa (1936) were in agreement that empyema was not a hazard of lung biopsy. Most of this work was done in the era preceding sulphonamides, penicillin and the other antibiotics. Is not the danger even less now that chemotherapy is available?

Martin and Stewart (1936) did not observe earlier or more frequent metastases in aspirated cases but they referred to tumour aspiration as a whole and not to lung biopsy in particular. Craver (1940) in his series on lung tumours was never able to demonstrate at autopsy growth of tumour along the needle tract. Gladhill et al. (1949) in 75 aspirations of cases of carcinoma of the lung also commented that there was no needle tract implantation.

However one must not gain the impression that lung biopsy is a completely innocuous procedure without any possible discomfort or sequelae and that it should be done on

the slightest provocation.

All investigators in this field must agree that pain, haemoptysis and pneumothorax may occasionally occur, and that death (whether it be from "pleural shock" or air embolism) although rare, is not an impossible sequela.

Pain has only been occasionally mentioned as a consequence of lung biopsy. Craver and Binkley (1938) stated that some patients coughed and complained of pain but a prescription of codeine sulphate gr. 1 as required for the first night was a sufficient analgesic. Nathanson et al. (1943) used a half grain of a codeine salt to "control the pain and anxiety". It was obvious that the pain experienced by their cases could not have been severe. Godlowski (1949) found that if the local anaesthesia was well performed, the majority of the patients felt only negligible pain during the whole procedure. A short stabbing pain for a few hours occurred in one or two of the "more sensitive individuals" but was not intensive and could easily be allayed by light analgesics. He did a routine check X-ray a week after lung biopsy and thus, if this pain was due to a very shallow pneumothorax, it would have been absorbed by this time.

Haemoptysis did occasionally occur after lung biopsy - Sappington and Favorite (1936) recorded three haemoptyses in 60 cases; Bullowa (1936) rarely in 1467 cases; Craver

and Binkley (1938) occasionally in 92 cases; Nathanson (1943) one haemoptysis in 10 cases; Godlowski (1949) one haemoptysis in 85 cases. Apart from those cases done with the large thoracocentesis trocars by the early investigators, there have been no deaths reported from haemorrhage and no cases were reported where the haemorrhage was severe enough to cause the slightest anxiety.

An occasional small pneumothorax was an uncommon complication and Craver and Binkley (1938) mentioned that it occasionally occurred. In Godlowski's series (1949) of 85 cases only three showed a small pneumothorax which was discovered only by routine X-ray. Other authors such as Sappington and Favorite (1936) agreed that pneumothorax was rare. There were no cases of tension pneumothorax recorded in the literature.

Air embolism would appear to be the only real danger in lung biopsy. The only cases to be reported were two patients of Craver (1940). Whilst the needle was still in the patient (in the sitting position) there was sudden collapse with tonic and clonic spasms and unconciousness. Recovery of conciousness occurred in 24 hours when various palsies were noted. These decreased "rapidly" so that within three weeks the patient was able to walk about but he still showed some residual motor impairment. They believed that these two cases were due to air embolism. Since then all their cases were

done in the recumbent position and there were no more accidents. No deaths have been recordéd.

It would seem unwise to aspirate a mass which might be a hydatid cyst. F. Stewart (1933) evacuated rather a large amount of fluid from a hydatid cyst and was rewarded with "a considerable immediate reaction".

If a reasonable amount of care is employed in choosing the biopsy site, the danger of penetrating the heart or great vessels can be discounted.

Thus one must expect in any reasonably large series of lung biopsies that occasional cases will have slight pain, haemoptysis or pneumothorax. One must be ready to deal with the rare case of air embolism.

COMPLICATIONS OF THE PRESENT SERIES:

These are summarised in Tables 3, 4, 5, 6, 7, 8 and 9. Eighty three biopsies on living patients are considered. The seven cases where biopsy was done after death and the four cases where liver cells were obtained are not included in this analysis.

Certain of the complications which were predicted as probable consequences of lung biopsy did not occur. There

were no cases of empyema in this series either following biopsies on cases of pneumonia or tuberculosis. There was no evidence that the cases of tuberculosis were any worse following the biopsy. In the one case of carcinoma the patient deteriorated at the same rate after as before biopsy and there was no clinical evidence of premature spread of secondaries. Unfortunately only a limited postmortem of the affected lung was allowed. Cases which might have been hydatid cysts were avoided in the present series.

Haemoptysis was the commonest complication and occurred in 34.9 per cent of cases. Of these a moderate haemoptysis accounted for 8.4 per cent, that is the patient soon after biopsy coughed up more than a tablespoonful of blood. The largest haemoptysis was in Case 69-2 who coughed up five tablespoonfuls of blood in the five minutes following biopsy. Blood streaking of the sputum occurred for never longer than twenty four hours. In no case did the amount of blood coughed up give any cause for anxiety. A small amount of blood was coughed up by 26.5 per cent of cases. In this group of small haemoptyses the record has been as scrupulously honest as possible, even the slightest speck of blood being recorded as a haemoptysis. In the majority of these cases the first sputum collected after biopsy simply contained a small streak of blood.

Pain occurred in 12 per cent of cases. After biopsy the

Table 3.

To Show the Incidence of Complications in 83 Lung Biopsies on Living Patients.

Group I (Normal Cases).

Case No.	Age Sex Race	Pathology	Situation of Biopsy	Haemoptysis	Pain	Pneumothorax
7	52 Male N.	Urethral stricture, fibrositis.	8th space left post. axillary line.	Nil	Nil	No check
8	45 Male C.	Syphylitic hemiplegia.	8th space 2cm. behind right post. axil. line.	Nil	Nil	Nil
11	51 Male C.	Gastric Ulcer.	7th space, below angle right scapula.	Nil	Slight	Present
13	54 Male C.	Gastric carcinoma.	8th space, below angle. left scapula	Nil	Nil	Nil
14	28 Male N.	Hemiplegia	7th space, 10cm. from midline of spine on right.	Nil	Nil	Nil

Table 3. (continued)

Case No.	Age Sex Race	Pathology	Situation of Biopsy	Haemoptysis	Pain	Pneumothorax
15	25 Fem. N.	Anaemia of pregnancy or steatorrhoea	8th space below angle right scapula.	Nil	Slight	Nil
16	40 Male C.	Tabes dorsalis.	8th space, below angle right scapula.	Two tablespoonfuls.	Nil	Nil
17	46 Male I.	Cirrhosis.	6th space, in right post. axil. line.	Nil	Slight	Present
18	49 Fem. N.	Menopausal symptoms.	7th space, in left post. axil. line.	Nil	Nil	Nil
25	20 Male C.	Ascariasis.	8th space, 4cm. behind right post. axil. line.	Trace	Slight	Present
36-1	35 Male C.	SBE, pulmonary embolus.	2nd space, 5cm. to right of midsternal line.	PM	PM	PM

Table 3. (continued)

Case No.	Age Sex Race	Pathology	Situation of Biopsy	Haemoptysis	Pain	Pneumo-thorax
61	28 Fem. C.	Hemiplegia, cerebral aneurysm.	2nd space, 5cm. to right of midsternal line.	PM	PM	PM
66	29 Male C.	Acute yellow atrophy.	3rd space, in left midclavic. line.	PM	PM	PM

Group II (Cases Done For Diagnostic Purposes).

Case No.	Age Sex Race	Pathology	Situation of Biopsy	Haemoptysis	Pain	Pneumo-thorax
1	49 Male C.	Hypertensive failure with pulm. infarct.	3rd space, 2cm. to right of sternal border.	PM	PM	PM
2	6 Fem. C.	TB empyema and pneumothorax.	3rd space 2 cm. to left of left sternal border.	Nil	Nil	Present before biopsy

Table 3. (Continued)

Case No.	Age Sex Race	Pathology	Situation of Biopsy	Haemoptysis	Pain	Pneumothorax.
3	48 Fem. C.	Hypertensive failure plus pneumonia.	8th space in left mid-axil. line.	PM	PM	PM
5	74 Fem. C.	Pulmonary TB.	2nd space, 3cm. to right sternal border.	Small for few hours.	Nil	Nil
5-1	74 Fem. C.	Pulmonary TB.	1st space, 2cm. to right of right sternal border.	Nil	Nil	Nil
10	58 Male N.	Pulmonary Carcinoma.	3rd space, just behind right ant. axil. line.	Sputum blood streaked few hrs.	Nil	Nil
12	46 Male N.	Pulmonary TB.	6 th space in left post. axil. line.	Nil	Nil	Nil
20	33 Male C.	? Pulmonary infarction.	6th space in right ant. axil. line.	Small	Nil	Nil

Table 3. (continued)

Case No.	Age Sex Race	Pathology	Situation of Biopsy	Haemoptysis	Pain	Pneumothorax
21	14 Fem. C.	? Rheumatic pneumonia.	7th space below angle right scapula.	Nil	Nil	Nil
22	82 Male C.	TB or pneumonia.	4th space in right midclav. line.	PM	PM	PM
27	14 Fem. C.	Congenital cystic lung.	2nd space just lat. to right midclav. line.	Nil	Slight	Nil
30	13 Male C.	Acute nephritis plus pneumonia.	8th space below angle of left scapula.	Tablespoonful then streaking for 1 hr.	Nil	Nil
32	23 Fem. N.	Pulmonary TB.	3rd space, 4cm. to right of right sternal border.	Nil	Nil	Nil
34	45 Male C.	TB lungs and meninges and asbestosis.	2nd space, 3cm. to right of right sternal border.	COLLAPSED AND DIED 17 HOURS LATER.		

Table 3. (continued)

Case No.	Age Sex Race	Pathology	Situation of Biopsy	Haemoptysis	Pain	Pneumothorax
39	18 Fem. N.	TB lungs and abdomen and brain.	5th space, 5cm. to right of mid-sternal line.	Nil	Nil	Nil
43	12 Male C.	Chronic nephritis plus ? uraemic lung.	7th space, 4cm. to right of midline spine.	Minimal	Slight	Present
44	18 Fem. C.	Bronchiectasis.	7th space in left post. axil. line.	Nil	Nil	Nil
44-1	18 Fem. C.	Bronchiectasis.	8th space below angle left scapula.	Nil	Nil	Nil
47	31 Fem. C.	Pulmonary TB.	7th space below angle left scapula.	Very slight	Nil	Nil
49	41 Male C.	Asthma and broncho-pneumonia.	7th space just behind right post. axil. line.	Nil	Slight	Considerable.
49-1			As above.	Nil	Nil	Nil

Table 3. (continued)

Case No.	Age Sex Race	Pathology	Situation of Biopsy	Haemoptysis	Pain	Pneumothorax
52	12 Male M.	? Rheumatic pneumonia.	2nd space, 4cm. to right of mid-sternal line.	Minimal	Nil	Nil
59	58 Male C.	Staph. aureus pneumonia.	7th space below angle right scapula.	Nil	Nil	Nil
59-1			As above	Nil	Nil	Nil
62	29 Male M.	Infected haematoma or amoebic abscess of lung.	7th space just lateral to angle right scapula.	Nil	Nil	Nil
62-1			As above	Nil	Slight	Present
64	40 Male M.	? CA oesophagus and broncho-pneumonia.	8th space just lat. to angle left scapula.	Four table-spoonfuls	Nil	Nil
				COLLAPSE ?SYNCOPE.		
68	4 Mths. Male C.	Pulmonary TB.	4th space in right midclav. line.	Nil	Nil	Nil
73	36 Male C.	Pneumonia of uncertain etiology.	3rd space, 5cm. to left of midsternal line.	Slight	Nil	Nil

Table 3. (continued).

Group III (Acute Lobar Pneumonia with Normal Resolution).

Case No.	Age Sex Race	Pathology	Situation of Biopsy	Haemoptysis	Pain	Pneumothorax
4	28 Male C.	Lobar pneumonia.	8th space in left post. axil. line.	Nil	Nil	Nil
9	30 Male M.	Lobar pneumonia.	8th space below angle right scapula.	Nil	Nil	Nil
23	49 Male C.	Lobar pneumonia.	2nd space, 5cm. to left left sternal border.	Slight	Nil	Nil
26	29 Male C.	Lobar pneumonia	4th space, 4cm. to right of right sternal border.	Three tablespoonfuls - 24 hrs.	Nil	Nil
				COUGH AND DYSPNOEA.		
28	29 Male M.	Lobar pneumonia	8th space in right post. axil. line.	Nil	Nil	Nil
33	49 Male M.	Lobar pneumonia	9th space just behind left post. axil. line.	Nil	Nil	Nil

Table 3. (Continued).

Case No.	Age Sex Race	Pathology	Situation of Biopsy	Haemoptysis	Pain	Pneumothorax
38	29 Male C.	Lobar pneumonia.	7th space below angle right scapula.	Nil	Nil	Nil
41	27 Male C.	Lobar pneumonia and asbestosis.	8th space below angle left scapula.	Nil	Nil	Nil
42	21 Fem. C.	Lobar pneumonia.	2nd space, 5cm. to left of midsternal line.	Slight	Nil	Nil
45	18 Male C.	Lobar pneumonia.	7th space below angle left scapula.	Nil	Nil	Nil
45-1			As above	Nil	Nil	Nil
48	23 Male C.	Lobar pneumonia.	2nd space 5 cm. to left of midsternal line.	Three tablespoonfuls - 12 hrs.	Nil	Nil
50	42 Male C.	Lobar pneumonia.	8th space, 2cm. behind left post. axil. line.	Nil	Nil	Present

Table 3. (continued).

Case No.	Age Sex Race	Pathology	Situation of Biopsy	Haemoptysis	Pain	Pneumothorax
51	23 Fem. N.	Lobar pneumonia	2nd space, 6cm. to right of midsternal line.	Slight	Nil	Nil
54	20 Male C.	Lobar pneumonia	8th space, 3cm. behind right post. axil. line.	Nil	Nil	Nil
55	26 Fem. C.	Lobar pneumonia	8th space below angle left scapula.	Slight	Nil	Nil
56	14 Male C.	Lobar pneumonia.	2nd space, 3cm. to right of right sternal border.	Slight - 2 hrs.	Nil	Nil
56-1			As above	Slight - 1 hr.	Nil	Nil
57	29 Male N.	Lobar pneumonia.	8th space below angle left scapula.	Slight	Nil	Nil
57-1			As above.	Two table spoonfuls - 1 hr.	Nil	Nil

Table 3. (continued).

Case No.	Age Sex Race	Pathology	Situation of Biopsy	Haemoptysis	Pain	Pneumothorax
60	21 Male C.	Lobar pneumonia.	7th space below angle left scapula.	Nil	Nil	Nil
60-1			As above	Nil	Nil	Nil
67	29 Male N.	Lobar pneumonia.	2nd space, 6cm. to right of midsternal line.	Nil	Nil	Nil
71	31 Male C.	Lobar pneumonia.	8th space below and lat. to angle left scapula.	Nil	Nil	Nil
71-1			As above	Nil	Nil	Nil
72	29 Fem. C.	Lobar pneumonia.	7th space below and medial to angle right scapula.	Nil	Nil	Nil
72-1			As above	Slight	Nil	Nil

Table 3. (Continued).

Group IV (Chronic Lobar Pneumonia).

Case No.	Age Sex Race	Pathology	Situation of Biopsy	Haemoptysis	Pain	Pneumothorax
6	31 Male C.	Chronic lobar pneumonia.	2nd space, 5cm. from right sternal border.	Slight - 10 mins.	Nil	Nil
6-1			5th space ant. to lat. border right scapula.	Nil	Slight -48 hrs	Present
19	36 Male C.	Chronic lobar pneumonia.	8th space, 5cm. behind left post. axil. line.	Three table-spoonfuls -24 hrs.	Present -7mins.	Nil
				COUGH AND DYSPNOEA		
24	40 Male C.	Chronic lobar pneumonia.	8th space, 5cm. from midline of back on left.	Slight -12hrs.	Nil	Nil
29	46 Male C.	Chronic lobar pneumonia.	7th space below angle left scapula	Nil	Nil	Nil

Table 3. (continued).

Case No.	Age Sex Race	Pathology	Situation of Biopsy	Haemoptysis	Pain	Pneumothorax
31	23 Fem. C.	Chronic lobar pneumonia.	8th space just behind right post. axil. line.	Nil	Nil	Nil
35	51 Male N.	Chronic lobar pneumonia.	8th space just behind left post. axil. line.	Nil	Nil	Nil
37	50 Fem. C.	Chronic lobar pneumonia.	5th space, 5cm. from midline post. on left.	Nil	Nil	Nil
37-1	50 Fem. C.	Chronic lobar pneumonia.	8th space, 2cm. behind left post. axil. line.	Nil	Nil	Nil
53	32 Male C.	Chronic lobar pneumonia.	8th space just lat. to angle right scapula.	Slight -10hrs.	Nil	Nil
53-1			As above	Nil	Nil	Nil

Table 3. (continued).

Case No.	Age Sex Race	Pathology	Situation of Biopsy	Haemoptysis	Pain	Pneumothorax
58-1	47 Male C.	Chronic lobar pneumonia.	7th space just below angle right scapula.	Nil	Nil	Nil
58-2			7th space just below and lat. to angle of right scapula.	Nil	Nil	Nil
63	52 Male N.	Chronic lobar pneumonia.	7th space below angle right scapula.	Nil	Nil	Nil
65	38 Male C.	Chronic lobar pneumonia.	3rd space in right mid-clavic.line.	One table-spoon-ful -2hrs. ? SYNCOPE	Nil	Nil
69	38 Male C.	Chronic lobar pneumonia.	2nd space, 3cm. to right of right sternal border.	Nil	Nil	Nil

Table 3. (continued).

Case No.	Age Sex Race	Pathology	Situation of Biopsy	Haemoptysis	Pain	Pneumothorax
69-1	38 Male C.	Chronic lobar pneumonia.	2nd space, 3cm. to right of right sternal border.	Slight -30mins.	Nil	Nil
69-2			As above	Five tablespoonfuls -1hr.	Nil	Nil
70	31 Male C.	Chronic lobar pneumonia.	7th space below and lateral to angle right scapula.	Nil	Nil	Nil
70-1			As above	Nil	Nil	Nil

The four cases in which Liver cells were obtained and the one autopsy case where the material was identified as spleen, are not included in this table. The other six autopsy cases are included for completeness so as to give a table which gives an idea of the type of patient and his pathology.

Table 4.

To Compare The Total Number Of Complications In The Various Groups And To Show The Total Number Of Complications Of The Whole Series.

Group	No. of Biopsies	Haemoptysis		Pain		Pneumothorax		Cough and Dyspnoea		Syncope or Air Embolism		Total number and percentage of biopsies with complications
		No.	%	No.	%	No.	%	No.	%	No.	%	
I	10	2	20	4	40	3	30	0	0	0	0	5 or 50%
II	26	9	34.6	4	15.4	3	11.5	0	0	2	7.7	13 or 50%
III	27	11	40.7	0	0	1	3.7	1	3.7	0	0	12 or 44.4%
IV	20	7	35	2	10	1	5	1	5	1	5	8 or 40%
Total	83	29		10		8		2		3		38 or 45.8%

Table 5.

To Show The Percentage Of Each Particular Complication In The Series As A Whole.

Complication		Percentage of 83 Biopsies.
Haemoptysis	Mild	26.5
	Moderate	8.4
Pain		12.0
Pneumothorax		9.6
Cough and Dyspnoea		2.4
Syncope or air embolism		3.6

Table 6.

To Show The Relationship Between Age And The Number Of Complications

Age	With Complications.	Without Complications.	Total	Percentage of Biopsies with complications.
Years	No. of Biopsies	No. of Biopsies		
0 - 9	0	2	2	0
10 - 19	6	6	12	50
20 - 29	11	13	24	45.8
30 - 39	10	7	17	58.8
40 - 49	8	8	16	50
50 - 59	2	8	10	20
60 - 69	0	0	0	0
70 - 79	1	1	2	50
Total	38	45	83	

Table 7.

To Show The Relationship Between Sex And The Number of Complications.

Sex	With Complications.	Without Complications.	Total	Percentage of biopsies with complications.
	No. Biopsies	No. of Biopsies.		
Male	30	33	63	47.6
Female	8	12	20	40
Total	38	45	83	

Table 8.

To Show The Relationship Of Complications To Situation Of Biopsy.

Lobe	No. of Biopsies	Haemoptysis		Pain		Pneumothorax		Cough and Dyspnoea		Syncope or air embolism		Total No. and percentage of biopsies with complications
		No.	%	No.	%	No.	%	No.	%	No.	%	
Right upper and middle.	20	11	55	2	10	1	5	1	5	2	10	14 or 70%
Right lower.	30	6	20	7	23.3	6	20	0	0	0	0	11 or 36.7%
Left upper.	6	4	66.7	0	0	0	0	0	0	0	0	4 or 66.7%
Left lower	27	8	29.6	1	3.7	1	3.7	1	3.7	1	3.7	9 or 33.3%

Table 9.

To Show Whether Experience Effects The Number Of Complications.

	First Forty Biopsies.	Second Forty Biopsies.
Number of biopsies with complications.	18	17
Number of biopsies without complications	22	23

patients were specifically asked if they had any pain and the slightest complaint was recorded as "pain present". Of the ten cases that complained of pain seven had an associated pneumothorax. The pain was very slight and in no case needed the use of analgesics. As can be seen it was almost always associated with pneumothorax and when a patient complained of pain one usually could predict that a small pneumothorax would be found on the subsequent X-ray. The pain was of an interesting type - it was in almost all cases (when associated with pneumothorax) situated in the infraclavicular region anteriorly irrespective of the site of the biopsy. It was stabbing, worse on coughing and deep breathing and often worse when the patient moved. It lasted longest in Case 6-1, namely for 48 hours. There was only one case of pneumothorax who did not complain of slight pain. In Cases 15 and 27 the pain was in the region of the puncture site and was not associated with a pneumothorax In Case 19 the pain was in the epigastrium and was probably associated with trauma to an intercostal nerve - no pneumothorax was present.

Pneumothorax occurred in 9.6 per cent of the biopsies. As stated it was usually associated with slight pain but the amount of pain was unrelated to the size of the pneumothorax. The pneumothorax was usually very small and shallow. In several cases the pneumothorax was probably due to a defect in the technique which was employed. In Case 11 the biopsy needle was pushed in and out of the lung four times before

suitable material was obtained. The needle thus remained in situ for rather a long time. In Case 49 the needle again remained in the lung somewhat longer than usual - this was a case with asthma and emphysema and the attachment of the needle to the syringe and the insertion of the needle was done rather more slowly than usual. In Case 50 the needle was inserted and the stylette removed, the syringe attached and suction applied; a mixture of fluid and air entered the syringe. Obviously the tip of the needle had been in the pleural space when the stylette was removed and a pneumothorax naturally resulted. The first attempt at biopsy on Case 31 is not included amongst the complications because lung biopsy was not actually performed; again on removing the stylette air sucked in giving a pneumothorax indicating that the needle was in the pleural cavity. The attempt at biopsy was abandoned without the needle being inserted into the lung. One must be quite certain that the needle point is in the lung parenchyma before the stylette is removed. This point of technique has already been discussed. Lastly in Case 62-1 a long 15cm. needle was used attached to the syringe from the outset. As the needle was inserted attempts were made at aspiration at different depths because fluid was suspected. The final depth was 8-9 cm. This was a comparatively slow affair and very different from the usual biopsy technique. From this it can be seen that in only four of the eight cases with pneumothorax was the technique reasonably perfect. An incidence of four cases (or even of eight cases)

of pneumothorax in 83 biopsied is small indeed. There were no cases of tension pneumothorax and in no case was the patient in any way distressed by the pneumothorax except for the slight pain. However in all fairness one must report one case of tension pneumothorax which strictly speaking did not follow lung biopsy but was related to it. This case was not included in the series because no lung biopsy was ever done. The patient was a 78 year old European male who had been subject to attacks of asthma. X-ray showed a peculiar type of bronchopneumonic lesion. His lungs were emphysematous. The chest was infiltrated with local anaesthetic in the 9th interspace in the right posterior axillary line. For various reasons it was then decided that it might be better to do the biopsy through the 8th interspace. Infiltration was then performed in this area and a pneumothorax was found to be already present and no biopsy was even attempted. One must conclude that the pneumothorax was the result of the first infiltration. This pneumothorax subsequently became a tension pneumothorax and although the patient became severely ill he recovered. It is probable that in the very exceptional case a tension pneumothorax might occur.

There were in the whole series only <u>five cases in which one was anxious about the condition of the patient subsequent to biopsy</u>. These cases will be described in some detail.

Case 19 was a Coloured male of 36 years with chronic

pneumonia. With the patient horizontal the needle was inserted into the 8th interspace about 5 cm. behind the posterior axillary line on the left side. As the needle was inserted with suction applied bloody material spurted into the syringe and then blood welled up into the barrel. The needle was immediately withdrawn. About a minute later the patient coughed up about three to four tablespoonfuls of blood and at the same time became very dyspnoeic with a raised pulse rate. About a minute later he complained of a stabbing pain in the epigastrium which lasted about 7 minutes. By this time he had settled down and felt quite comfortable. There was slight blood streaking of the sputum for about 24 hours. X-ray showed no pneumothorax.

Case 26 was a Coloured male of 29 years with a lobar pneumonia. Lung biopsy was performed through the fourth interspace about 4 cm. to the right of the right sternal border (the patient was horizontal). This was followed almost immediately afterwards by a quite alarming reaction with much coughing and dyspnoea and he had a haemoptysis of three tablespoonfuls of blood. The whole occurrence lasted only a very few minutes. He complained afterwards of a slight headache. There was slight blood staining of the sputum for 24 hours. No pneumothorax was present on the subsequent X-ray.

It was rather uncertain as to the cause of these reactions but it would appear that quite a big bronchus was

probably entered and there was then, an irritating gush of blood with the subsequent cough, dyspnoea and haemoptysis.

A native male (40 years) was a case of chronic bronchopneumonia (Case 64). Lung biopsy was performed through the 8th interspace just lateral to the line of the angle of the left scapula. The patient was lying flat on his side with his head low. The needle was inserted, the plunger withdrawn and on one insertion a little bloody material oozed into the syringe. For about a minute afterwards he appeared to be perfectly well but then he suddenly coughed up a tablespoonful of bloody sputum, sat up, attempted to wretch and then became unconscious, cold and pulseless. Within a few seconds he had been given 8m. of adrenaline subcutaneously and oxygen started. He immediately resented the nasal cathater and was thus in the absolutely collapsed state for only 30-60 seconds. By auscultation his heart rate was noted to be slow. He then sweated a lot (possibly an adrenaline effect) and over the next 2-3 minutes regaindd full consciousness and the pulse became palpable but the rate was still slow though faster than before. He subsequently coughed up three tablespoonfuls of blood-stained mucoid sputum. About ten minutes later he was perfectly normal with a blood pressure of 120/90 mm. Hg. but he complained of a slight headache. Blood-staining of the sputum continued for about an hour. X-ray showed no pneumothorax. This reaction might have been due to a small air embolus or more probably,

because of the slow pulse, a syncope possibly of the vaso-vagal type.

Case 65 was a Coloured male (38 years) with chronic lobar pneumonia. Lung biopsy was performed through the third interspace in the right midclavicular line (the patient was in the supine position). The biopsy was uneventful but about a minute later he coughed up a tablespoonful of blood, looked "peculiar" and began to sweat. The pulse diminished in force. He said that he was alright except that he felt hot and had experienced a "shock" in the left corner of his mouth and in his left hand. He then coughed up a little more blood. About five minutes later he said he felt nauseous and vomited up his breakfast. After this he was quite alright. His sputum was blood streaked for about two hours. X-ray showed no pneumothorax. This might well also have been vaso-vagal in nature but the "shock" suggested that there might have been a small air embolus to the cerebral cortex.

The only death in the series was Case 34, a Coloured male of 45 years who had widespread bilateral pulmonary tuberculosis and "asbestosis". The patient was placed in the supine position but his head was raised on one low pillow because he complained of considerable dyspnoea and discomfort when lying absolutely flat. The needle was inserted through the second interspace about 3 cm. to the right of the right border of the sternum. As the needle with syringe attached

was inserted material spurted into the syringe and the needle was immediately withdrawn. The patient at first appeared to be perfectly alright but about 10 seconds later he attempted to sit up, turned towards the right side and attempted to cough and wretch. He then went absolutely rigid and very pale and became unconscious. Within seconds adrenaline was given subcutaneously and oxygen started; an extra pillow was placed under his head and the bed blocked. The patient's eyes had a glassy stare and he breathed stertorously with a white froth forming round his lips. He was pulseless but the heart was heard beating very rapidly. There was no clinical pneumothorax. The pupils reacted to light. After about three or four minutes he began to sweat profusely and breathing became more vigorous. A few minutes later he became less rigid (before this all his limbs had been in stiff extension), moved his one arm slightly and made facial grimaces. After 30 minutes he was less deeply unconscious, his pulse rapid but of fair volume and his colour good. After an hour he had improved still further but began sweating again profusely. The blood pressure was 180/110 m.m. Hg. and there was a gross pulsus paradoxus. After an hour and a half his state was unchanged but his heart could only be heard beating during expiration. After two hours his breathing was quieter and his pulse 130 per minute and regular (the pulsus paradoxus had disappeared.) At two and a half hours breathing was regular, pulse regular at 160 per minute, sweating still profusely, blood pressure

120/85 m.m. Hg, pupils equal and reacted to light, left arm very stiff but reflexes obtained, plantar responses equivocal, ankle and knee clonus on left, ankle clonus on right, and left leg stiffer than right. After four hours there was less sweating, breathing was quieter, and signs unaltered except that left arm was less spastic and both plantars were extensor. At seven hours his colour was good, pulse 110 and regular, breathing quietly and recovery seemed a matter of course. However, during the night he had several twitchings of the left side of his face and his left arm and during the early morning he deteriorated. The pulse became rapid and weak and respiration Cheyne-Stokes in type. In spite of Coramine and oxygen he died at 5 a.m. that morning, that is 17 hours after the lung biopsy had been performed. His temperature throughout the episode had remained between 101 and 102 degrees.

At autopsy both pleural cavities were obliterated by dense adhesions so that a tension pneumothorax could have played no part in the clinical picture and clinically there had been no evidence of it. In the right lung there was a large cavity at the right apex with very large vessels lying on its inner surface. No needle mark or track could be seen but from the position of the cavity it was obvious that it had been entered by the point of the needle. There was also a small cavity in the leftapex. Widespread tuberculous infiltration was present throughout both lungs. The lung parenchyma between the areas of tuberculosis was

very firm and had a slightly brownish appearance of asbestosis. There was some hypertrophy of the right ventricle which suggested that the asbestosis had been of such duration as to give a mild bhronic cor pulmonale. The brain showed a greenish gelatinous exudate over the vertex and this was more prominent at the base where there were in addition small groups of tubercles in the membranes. Histologically the meninges showed a moderate polymorph and macrophage infiltration compatable with a diagnosis of tuberculous meningitis. The vessels and branches of the Circle of Willis were carefully dissected out but no obvious air embolus was found.

It seemed obvious that this patient's collapse and death was a direct result of the lung biopsy. It was probable that the needle entered one of the pulmonary veins in the wall of the cavity and thus produced a communication between the vessel and the air in the cavity to cause an air embolus. The patimnt's head was slightly raised and the air probably passed to the brain to give a picture almost idmntical with the decembrate rigidity of the experimental animal. He seemed well on the way to recovery when he gradually deteriorated and died. Probably the presence of the tuberculous meningitis prejudiced his chances of recovery.

This shocking experience changed ones whole attitude towards lung biopsy. From a completely harmless procedure it became a possibly lethal weapon. After this death no more

biopsies were done on living normal patients. I should like to record that had it not been for the encouragement of Professor Forman and Dr. Landau the investigation might well have proceeded no further. Having seen one case of air embolism one never wants to see another. From this time onwards no patient was biopsied who could not lie absolutely flat and cases where a cavity was suspected were also avoided.

Thus in the series of 83 biopsies although complications occurred in 45.8 per cent these figures are not nearly as bad as would appear at first sight. Only in five cases was there any anxiety attached to the sequelae of the biopsy.

There seemed no danger in doing serial biopsies and in many cases two biopsies were done on the same patient and two cases were subjected to three biopsies each. Case 37 had two biopsies done on the same side - one on the upper and the other on the lower lobe - within fifteen minutes of each other. She tolerated this procedure without any sequelae.

A feature of lung biopsy is that if complications are going to occur then they do so very soon after the biopsy. If nothing untoward has happened within five minutes of removal of the needle then one probably need have no fear that there will be any alarming events. This is important as it was not necessary to keep any special watch on the patient after the first five minutes.

It was thought that it might be of interest to see if the number of complications and their type occurred more commonly in any particular pathological condition or in relationship to certain lobes of the lung. In addition the frequency of complications as related to the age and sex of the patients was analysed. Whether complications become less as the experience of the doctor performing the biopsies becomes greater has also been considered.

It will be seen from Table 4 that the incidence of complications as a whole differed but little between the four large groups of biopsies - normal cases, cases done for diagnostic purposes, acute pneumonias, and chronic pneumonias. Haemoptysis occurred less frequently in the normal than in the other groups. Pneumothorax and its accompanying pain appeared to be at least twice as frequent in normal patients as in any of the other groups and was found least often in acute pneumonia cases. The two cases of cough and dyspnoea occurred in the pneumonia groups. The cases of syncope and air embolism occurred in the diagnostic and chronic pneumonia sections. Probably the only figure of significance was the high incidence of pneumothorax in the cases with normal lungs.

The distribution of complications was fairly equal in the various age groups (Table 6) except for the smaller incidence, surprisingly enough, in the sixth decade. There was almost an equal incidence of complications in the male and the female patients (Table 7).

The most interesting results were found when the relationship between the number of complications and the lobe of the lung on which biopsy had been performed, was considered (Table 8). When the situation of biopsy was in the upper lobes the total incidence of complications was 70 per cent and 66.7 percent for the right and left respectively (although in all fairness very few biopsies were done on the left upper lobe) and the corresponding figures for the right and left lower lobes were 36.7 per cent and 33.3 per cent respectively. The incidence of haemoptysis showed a similar trend. Pneumothorax seemed most commonly related to biopsies of the right lower lobe. Three of the five cases of serious complications occurred when the right upper lobe was the site of biopsy and the remaining two after biopsy of the left lower lobe. There seemed no reason for this apparently greater risk of sequelae following biopsy of the upper lobes of the lung.

A consideration of Tables 4 and 8 might suggest that there was some discrepancy between the number of complications and the total in the last column. For example, in Group I of Table 4 if one adds up the number of cases of haemoptysis, pain, pneumothorax, cough and dyspnoea, and syncope or air embolism the total is nine; but in the final column a total of five is given; the final column records the number of <u>biopsies</u> with complications not the total number of complications. The apparent discrepancies are due to more than one complication occurring in a single biopsy.

When one analysed the number of complications that occurred during the first forty biopsies as compared to those that resulted from the second consecutive forty biopsies the results were surprising. One would have expected that as one gained more experience with the method that the number of complications would diminish but complications during the second forty cases appeared to be as common as during the first forty. It would seem that whether complications occur or not depend almost entirely on the anatomy of the part of the lung penetrated by the needle.

The general conclusions from this analysis were that:

(1) Complications of a very mild nature, such as slight haemoptysis, slight pain or a shallow pneumothorax, must be expected in almost 50 per cent of cases.

(2) Serious complications are very infrequent but one must be prepared to deal with the very occasional case of tension pneumothorax or air embolism.

(3) If material spurts into the barrel of the syringe during the insertion of the needle these cases are the ones most likely to give trouble in the form of a moderate haemoptysis or one of the more serious sequelae.

(4) Complications are more likely to occur when an upper rather than a lower lobe is the site of biopsy.

(5) The age, sex and the actual underlying pathology of the patient probably play little part in determining whether or

not complications will follow biopsy.

(6) Cases should be done in the horizontal position and cases with suspected cavities or hydatid cysts are probably best avoided.

(7) Although lung biopsy is a relatively safe procedure it should not be done without due consideration of the fact that death may occur in the very occasional case. However if it is felt that useful information might be obtained by lung biopsy one should not hesitate to use the method.

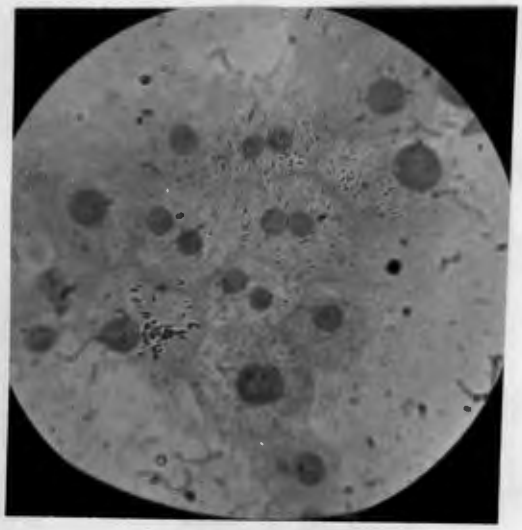
Under this section it would be best to deal with those five cases in which the material obtained was of hepatic or splenic origin. The case where tissue from the spleen was found in the needle was done after death, but the four cases of liver biopsy were done on living patients and there were no complications. The groups of cells did not correspond to any that occur in the lung and Professor Thompson (Department of Pathology) kindly confirmed the suspicion that these were liver cells.

All four of the liver cases had had biopsies done on the right side. The needle was inserted into the 8th interspace in the midaxillary line in Case 7-1 (crepitations at right base); in the 8th interspace below the angle of the scapula in Case 40 (bilateral lobar pneumonia); in the 5th interspace in the anterior axillary line in Case 46

(bronchopneumonia); and in the 8th interspace below the angle of the scapula in Case 58 (chronic pneumonia). In all these cases the needle was inserted into the area of maximal physical signs and thus it was surprising to find liver cells. However it must be remembered that these patients were in the horizontal position at the time of the biopsy and that the diaphragm might be at least one space higher than shown on an X-ray taken in the upright position. One was also liable to go into the liver if there was in addition any degree of pulmonary collapse with a slightly raised diaphragm. It was peculiar that in no case was the resistance of the diaphragm felt during the insertion of the needle. The material was a pale brownish colour and seemed in threads which made one suspect that the liver rather than the lung had been entered. In the latter a drop of fluid was usually obtained which might contain small pieces of material. It is felt that even knowing of the possibility that the liver might be entered and taking all precautions to avoid it occasionally liver cells will be obtained in biopsies on the right lower lobe.

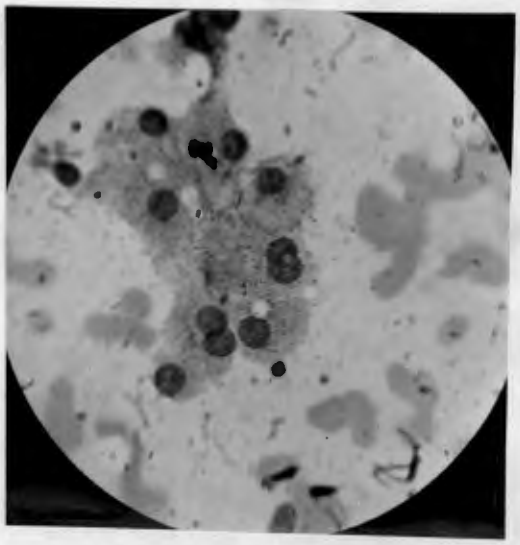
Splenic cells were obtained when Case 36 was biopsied through the left 6th interspace about 7 cm. from the midline of the sternum. This was more or less the area where numerous crepitations had been heard during life and where the situation of a pulmonary infarct was suspected. The smear contained no pulmonary cells and the innumerable small

CELLS FROM THE LIVER AND SPLEEN.



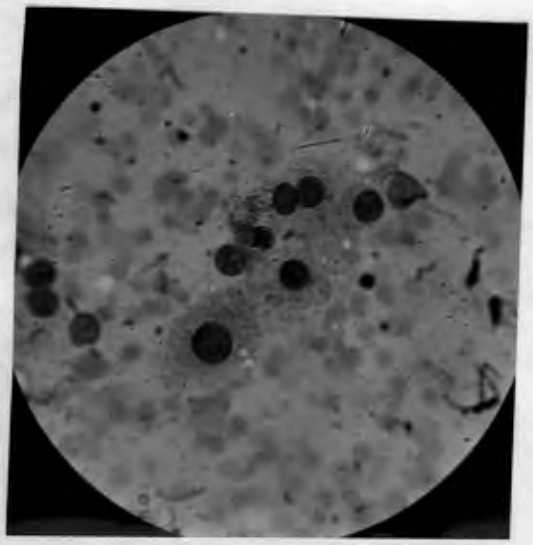
Case 7-1

Hepatic Cells
Oil Immersion



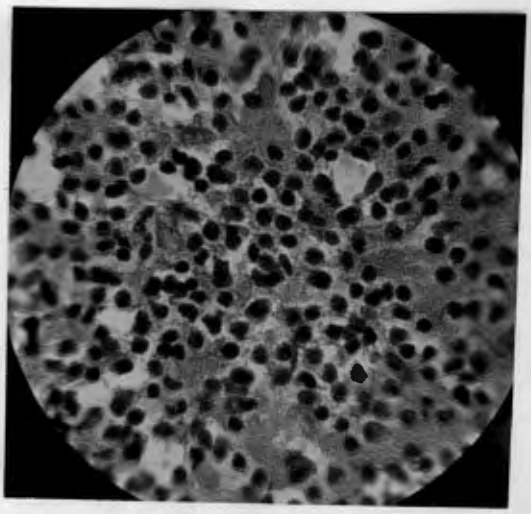
Case 40

Hepatic Cells
Oil Immersion



Case 46

Hepatic Cells
Oil Immersion



Case 36

Splenic Cells
Oil Immersion

round cells were obviously from the spleen. It seems very unlikely that with reasonable precautions splenic puncture would occur during life during an attempted lung biopsy.

In none of the series of lung biopsies described in the literature have liver or splenic cells been recorded.

SECTION II

LUNG BIOPSY OF THE NORMAL LUNG.

LUNG BIOPSY OF THE NORMAL LUNG.

Before one may enter into a discussion on the lung biopsy findings in pathological conditions, it is necessary to have as clear an idea, as possible, of the types of cells that may be obtained from a normal lung. Lung biopsy material if often difficult to interpret; in my ignorance at the onset of this investigation, I not infrequently labelled cells pathological which with wider experience I was able to identify as normal constituents of the lung.

Investigators have used lung biopsy mainly in the diagnosis of tumours and to obtain organisms from cases of pneumonia. The importance of a knowledge of the normal lung is illustrated by the fact that it is by no means difficult to confuse a group of non-ciliated bronchiolar epithelial cells or a group of alveolar cells which have undergone some metaplasia with a group of tumour cells; also no one, to date, has shown that the healthy human lung is sterile and does not normally contain pneumococci or other organisms.

THE STERILITY OF THE NORMAL HUMAN LUNG.

There is, to my knowledge, no direct information available as to whether or not the human lung is normally sterile. There does not appear any method of determining this other than by lung biopsy of living healthy human beings. Robertson (1941) quoted Bloomfield as stating that the

lungs of human beings were sterile. However, Bloomfield, in his original paper of 1922, was by no means so definite. All that he actually said was that, in health, few or no bacteria were present below the larynx; cultures made from the lungs of healthy animals were almost uniformily sterile; and finally "direct evidence from human beings is not readily obtainable". Godlowski (1949), who wrote the only paper on the normal lung biopsy, did not culture his material nor did he stain any of the slides to show organisms.

In the present series there were thirteen normal cases. The first ten cases (Cases 7, 8, 11, 13, 14, 15, 16, 17, 18 and 25) were on living patients whose lungs were both clinically and radiologically normal. After the death of Case 34, it was felt that it was not justifiable (however small the risk) to continue to biopsy patients whose lungs were normal. Thus the final three normal biopsies (Cases 36-1, 61 and 66) were done on cases soon after death, namely 5 hours, 1 hour and 5 minutes respectively. These biopsies done after death were not cultured but Gram stains were made; in the former two cases organisms were seen, but none were observed in the bbopsy done almost immediately after death. One may assume that in the former cases these organisms were post-mortem invaders.

These "control cases" were admitted with the following conditions:

Case 7 - pyuria with urethral stricture, and cervical fibrositis.

Case 8 - hemiplegia due to thrombosis probably on the basis of a syphilitic endarteritis.

Case 11 - uncomplicated gastric ulcer.

Case 13 - carcinoma of the stomach with hepatic secondaries.

Case 14 - hemiplegia due probably to thrombosis associated with essential hypertension.

Case 15 - anaemia of pregnancy or steatorrhoea.

Case 16 - tabes dorsalis.

Case 17 - cirrhosis of the liver and pyrexia of uncertain origin.

Case 18 - menopausal symptoms.

Case 25 - ascariasis and pyrexia of uncertain etiology.

Case 36-1 - rheumatic heart, S.B.E. and left sided pulmonary embolus.

Case 61 - hemiplegia, cerebral aneurysms and cerebral haemorrhage.

Case 66 - acute yellow atrophy following infectious hepatitis.

Cultures of the lung biopsy material were carried out in the 10 living cases. Of these six showed no growth on any of the culture media and no organisms were seen on the slides stained by Gram and Ziehl-Neelsen methods. Occasional large Gram positive budding organisms were observed but these were almost certainly contaminants of the non-sterile slides or organisms which had settled on the slides before staining.

Organisms were grown in four cases:

Case 8 - on the blood agar there were scanty colonies of diphtheroids and the serum broth grew scanty colonies of staphylococcus albus. There was no growth on the Lowenstein medium.

Case 11 - there was no growth on the inoculated area of the blood agar but the plate was heavily contaminated; coliform organisms were grown from the serum broth, and the Lowenstein medium was sterile.

Case 13 - there was no growth on the blood agar, the serum broth grew diphtheroids, and the Lowenstein medium was sterile.

Case 16 - on the blood agar there were two colonies of staphylococcus albus and two colonies of B. subtilis but both the serum broth and Lowenstein medium were sterile.

The growth in these cases was probably due to contamination of the culture medium before or during inoculation.

It might be argued that the biopsies that were sterile were due to the fact that with the technique used even if organisms were present they would not have grown. This was very unlikely as biopsies of cases of pneumonia which had not had chemotherapy almost invariably showed a growth of pneumococci; from other cases positive cultures of staphylococcus aureus and tubercle bacilli have been obtained.

It would appear to be fair to state that it is very probably that the normal human lung is sterile.

THE NORMAL PULMOGRAM.

The term "pulmogram" used by Godlowski (1949) means the cellular analysis of a smear of the material obtained by aspiration lung biopsy. Cells may be present which have their origin from the skin and thoracic wall, the pleura, the lung itself and from the blood in the pulmonary vascular tree.

In none of the 94 biopsy smears of this series were cells identified which might have come from the skin or thoracic wall. Using the technique described "contamination" of the slide by these cells became only a theoretical possibility.

Cells derived from the pleura were found in only very occasional cases. These were very easy to identify as they were very large cells and appeared to be well over 100 mu in diameter. The cytoplasm was rather fibrillar and stained eosinophilic with eosin and basophilic with Leishman; the nucleus was small and central or eccentric (see Fig. 18).

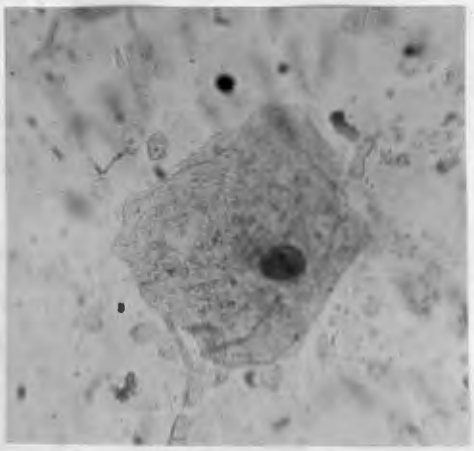


Figure 18. Case 61.
Pleural Cell.
Oil Immersion.

In all pulmograms cells were found from the pulmonary vessels. Red cells were seen in all cases and might be very numerous. The presence of white cells naturally depended on the amount of blood present and Godlowski (1949) showed that the differential count of these cells corresponded closely to the differential count in capillary blood obtained from the finger.

Most important were those cells derived from the lung tissue itself. Depending on the structures through which the needle passed one expected to find ciliated bronchial epithelium, ciliated bronchiolar epithelium, non-ciliated bronchiolar epithlium, macrophages, possibly peribronchial connective tissue and cells derived from the alveolar walls. Difficulty at once occurred when one considered the histology of the alveolus. There was no general agreement on what exactly constituted the alveolar wall and especially as to whether or not there was a continuous alveolar epithelial lining. Geever et al. (1943) summarised the views of the two opposing schools of thought. Maximow and Bloom, Lang, Fried, Loosli and others did not believe that there was an epithelial lining in the alveoli during normal postnatal life; Miller, Bremer, Cooper and others believed that a continuous epithelial lining existed; Aschoff, Bargmann, Seeman and others stated that the isolated septal cells in the capillary niches were epithelial. Geever et al. (1943) basing their opinion on 4000 autopsies performed at the

Colorado General Hospital, stated that the epithelium of the respiratory tract appeared to terminate more or less abruptly at the beginning of the alveolar ducts. The walls of both the alveoli and ducts were composed of capillaries in a delicate reticular and elastic stroma. The septal cells scattered therein could usually easily be distinguished from bronchiolar epithelium. They concluded that there was no evidence of a continuous alveolar epithelium in normal adult lungs. Robertson (1941), in his description of the anatomy of the lung, came to very much the same conclusions. He stated that the continuous epithelial lining ended with the ductus alveolaris. Ciliated epithelial cells extend only to the first part of the respiratory bronchiole. The wall of the alveolus was composed of an interlacing network of capillaries supported by a framework of elastic and collagenous fibrils and contained varying numbers of "septal" cells. These cells included the so-called "alveolar epithelium", histiocytes such as were found in the connective tissues, as well as undifferentiated mesenchymal cells and fibroblasts. The capillary walls were in direct contact with the air space except for a thin ground membrane and occasional septal cells attached to the wall. These septal cells did not form a continuous layer. Between the capillary loops were frequent window-like openings (the pores of Kohn) which constituted direct communication between adjacent alveoli. The plexus of lymphatics surrounding the bronchi did not extend beyond

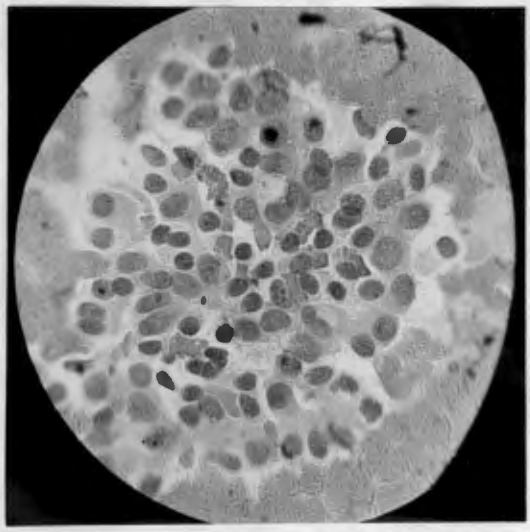
the ductus alveolaris. The only vessels in the alveolar walls were capillaries. At a round table conference at Duke University (Durham, N.C.) in 1936, Dr. Bremer of Harvard, Dr. Palmer of the Ohio State University and Dr. Bloom of the University of Chicago all aired their conflicting views. Finally the chairman, Charles C. Macklin, commented that the number of investigators who denied the presence of a continuous epithelium on the ground of their inability to demonstrate it, was increasing.

Godlowski (1949) described in his biopsy material groups of cells which he identified as alveolar epithelial cells. On many occasions similar cells have been seen in the present investigation. These cells were different from those lining the bronchioles, and appeared singly and in small groups. If they did not arise from the bronchioles and if they were not macrophages (and they definitely did not resemble these and never showed any phagocytic properties) then by elimination they must have their origin in the alveolar wall. Throughout this paper these will be designated "alveolar epithelial cells".

The following "pulmonary" cells might be found in normal lung biopsy material:

(1) Ciliated bronchial epithelial cells - these were found singly and in small groups. The cells were columnar with rather a large oval nucleus and cilia were clearly seen. In groups they might be arranged in palisade formation, the bottom of the row showing polygonal epithelial cells with round or oval nuclei. The chromatin of the nucleus was coarse and a nucleolus was clearly seen. Godlowski (1949) stated that they were very seldom seen in a normal biopsy and that they were frequently seen in conditions such as venous congestion and chronic bronchitis. However four of the thirteen normal cases in this series contained these cells. Although Godlowski's opinion was based on 75 normal biopsies it seemed logical that if the needle penetrated one or more bronchi then the biopsy material would contain these ciliated bronchial cells irrespective of whether the lung was normal or the seat of a pathological process.

These cells are illustrated in Figures 19 to 23.



Groups of Ciliated
Bronchial Epithelial Cells.

Oil Immersion.

Figure 19. Case 66.

Figure 20. Case 11.

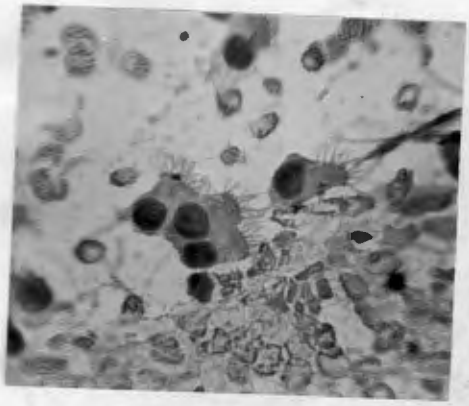


Figure 21. Case 26.

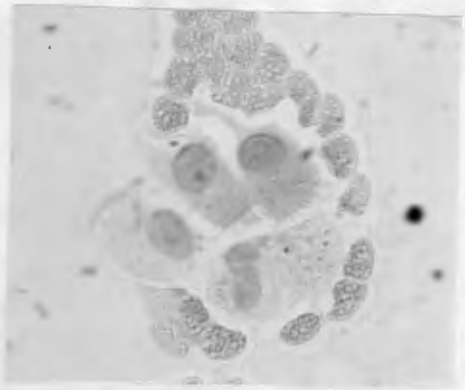


Figure 22. Case 11.

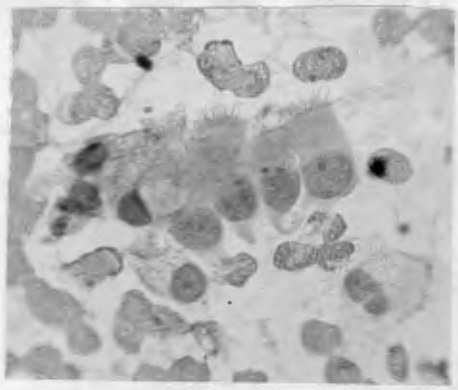


Figure 23. Case 11.

(2) Ciliated bronchiolar epithelial cells - these were essentially similar to the bronchial epithelial cells but were cuboidal and often arranged in small or large sheets. The cilia might be obvious or only showed as fine reddish dots lying between the adjacent cells. These were difficult to demonstrate on a microphotograph (Figure 24.) but could be clearly seen under oil immersion. The nuclei of these cells were large and varied considerably in size and contained one or more nucleoli. These cells were seen in only one of the normal cases.

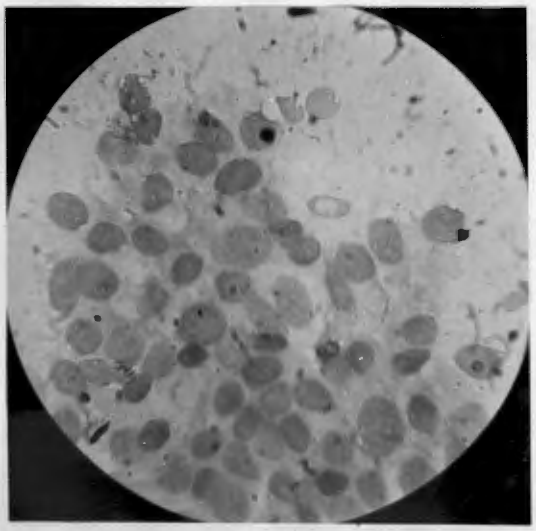


Figure 24. Case 6.

Ciliated Bronchiolar Epithelial Cells.

Oil Immersion.

(3) Non-ciliated bronchiolar epithelial cells - these appeared usually in sheets and dense groups. The individual cells resembled those of the ciliated type except for the absence of cilia. Again there was some variation in size and even in shape of the nucleus, some being round, oval or slightly kidney shaped. There might be one or more nucleoli. They were larger than the alveolar epithelial cells and had a much less vacuolated cytoplasm. These were seen in three of the normal biopsies.

Non-ciliated Bronchiolar Epithelial Cells.

Figure 25. Case 36-1.

Low Power.

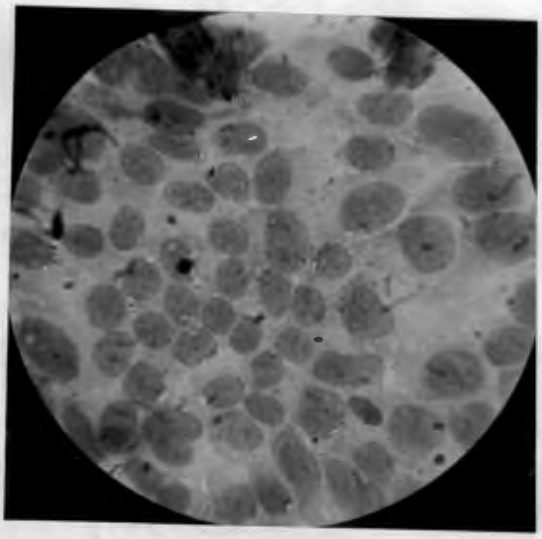


Figure 26. Case 36-1.

Oil Immersion

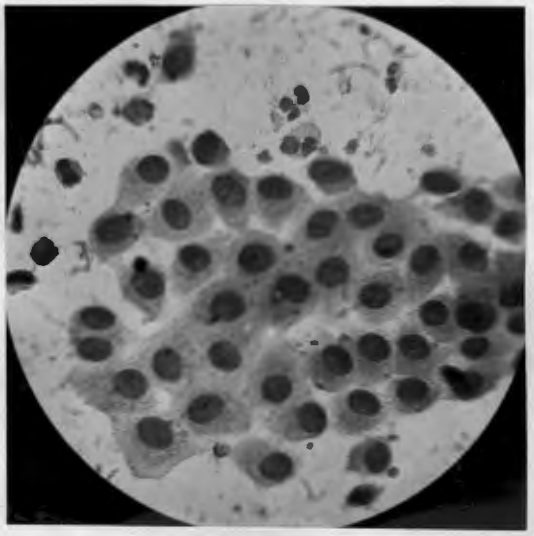
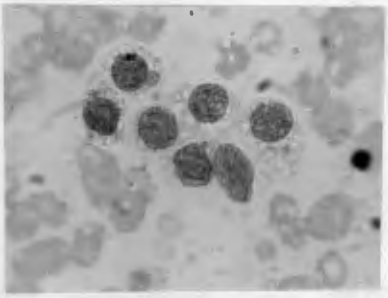


Figure 27. Case 50.

Oil Immersion

(4) Alveolar epithelial cells - these were smaller than the bronchiolar cells and were found singly or in small or large sheets. When isolated they showed a tendency to be round but in the sheets they took on a polygonal shape. The nucleus was small as compared to bronchiolar cells and was often central but might be eccentric and contained one or more nucleoli. The nuclei varied but little in size and took up about half the volume of the cell. The cytoplasm was finely or moderately vacuolated. These cells were present in most pulmograms and might be scanty or very numerous. They were found in 12 of the 13 control normal cases. Case 13, which did not show these cells, was a rather unsatisfactory biopsy where only very little material was obtained.



Alveolar Epithelial Cells.
Oil Immersion.

Figure 28. Case 11.

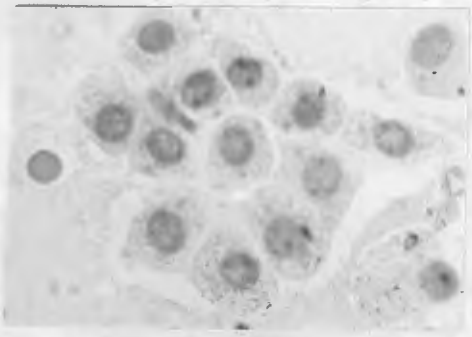


Figure 29. Case 11.

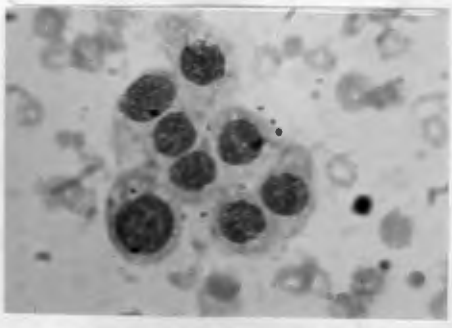


Figure 30. Case 28.

(5) Macrophages - these were of three main types and were found to a greater or lesser extent in all lung biopsies. They were essentially phagocytic cells.

(i) Small Macrophages with a single nucleus, vacuolated cytoplasm and few or no ingested particles. The nucleus was round, oval or kidney-shaped and contained one or more nucleoli. The nucleus was usually eccentric and took up about a third to a quarter of the cell. The cytoplasm might be finely, moderately or coarsely vacuolated. The cell was usually about 15 to 30 mu in diameter. These cells had probably been recently mobilised and were the precursors of the older fully developed "dust cells".

(ii) "Dust cells" - these were macrophages which appeared older than the smaller cells by virtue of the number of particles that they contained or by their size. These varied from 30 mu to over 100 mu in diameter. The smaller cells had numerous black or brown particles which varied in size and shape whilst the larger cells might be packed with particles or contain but few. The larger cells might have many nuclei (in one cell, there were eleven nuclei) which varied in shape and size but retained the same characteristics as those of the small macrophages. The variation in the shape and the size of the particles and the fact that they were not obviously stained by Gram's method seemed to indicate that they were not organisms; they were probably inhaled dust which had been ingested. Godlowski

stated that these cells were most frequently found in cases who were heavy tobacco smokers but in Case 11 there were very numerous macrophages and the patient smoked only 10 cigarettes a day; Case 36, who was a non-smoker, showed very many macrophages (in all fairness he died in acute rapidly fatal congestive heart failure which might have accounted for the increased macrophages). One could not agree with Godlowski that the large macrophages with the multiple nuclei were found rarely in the normal pulmogram as they were seen in five of the thirteen cases. The macrophages showed a tendency to collect towards the periphery of the smear. Godlowski put his limit of normal at three to five macrophages per high power field but this could not be accepted as in some of the present normal cases the macrophages were very frequent.

(iii) Alveolar histiocytes - these were apparently phagocytic cells having a permanent residence in the alveolar wall. These have been described by Godlowski and were frequently identified in the present series. The size was about the same as that of the small macrophage; they contained many or few particles. The nucleus was round or oval and usually eccentric and the chromatin was rather dense. One or more nucleoli might be seen. The cytoplasm was "smoother", less vacuolated and stained more deeply basophilic (with Leishman stain) than that of the small macrophage and this was really the only characteristic point

of differentiation. The alveolar histiocyte was indistinguishable from the small macrophage or small dust cell in a slide stained with haematoxylin and eosin. These cells were always scanty as compared with the other types of macrophage.

The origin of the macrophage is a much discussed problem and will be discussed under the section on the resolution of acute lobar pneumonia.

Macrophages were found in twelve of the normal cases. The one case which did not show them was Case 8 which was a very unsatisfactory biopsy and might be classed as one where almost no material was obtained.

Macrophages of various types are shown in Figures 31 to 41.

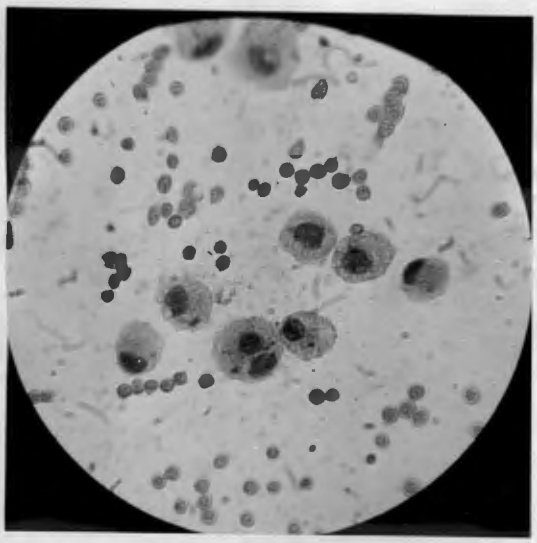


Figure 31. Case 61.

Small Macrophages and a Macrophage with two Nuclei. These Macrophages will be frequently illustrated in the sections on pneumonia.

Oil Immersion.

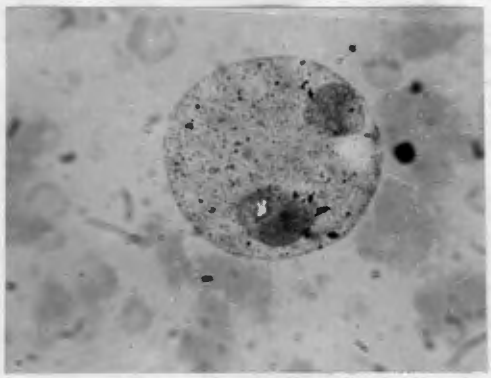


Figure 32. Case 11.

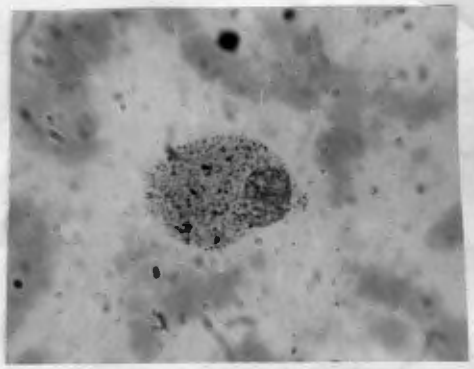


Figure 33. Case 11.

Dust Cells of Different Sizes with One, Two and Three nuclei. The Ingested Particles are well demonstrated.

Oil Immersion

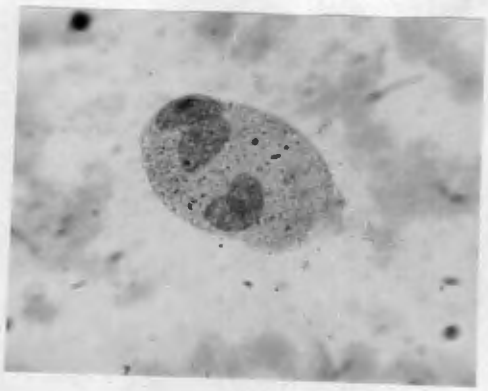


Figure 34. Case 11.

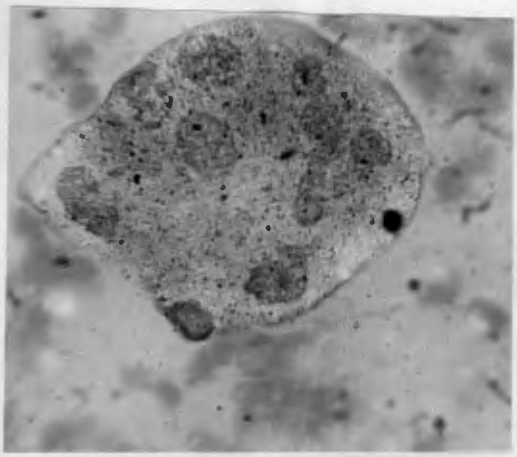


Figure 35. Case 11.

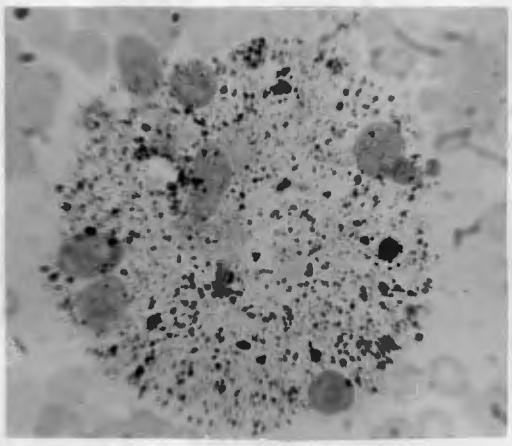


Figure 36. Case 10.

Large Multinucleated Dust Cells. The Number of Ingested Particles Shows Considerable Variation.

Oil Immersion.

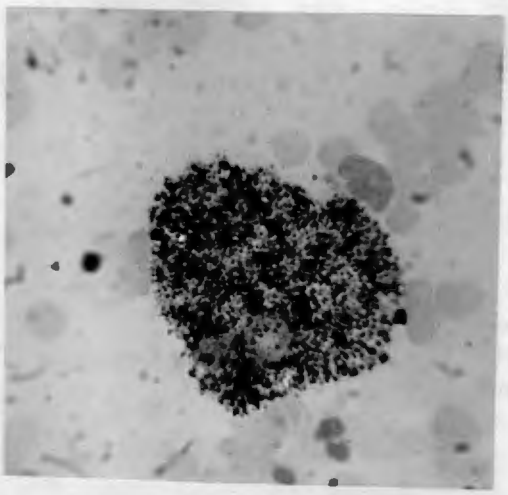


Figure 37. Case 10.

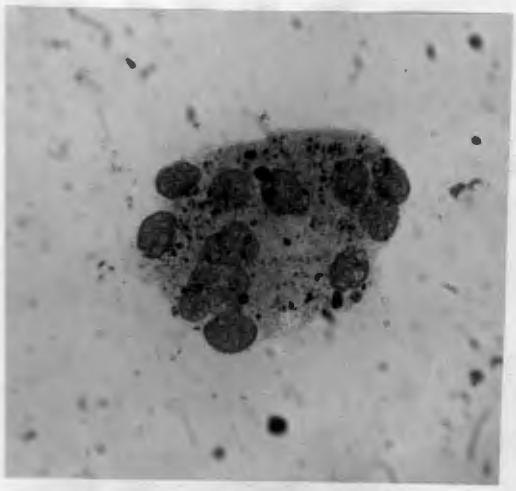


Figure 38. Case 11.

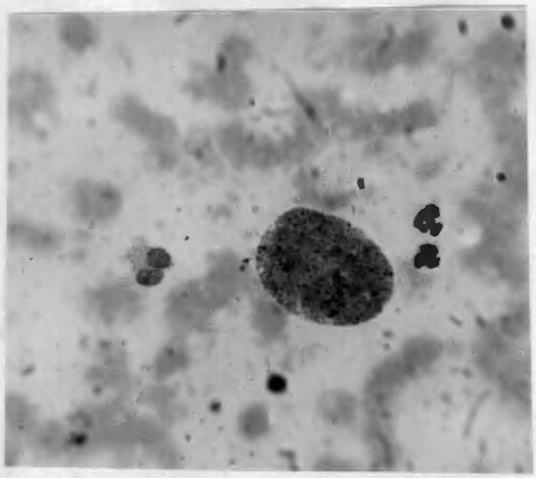


Figure 39. Case 11.

Alveolar Histiocyte.

Oil Immersion

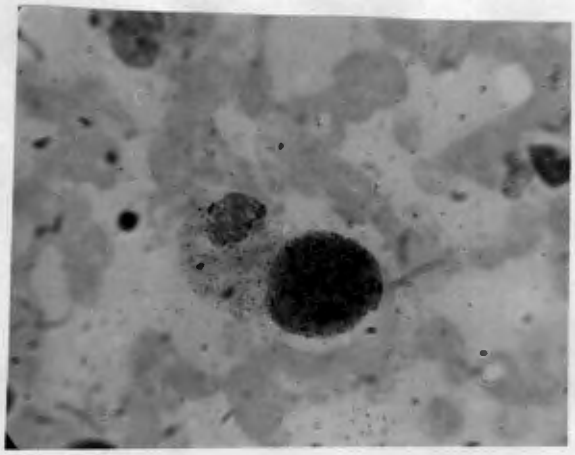


Figure 40. Case 17.

Alveolar Histiocyte and Small Macrophage.

Oil Immersion.

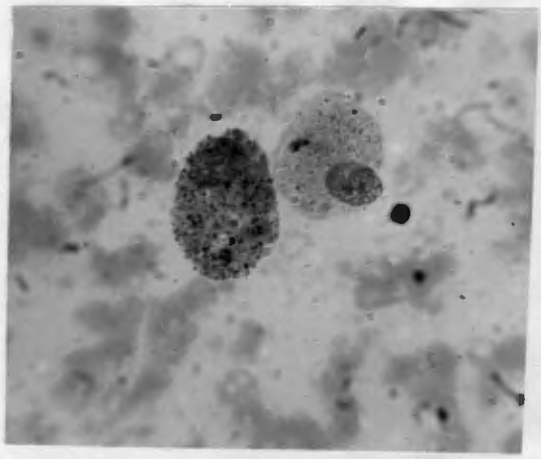


Figure 41. Case 11.

Alveolar Histiocyte and Small Macrophage.

Oil Immersion.

(6) "Non-nucleated plates" - These were thin structureless plates which were polygonal or quite irregular in outline. They were a pale blue with Leishman stain and a pale pink with eosin. Their presence was noted in two of the normal biopsies. Their origin was uncertain but Godlowski considered them definitely to be of pulmonary origin and that they might possibly form part of the structure of the alveolar wall. There was no doubt that some were artefacts due to the removal of the nuclei from macrophages during the smearing and crushing process. These plates seemed to have little or no significance

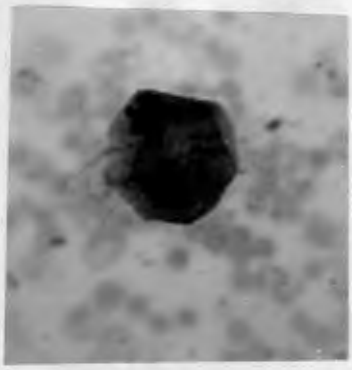


Figure 42. Case 69-2.

Non-nucleated plate. This is not a very typical example but was used because the microphotograph showed up so well. Usually they stain poorly and are much less well defined.

Oil Immersion.

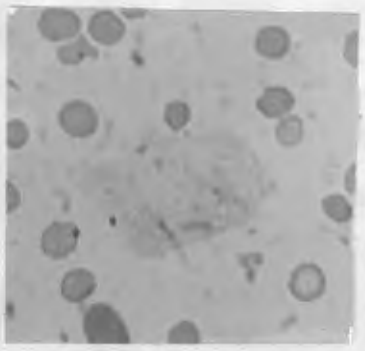


Figure 43. Case 17.

Non-nucleated plate artificially produced by separation of the nucleus from a macrophage. The nucleus is seen adjacent to the "plate".

Oil Immersion.

The pulmogram did not consist solely of a smear of individual cells and groups of cells but frequently showed actual masses of crushed tissue, in other words "pieces of lung". These masses of solid tissue were of two types; (1) There was the rather openwork type of tissue consisting of thick twisted threads (probably collagen) and thin straight fibrils with curled ends (probably elastic fibres) and amongst these lay alveolar cells, sometimes macrophages and not infrequently long thin cells with long thin nuclei (probably fibroblasts). This was exactly what was said to be found in the alveolar walls and thus these masses were probably pieces of <u>lung parenchyma</u>, that is a crushed conglomeration of many alveolar walls.

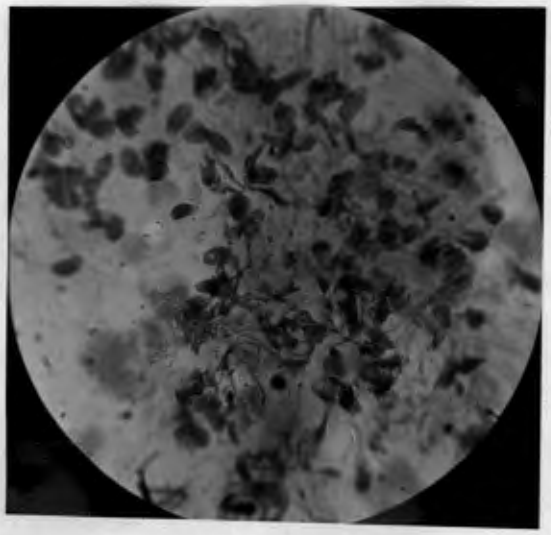


Figure 44. Case 17.
Lung Parenchyma.
Oil Immersion.

(2) Masses were seen which consisted of a rather dense

almost structureless material staining eosinophilic or basophilic with eosin and Leishman stain respectively. In this tissue there were a fair number of nuclei some round, some oval and some long and thin. In addition occasional elastic fibrils might be seen. The impression was that this was a rather dense connective tissue and might have its origin from the peribronchial or peribronchiolar regions. This was termed, for convenience, <u>interstitial tissue</u>. It was possible that the distinction between parenchyma and interstitial tissue was an artificial one and that interstitial tissue might be parenchyma which had been insufficiently crushed

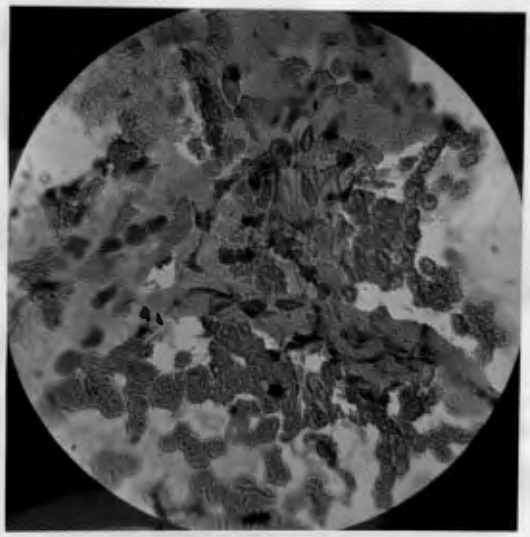


Figure 45. Case 17.
Interstitial Tissue.
Oil Immersion.

In ten of the normal cases either interstitial tissue or parenchyma or both were present.

Lastly there was the question of <u>black or dark brown particles</u>. As has been mentioned these were frequently seen ingested by macrophages but in addition these particles were often found lying free in the parenchyma and in the interstitial tissue. Not only were small particles present but occasionally large conglomerate masses were seen. These particles were probably inhaled dust and other foreign material.

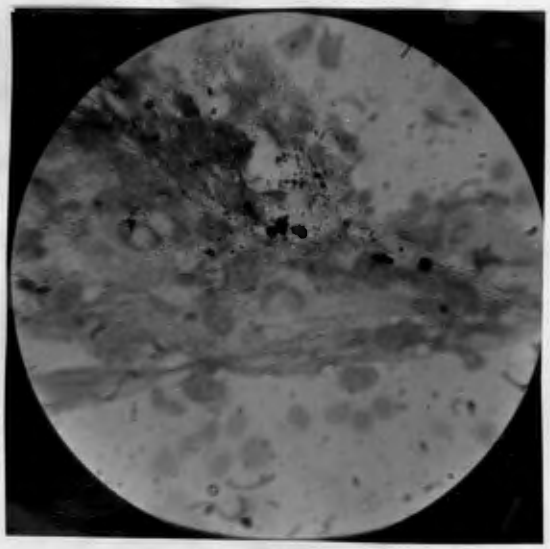


Figure 46. Case 39.

Black Particles and Small Masses.

Oil Immersion.

Thus, to summarise, in a lung biopsy of a normal lung one might expect all or some of the following elements:

(1) Red cells and white cells as in the peripheral blood.
(2) Pleural squamous epithelial cells.
(3) Ciliated bronchial epithelial cells.
(4) Ciliated bronchiolar epithelial cells.
(5) Non-ciliated bronchiolar epithelial cells.
(6) Alveolar epithelial cells.
(7) Macrophages which might be small with a single nucleus or large with many nuclei or which might be of the alveolar histiocyte type.
(8) Non-nucleated plates.
(9) Parenchyma.
(10) Interstitial tissue.
(11) Small and large black particles.

The pulmograms of the thirteen normal cases were as follows:

Case 7: Numerous red cells with a corresponding number of white cells; occasional groups of alveolar cells; several large masses of parenchyma.

Case 8: Few red cells; few non-nucleated plates; very scanty groups of cells probably alveolar; material obtained minimal.

Case 11: Numerous red cells with corresponding white cells; numerous macrophages of all types; occasional groups of alveolar cells; many groups of ciliated bronchial epithelium; large masses of parenchyma; small portions of interstitial tissue; scattered black pigmented particles.

Case 13: Fair number of red cells; fair number of small macrophages.

Case 14: Many red cells; few groups of pleural cells; macrophages of all types; small groups of alveolar cells; occasional groups of ciliated bronchial epithelial cells; occasional masses of parenchyma; scattered pigmented particles.

Case 15: Many red cells; macrophages of all types; alveolar cells; many areas of parenchyma.

Case 16: Many red cells; macrophages of all types; many alveolar cells singly and in groups; groups of non-ciliated bronchiolar epithelial cells; scanty interstitial tissue.

Case 17: Numerous red cells; macrophages of all types;

alveolar cells singly and in groups; non-nucleated plates; parenchyma; occasional masses of interstitial tissue; scattered pigmented particles.

Case 18: Fair amount of blood; scattered macrophages both small and large; parenchyma and interstitial tissue.

Case 25: Numerous red cells; scanty small and large macrophages; occasional masses of parenchyma; small groups of non-ciliated bronchiolar epithelial cells.

Case 36-1: Little blood; frequent macrophages of all types; numerous alveolar cells singly and in groups; groups of ciliated and non-ciliated bronchiolar epithelial cells; areas of interstitial tissue.

Case 61: Much blood; macrophages of all types; alveolar cells; ciliated bronchial cells; occasional pleural cells.

Case 66: Many red cells; macrophages of mainly the small type; scanty alveolar cells; ciliated bronchiolar epithelial cells; interstitial tissue; scattered black particles.

The situation of the biopsy was varied so that normal biopsies from all lobes were represented (for exact biopsy sites see Table 3, Group I, page 54).

SECTION III

LUNG BIOPSY USED FOR DIAGNOSTIC PURPOSES.

LUNG BIOPSY USED FOR DIAGNOSTIC PURPOSES.

The scope of lung biopsy in the field of diagnosis has been indeed narrow. The method was used mainly in the diagnosis of pulmonary tumours and it is unnecessary to recapitulate the work of Menetrier (1886), Fränkel (1896), Sokolowsky (1898), Jacobson (1899), Hellendall (1899), Ellis (1922), Ellis and Martin (1930), Sharp (1931), Fernandez and Tobias (1931), F.W. Stewart (1933), Martin and Ellis (1934), Lanari and Pavlovsky (1937), Craver and Binkley (1938), Blady (1939), Craver (1940), and van Ordstrand and Lambert (1941).

Lipoid pneumonia was diagnosed by lung biopsy by Faber, Carpenter and Pellicano (1942) and by Nathanson et al. (1943).

Horder (1909), van Ordstrand and Lambert (1941) and Godlowski (1949) all visualised a much wider field of application. Horder (1909) felt that the procedure was indicated in any case of consolidation where the causal organism was not isolated from the sputum, and in cases of lung abscess and bronchiectasis to obtain the organisms from the actual seat of the pathology. He described in some detail six of his cases - two of lung abscess, one pneumonia with mixed organisms (pneumococci, B.coli and B.influenzae), two staphylococcal pneumonias and one case of pneumonia with delayed resolution. Van Ordstrand and Lambert (1941) diagnosed as bronchogenic carcinoma cases which had been

labelled aneurysm, tuberculosis, interlobar empyema and interlobar effusion. In addition, of two cases diagnosed as lung tumours one was proved to be an unresolved pneumonia and the other a fuso-spirochaetal lung abscess. Godlowski (1949) performed ten biopsies on cases with "various pathological conditions" but gave no details of his results. He concluded, however, that lung biopsy might be used as a diagnostic procedure in various pathological conditions of the lung such as pneumoconiotic or chronic and acute inflammatory processes. The pathological alterations might be viewed on the bases of quantitative and qualitative changes of the cellular elements as well as bhanges of micro-histochemical analysis; this latter might be of particular value in the various types of pneumoconiosis, which offered clinically diagnostic difficulties.

It is not within the scope of this section to deal with the isolation of organisms in cases of pneumococcal pneumonia. Although this probably could be included under the diagnostic uses of lung biopsy, it falls more naturally in the sections dealing with pneumonia.

In this paper one hopes to touch the fringe of the wider application of lung biopsy for the diagnosis of many pulmonary conditions. It would be foolhardy to claim that, in every case with a puzzling pulmonary lesion, lung biopsy will reveal the diagnosis but, in selected cases, it is

Table 10.

The Types of Cases on which Lung Biopsy was Performed for Diagnostic Purposes.

Type of Case	Number of Cases
Pulmonary tuberculosis	8
Various pneumonias	7
Pulmonary infarction	2
?Rheumatic pneumonia	2
?Uraemic lung	1
Peripheral carcinoma of the lung	1
?Amoebic abscess of the lung	1
Bronchiectasis and lung abscess	1
Congenital cystic lung	1
Total	24

usual for lung biopsy to give information of value.

In this series, 29 lung biopsies were performed on 24 cases; three of these biopsies were performed after death. Table 10 gives some idea of the scope of this work and shows the varied conditions in which lung biopsy was used.

For the sake of brevity the following case histories have been much simplified but more detailed accounts with a few additional photographs and microphotographs may be found in the case reports in the appendix.

PULMONARY TUBERCULOSIS.

CASE 2:

S.S. (C. fem. 6 years) presented with a left sided hydro-pneumothorax with calcified areas in the collapsed left lung and an area of consolidation in the right lung. (See Figure 47).

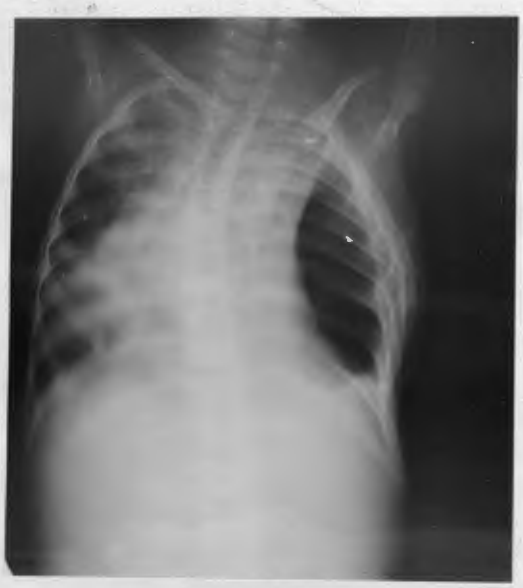


Figure 47. Case 2.
X-ray Chest. PA.
(On admission).

There were signs of congestive cardiac failure. The differential diagnosis lay between tuberculosis and histoplasmosis. Biopsy of the left lung was attempted but only a little sterile pus was obtained. The patient did not respond to penicillin and died immediately after a thoracentesis about a week later. Autopsy showed tuberculosis of both lungs. The clue to the diagnosis was the sterile pus obtained at biopsy. This could not have come from an "ordinary" lung abscess or empyema as the patient had had no chemotherapy and organisms would have been cultured. Tubercle bacilli were not seen in nor grown from the biopsy material.

CASE 5 AND 5-1:

S.M. (C. fem. 74 years) was a diabetic who presented with haemoptysis. Examination of the chest showed no abnormality but on X-ray there was a diffuse shadow involving the right upper lobe (see Figure 48). The differential diagnosis lay between carcinoma, tuberculosis and a low grade pneumonia. The right side of the diaphragm, although raised moved well and bronchoscopy revealed no abnormality; three specimens of gastric juice were negative for tubercle. Lung biopsy showed a low grade inflammatory lesion and the material was sterile. Six weeks later there had been no change in the patient's condition nor in the X-ray appearance and lung biopsy was repeated (5-1). Again the histological picture was that of a low grade inflammation, no organisms were seen and the blood agar and serum broth remained sterile. Tubercle bacilli were grown on the Lowenstein medium. The diagnosis of tuberculosis was confirmed at autopsy a month later.

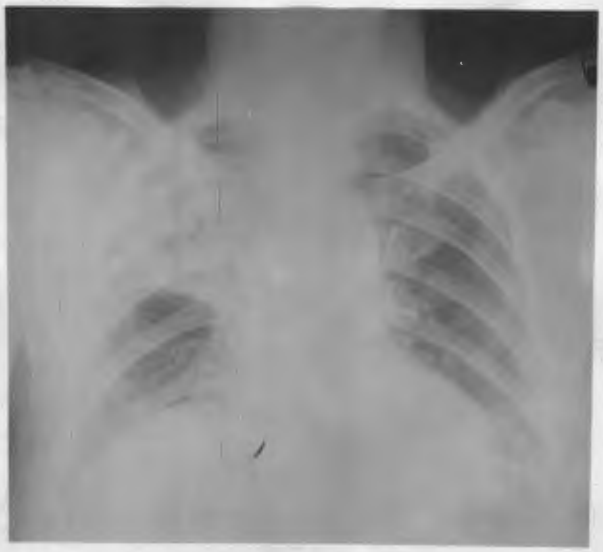


Figure 48. Case 5.
X-ray Chest. PA.
(On Admission).

CASE 12:

W.T. (N. male 46 years) was a proved case of tuberculosis with infiltrations in the left midzone and right base. The organisms had been found in the gastric juice. Lung biopsy was performed on the left side and showed a chronic inflammatory lesion but no organisms were seen. The cultures were sterile. Biopsy had been performed through the periphery of the lesion and the patient had been on streptomycin for 19 days; a subsequent gastric juice was negative for tubercle. The antibiotic therapy and the site of the biopsy possibly explained why the organisms were not found in nor grown from the biopsy material.

CASE 32:

M.H. (N. fem. 23 years) presented with a history strongly suggestive of a lung abscess. She was very ill, pyrexial, had copious foul sputum, signs of consolidation of the right upper lobe and a neutrophil leucocytosis. X-ray showed cavitation with surrounding pneumonitis in the right upper lobe (see Figure 49). She showed no response to penicillin and sulphatriad although the sputum lost its foul odour. X-ray showed the process to have spread to both lower lobes (see Figure 50). A fresh sputum grew no significant organisms and two fresh and four 24 hour sputa were negative for tubercle. Her temperature and general condition seemed to respond to streptomycin and P.A.S. but on X-ray the lesions were seen to have extended. Material resembling

caseation was obtained from the lung biopsy (see Figure 51) and tubercle bacilli were seen on the direct smear although none were grown on the Lowenstein medium.

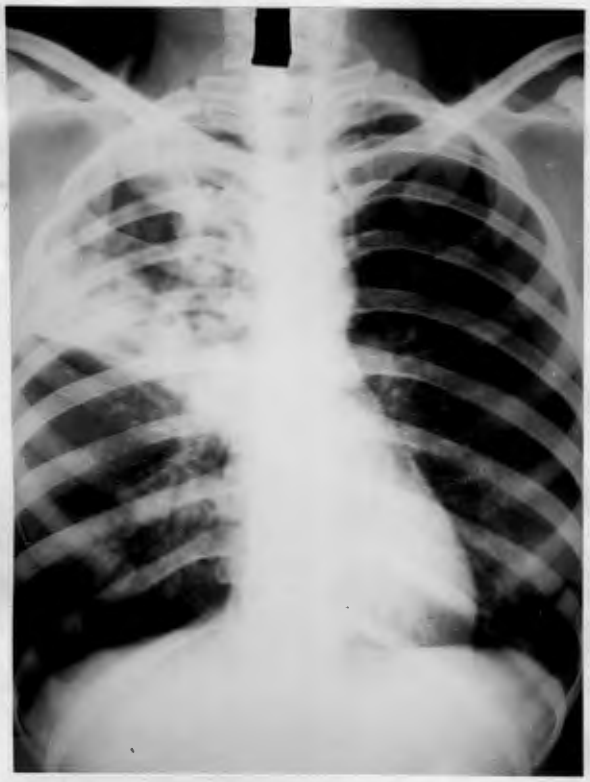


Figure 49. Case 32.
X-ray Chest. PA.
On Admission

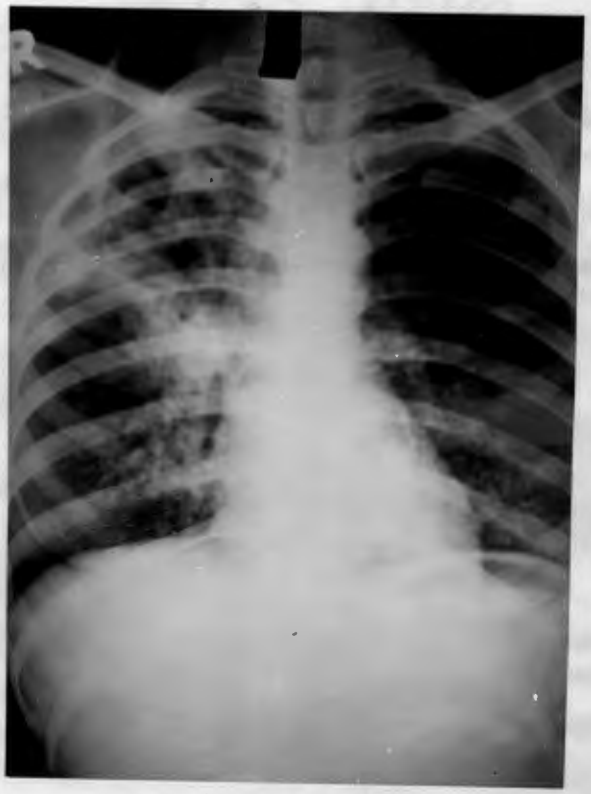


Figure 50. Case 32.
X-ray Chest. PA.
Two Weeks Later.

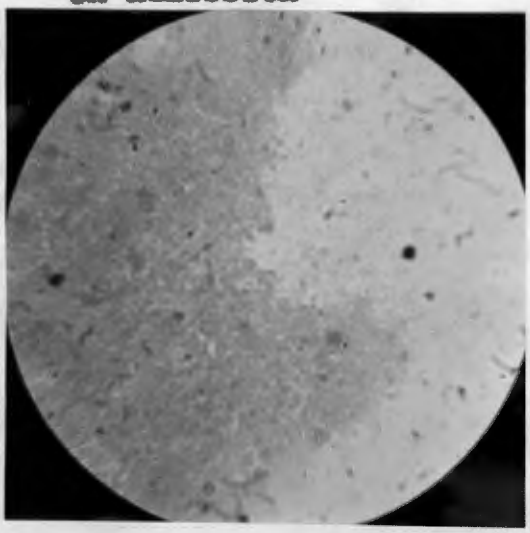


Figure 51. Case 32.
Lung Biopsy Material.
Caseation.
Oil Immersion.

CASE 34:

J.M. (C. male 45 years) gave a history of dyspnoea, left sided pleuritic pain, copious yellow sputum, loss of weight and night sweats for about 4 weeks. There were signs of consolidation of the right upper lobe and the left midzone. X-ray showed a large cavity in the right upper lobe with bronchogenic spread to the middle and lower lobes and throughout the left lung there was extensive infiltration with cavitation(see Figure 52). He was an obvious case of tuberculosis. A sputum was sent to the laboratory for investigation. Lung biopsy of the right upper lobe was followed by collapse and unconsciousness and the patient died about 17 hours later. The histological picture was that of a rather acute inflammation and in addition numerous asbestosis bodies were present. Tubercle bacilli were seen in the direct smear and grown on the Lowenstein medium. The sputum contained numerous tubercle bacilli. The diagnosis was confirmed at autopsy but in addition he was found to have had an early tuberculous meningitis.

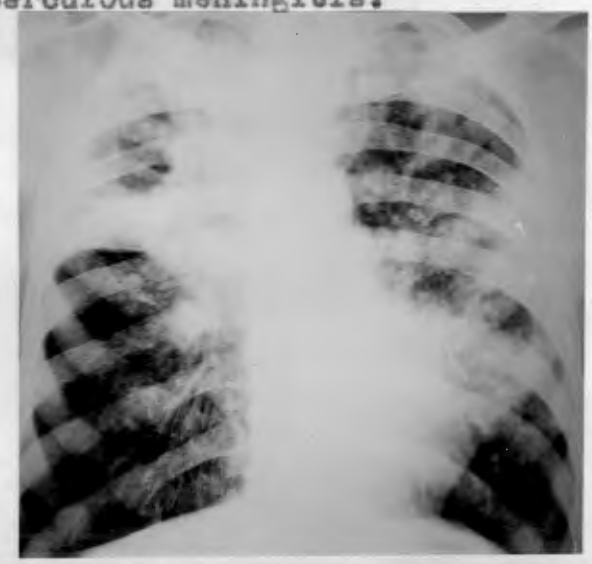


Figure 52. Case 34.
X-ray Chest. PA.

CASE 39:

C.M. (N. fem. 18 years) presented with vague symptoms of about two months duration - anorexia, loss of energy, abdominal pains, headaches and neck stiffness. For two weeks she had had a dry cough and pain in the interscapular region. She was about 16 weeks pregnant. She was very ill with a high temperature, signs of consolidation at the right base and generalised abdominal tenderness. There was no leucocytosis. X-ray showed consolidation at both bases. She showed no response to penicillin nor aureomycin. Sputum culture grew Friedlander's bacillus. Lung biopsy culture was sterile and the histology was that of a chronic inflammatory process. Sputa and gastric washings were negative for tubercle. She died about three weeks later. Autopsy showed small areas of tuberculosis in both lungs especially the right, an extensive tuberculous peritonitis and mensenteric and para-aortic adenitis, tubercles in the liver and spleen and over a hundred small tuberculomata scattered through the brain. The biopsy was of value in the it showed that the case was not a Friedlander's bacillus pneumonia and that the pulmonary condition was a chronic one and probably did not account for the whole clinical picture.

CASE 47:

F.A. (C. fem. 31 years) had had a cough with yellow and pink sputum for 4 months and had lost weight for two months. She was about 20 weeks pregnant. There was dullness on percussion and rhonchi and crepitations were heard at both lung bases but she was apyrexial. X-ray showed both lung fields to be unevenly stippled throughout by a hard fine miliary type of lesion but the infraclavicular regions and the apices seemed to be clearer than the rest; cavities appeared to be present in the right apex and midzone and in the left midzone. Gastric washings and sputa were negative for tubercle and the Mantoux test was positive . The diagnosis lay between tuberculosis (which was naturally most strongly favoured) and Boeck's sarcoid. Lung biopsy showed a chronic inflammatory lesion and no organisms were seen in the smears nor cultured on the blood agar or in the serum broth. On the Lowenstein medium there was a good growth of tubercle bacilli.

CASE 68:

O. van N. (C. male infant 4 months) was probably the most fascinating case of the diagnostic series. For two weeks he had had a cough and slight diarrhoea. He ran a pyrexia varying from 99 to 102 degrees and X-ray showed a homogeneous consolidation of the whole right upper lobe (see Figure 53). In spite of this the infant looked remarkably well. The X-ray appearance remained unchanged in spite of weeks of penicillin with and without sulphadiazine, and then weeks of terramycin. Lung biopsy was done using a 5 c.c. syringe

and an intramuscular needle. Caseous material was obtained (see Figure 54) and tubercle bacilli were seen on the direct smear and grown on the Lowenstein medium. This was probably a case of epituberculosis and the biopsy material was obtained from the primary focus.

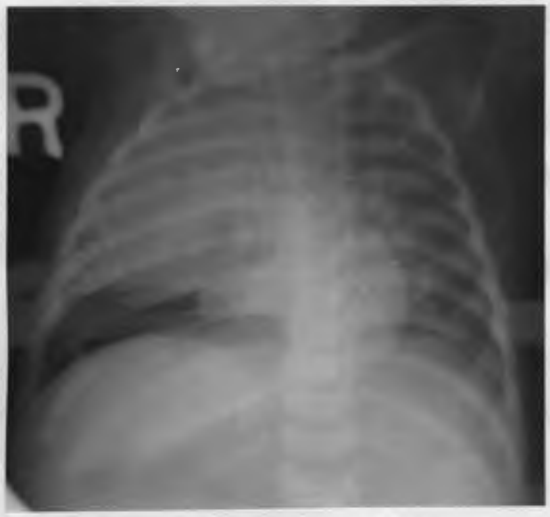


Figure 53. Case 68.

X-ray Chest . PA.

(Appearance the day before lung biopsy).

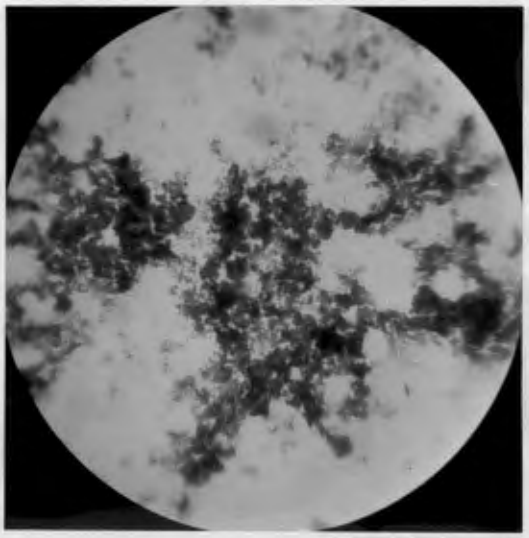


Figure 54. Case 68.

Lung Biopsy material. Caseation.

Oil Immersion.

Thus in these eight cases of pulmonary tuberculosis five showed the tubercle bacilli either on direct smear or culture or both; in one a tuberculous empyema should have been suspected; and in the last two cases it could be stated that the process was a chronic inflammatory one.

UNUSUAL PNEUMONIAS.

CASE 3:

A. van G. (C. fem. 48 years) gave a history of dyspnoea on exertion with oedema of the feet for 3 years and angina pectoris for two years. For five days she had been coughing blood-stained sputum, felt feverish and sweated excessively. She was apyrexial but very ill and dyspnoeic; hypertension with cardiomegaly and slight oedema of legs and sacrum; at left base dull with medium crepitations; leucocytosis of 37,000. She was treated as a cardiac failure with no response. Penicillin was started on the third day and X-ray showed consolidation of the left lower lobe. She died some hours later. The diagnosis had been pulmonary infarction. Lung biopsy done about 12 hours after death showed large masses of fibrin with innumerable neutrophils - the picture of an acute pneumonia. This was obviously a case where the wrong diagnosis had been made.

CASE 22:

J.L. (C. male 82 years) collapsed in the Docks and was too ill to state more than that he had been short of breath and had had pain in the chest for two days. He was very ill and pyrexial with the physical signs of consolidation of the right midzone and there was no leucocytosis. X-ray showed extensive infiltration of both lungs with probable cavities in the right midzone and left subclavicular region. He was

given large doses of penicillin and his temperature fell to subnormal but he died on his third day in hospital. No pathogens had been cultured from the sputum and no tubercle bacilli had been found. Biopsy of the right midzone six hours after death showed innumerable polymorphs associated with rather scanty fibrin (see Figure 55). No tubercle

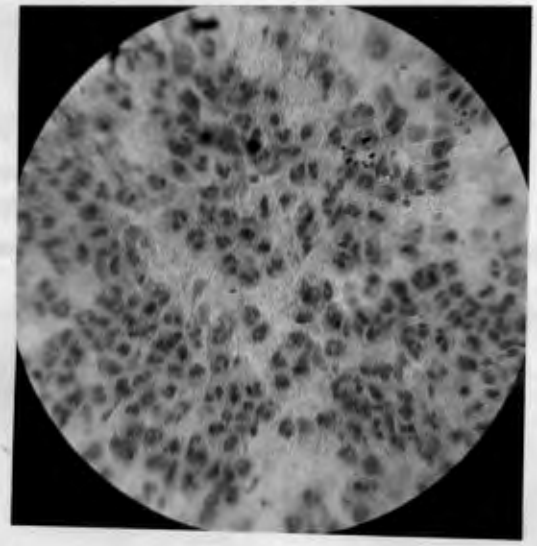


Figure 55. Case 22.

Lung Biopsy Material. Innumerable Polymorphs.

Oil Immersion.

bacilli nor pneumococci were seen. This was the picture of a very acute pneumonia in the stage of red hepatisation and was quite unlike the picture of tuberculosis. With such an acute lesion one would have expected tubercle bacilli to have been easily identified. The apparently short history and the acute inflammation was in favour of possibly a severe pneumococcal pneumonia but the explanation of the cavitation was difficult. Pneumococci disappear very rapidly from the lung when the patient is on penicillin. The possibility of multiple lung abscesses could not be excluded.

CASE 30:

S.C. (C. male 13 years) presented with the general appearance, blood pressure and urinary findings of an acute nephritis. In addition he was pyrexial, dyspnoeic and had a left basal consolidation. His blood showed a neutrophil leucocytosis. His temperature fell by crisis in response to penicillin and biopsy the day after admission showed the picture of an early resolving pneumonia. Within two weeks his chest was clear both clinically and radiologically and within four weeks his acute nephritis had completely subsided. This patient was included in this section, rather than in the section on acute pneumonia, because of this rather unusual association of acute nephritis and lobar pneumonia.

CASE 49 AND 49-1:

P.F.(C. male 41 years) had had attacks of apparently allergic asthma for 10 years and was admitted five days after the cessation of an acute attack. He did not appear ill although his temperature was 102 degrees. His chest was emphysematous and occasional rhonchi were heard. There was a slight leucocytosis. X-ray showed patchy areas of consolidation at the lung bases particularly on the right. His temperature fell to normal over six days without chemotherapy but crepitations were persistently heard at the right base posteriorly. Very little material was obtained by lung biopsy of the right base. This was sterile and the

histology showed small macrophages, dust cells and occasional alveolar cells. About two weeks later the lung was clear on X-ray and biopsy was repeated and showed the same histological appearance as before. Bronchogram of the right lung showed no abnormality. The absence of eosinophils excluded a Loeffler pneumonia and the picture was that of a resolving bronchopneumonia of uncertain etiology.

CASE 59 AND 59-1:

D.A. (C. male 58 years) had had a sticking pain in the right chest, a cough with white sputum and dyspnoea on exertion for about two months. He was not particularly ill but showed weight loss and early clubbing of the fingers. There was a right sided effusion which was found on aspiration to be sanguinous and sterile (even guinea pig inoculation was negative). The effusion was tapped several times but he continued with a pyrexia between 99 and 102 degrees. Gradually the fluid diminished in amount but the underlying atelectasis persisted and the mediastinum became gradually drawn over tb the right. Courses of penicillin and streptomycin had no effect on the pyrexia. Sputa and gastric washings were negative for tubercle and fresh sputa grew no significant organisms. Carcinoma of the lung had been suspected but bronchoscopy had shown no abnormality and thoracoscopy had demonstrated a fibrinous pleurisy suggestive of tuberculosis. A bronchogram showed

the collapse but there was no obvious bronchostenotic cause. Lung biopsy was performed two and a half months after admission. The slides showed large masses of fibrin with scanty polymorphs and macrophages with here and there groups of very pleomorphic cells which were probably metaplastic alveolar cells (see Figures 56 and 57). The culture media showed a pure growth of staphylococcus aureus

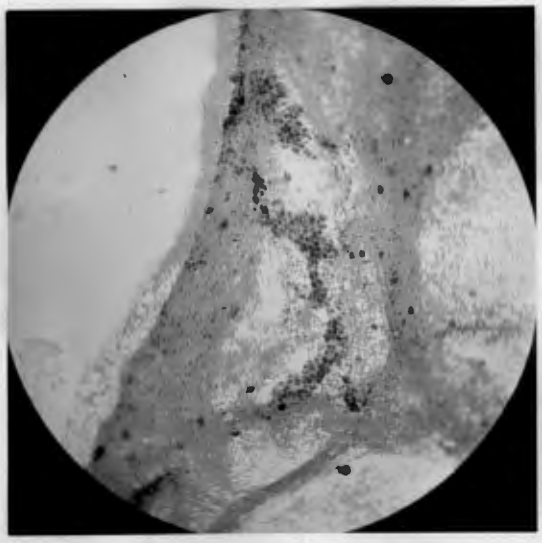


Figure 56. Case 59.
Lung Biopsy Material.
Groups of Pleomorphic
Cells and masses of Fibrin.
Low Power.

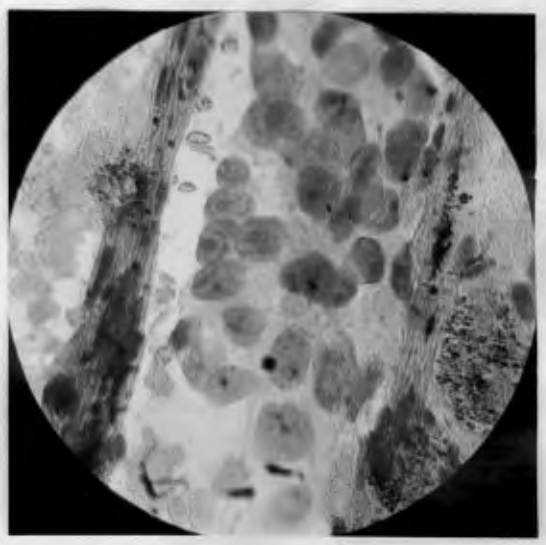


Figure 57. Case 59.
Lung Biopsy Material.
Group of Pleomorphic Cells.

Oil Immersion.

sensitive to penicillin and streptomycin. He was given courses of penicillin, streptomycin and aureomycin with no effect. Lung biopsy was repeated a month later and now there were in addition cells resembling fibroblasts associated with the fibrin. Cultures again grew staphylococcus aureus but this was now insensitive to penicillin. Penicillin inhalations caused no improvement and he was

transferred to a chronic sick home, The lung biopsy material seemed to indicate that this was a case of chronic staphylococcal pneumonia which had gone on to fibrosis, the organisms being isolated in small locules inaccessible to the action of the antibiotics.

CASE 64:

B.B. (N. male 40 years) was admitted with the signs and symptoms of a left basal bronchopneumonia. In addition there was dysphagia. His pyrexia responded very slowly to penicillin, sulphatriad and later streptomycin. About 4 weeks after admission, although his general condition was much improved, there were few signs of resolution of the pneumonia. Lung biopsy was followed by a bad reaction. The histological picture was that of a resolving pneumonia. A coagulase positive staphylococcus albus was grown in the serum broth only and this was probably a contaminant. A course of Calgluquine appeared to cause some degree of resolution. His dysphagia became worse and X-ray showed a marked stricture of the oesophagus at the level of the bifurcation of the trachea, the trachea itself being indented and displaced anteriorly. Oesophagoscopy revealed little additional information. He developed acute respiratory obstruction and died. The biopsy had shown that the pneumonia was resolving and that the pulmonary pathology was of little importance in relationship to the patient's

general condition at that time.

CASE 73:

G.T. (C. male 37 years) gave a history of slight cough and malaise for three days and feverishness for one day. He was not toxic and was apyrexial. Over the left chest anteriorly there was slight dullness and fine crepitations. The total white count was 21,000 with neutrophils 51 per cent and lymphocytes 41 per cent; the E.S.R. was 115 m.m. in one hour (Westergren). X-ray showed a peculiar stippled non-homogeneous opacity of the left upper lobe and to a lesser extent involving the right side (see Figures 58 and 59). The sputum was purulent.

He was started on penicillin and eight days later the physical signs were but little altered and lung biopsy was done. The biopsy material was sterile and from the sputum there grew only salivary organisms. The biopsy histology showed some fibrin with a fair number of polymorphs but there was also rather an excessive amount of tissue consisting of elastic and collagen fibrils with scattered black particles - there seemed both a subacute and a chronic inflammatory lesion. X-ray the next day showed that there had been marked clearing of the consolidation. He was discharged after 22 days and two weeks later his chest was normal on clinical examination in the outpatient department.

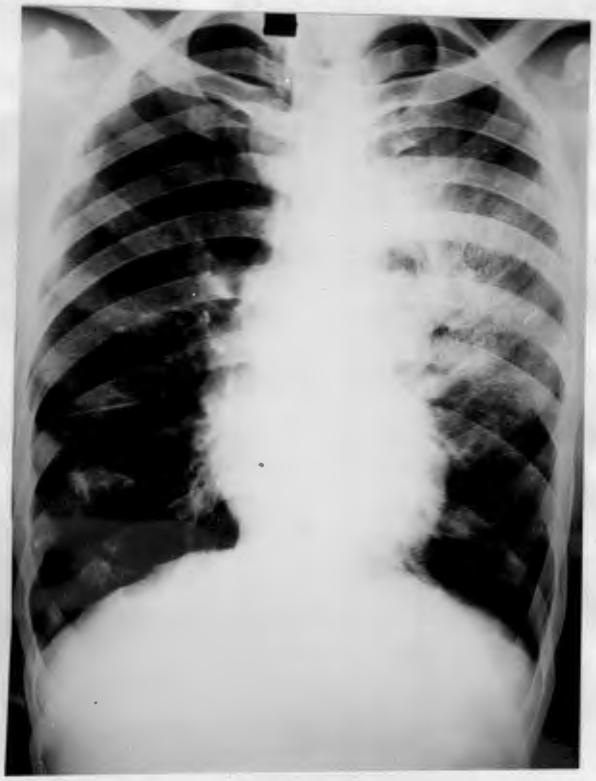


Figure 58. Case 73.
X-ray Chest. PA.
(On admission)

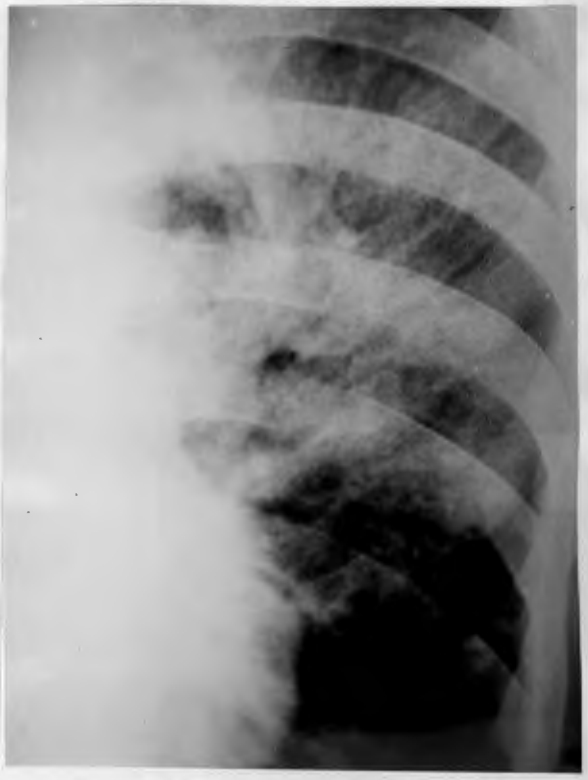


Figure 59. Case 73.
Enlarged View to show the unusual stippled appearance of the consolidation in the left midzone.

No check X-rays were done. The etiology of the consolidation was obscure - the X-ray appearance most closely resembled tuberculosis but the rapid resolution was against this; neither the clinical, radiological nor biopsy findings were in favour of a virus pneumonia; one was forced to conclude that this was a peculiar type of probably bacterial pneumonia.

In this group lung biopsy was used to diagnose two cases of bacterial pneumonia after death where the antemortem diagnosis had been pulmonary infarction and tuberculosis; one case was shown to be a pneumonia associated with acute nephritis; a chronic staphylococcal pneumonia was diagnosed mainly from the biopsy findings; a chronic bronchopneumonia was shown to be pathologically similar to chronic lobar pneumonia; little information was obtained in connection with a bronchopneumonia associated with allergic asthma but "an allergic lung" was probably excluded; and in the last case the biopsy made the etiology of the pneumonia even more obscure.

PULMONARY INFARCTION.

CASE 1:

G.S. (C. male 49 years) was a case of chronic congestive cardiac failure due to hypertension. He had had two episodes of shock with haemoptysis considered to be due to pulmonary infarction. On his last admission he complained of pain in the right chest, produced heavily blood stained sputum and crepitations were heard in the upper chest just to the right of the sternum. He died three days later in severe congestive failure. Lung biopsy was performed (using a 19 gauge aspirating needle without a stylette) 36 hours after death. The smear showed much blood, not infrequent heart failure cells and in one area these seemed associated with

a fibrinous mass. Little information was obtained from this first lung biopsy.

CASE 20:

H. du P. (C. male 33 years) was admitted with congestive cardiac failure associated with a nephritic lesion. The cardiac failure responded to therapy but a week after admission he developed a sudden pain in the right axilla and medium crepitations were heard in this region. X-ray showed a small area of "pneumonic" consolidation in the right middle lobe. His temperature was never more than 99 degrees. The lung biopsy material was sterile and the histology showed masses of a fibrinous material with rather scanty cells mainly small macrophages and a fair number of polymorphs. There was much blood present. The picture was compatible with that of a pulmonary infarct. He recovered well without chemotherapy.

Lung biopsy in these cases yielded little information. In Case 20 an ordinary bacterial pneumonia was probably excluded.

RHEUMATIC PNEUMONIA.

CASE 21:

D.A. (C. fem. 14 years) was admitted with acute rheumatic fever. There was a mitral stenosis. She responded well to salicylates but two weeks after admission she developed signs of consolidation at the right base and in the right axillary region. She was apyrexial and had a slight leucocytosis. Lung biopsy showed a fibrinous or albuminous exudate with a fair number of small macrophages. The cultures were negative. The chest condition cleared without chemotherapy. The picture was compatible with that of a mild early rheumatic pneumonia, or possibly a pulmonary infarct.

CASE 52:

S.I. (M. male 12 years) was admitted with acute rheumatic fever and slight left sided cardiac failure. Mitral stenosis was present. He responded to salicylates but in the second week suddenly developed signs of acute nephritis, congestive cardiac failure and consolidation of the whole right upper lobe. At no time was his temperature over 99,5 degrees. He responded to mersalyl and digitalis and was given penicillin. About a week later the consolidation was unchanged and lung biopsy was performed. The material was sterile. Histology showed large masses of fibrin with a poor cell response mainly in the form of small macrophages. The consolidation

gradually resolved over a period of about a month. The blood urea had never been raised. The biopsy findings were compatible with the diagnosis of a rheumatic lung.

In both these cases the findings were compatible with that of a rheumatic pneumonia although it was impossible to give a definite answer. However, one was able to state that a bacterial pneumonia was very unlikely.

URAEMIC LUNG.

CASE 43:

L.C. (C. male 12 years) was admitted in severe congestive cardiac failure with hypertension (blood pressure 205/155 m.m.Hg) and a renal lesion of either acute nephritis or an acute exacerbation of a chronic nephritis. At the right base there was dullness and resonating medium crepitations. His blood urea was 128mg. per cent. A week later there were more definite signs of right basal consolidation. Biopsy was performed to try and distinguish whether the physical signs were of a bacterial, uraemic or congestive nature. The cultures were sterile. There appeared to be masses of a fine fibrinous material containing small macrophages, a few polymorphs, alveolar cells and cells which closely resemble the ordinary monocytes of the blood. The patient went steadily downhill to die in congestive failure and uraemia. The biopsy histology was compatible with the

diagnosis of an uraemic lung. There is no information on the appearance of biopsy material from chronic passive congestion and until such information becomes available a definite statement that this was not just congestion could not be made.

CARCINOMA OF THE LUNG.

CASE 10:

B.B. (N. male 58 years) complained of a dry irritating cough for a year, and loss of weight and hoarseness of the voice for two months. There was slight dullness at the right apex and X-ray showed a well marked peripheral rounded opacity. (See Figures 60 and 61). Bronchoscopy showed no abnormality

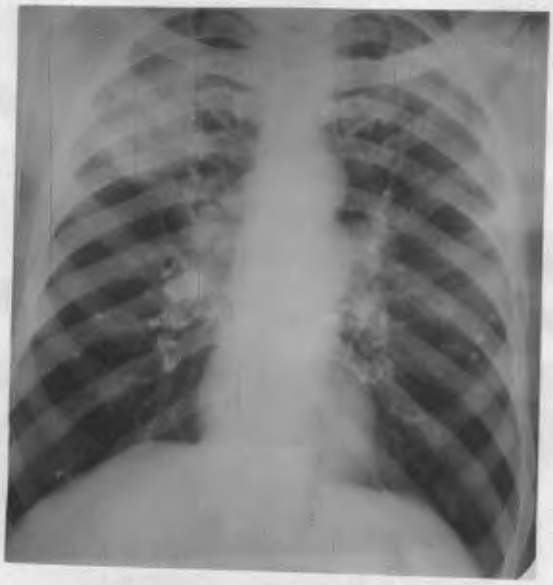


Figure 60. Case 10.
X-ray Chest. PA.

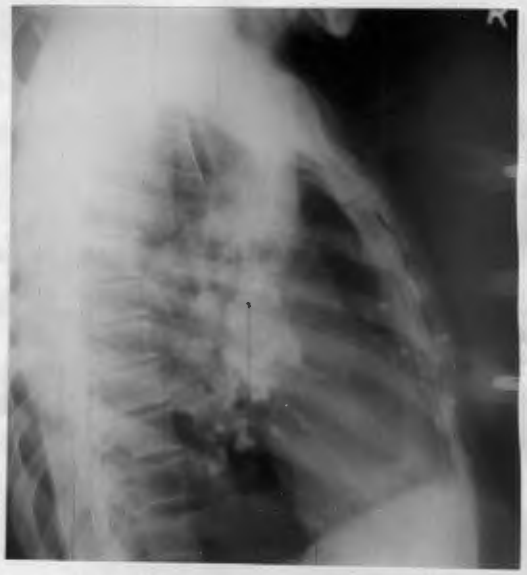
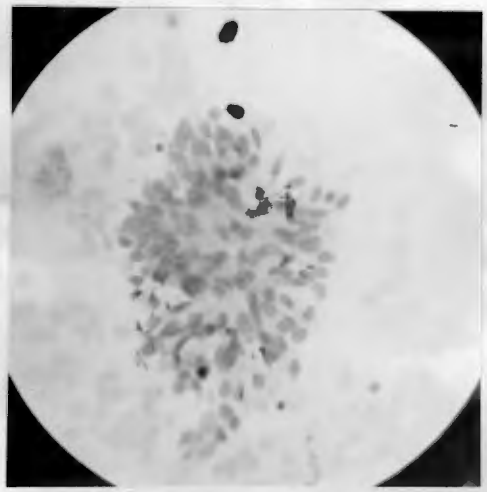
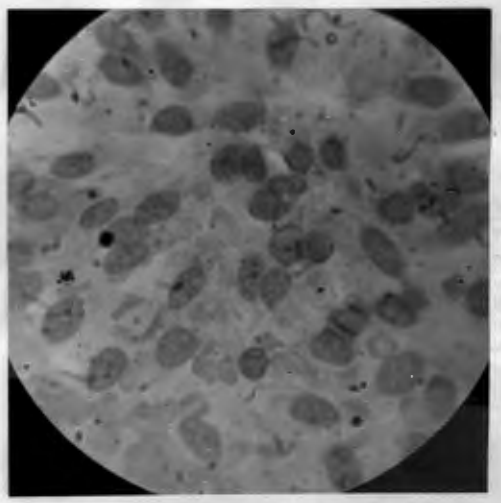


Figure 61. Case 10.
X-ray Chest. Lateral.

and sputa were negative for tubercle. On lung biopsy a solid mass was encountered. The milky bloody material was sterile and microscopically showed many groups of large cells with large nuclei showing some variation in size. These cells were probably malignant (see Figures 62 and 63). In addition there were some areas of fibrin with polymorphs indicating an associated inflammatory reaction. In spite of these findings the patient was treated as a lung abscess. He gradually deteriorated and died about two months later. At autopsy there was a carcinoma of the lung of the spheroidal cell type showing some secondary suppuration.



Case 10. Figure 62.
Lung Biopsy Material
Carcinoma Cells.
High Power.



Case 10. Figure 63.
Lung Biopsy Material
Carcinoma Cells.
Oil Immersion.

During the eighteen months of this investigation this was the only carcinoma of the lung which was seen.

AMOEBIC ABSCESS OF THE LUNG.

CASE 62 AND 62-1:

J.M. (N. male 29 years) sustained a blow by a chain on the right side of the chest two months before admission and had had slight pain in this region ever since. For a month he had had a mild diarrhoea. For about a week there had been an acute episode with severe pain in the right chest, dyspnoea and sputum which was at first purulent and then bloody. He was slightly dyspnoeic and pyrexial; at the right base there was dullness with grossly diminished air entry but increased vocal resonance; liver just palpable, of normal consistency but tender; urine contained a little urobilin, leucocytes 14,450 with 80 per cent neutrophils. X-ray showed a postero-lateral shadow with a rounded upper border in the right costophrenic angle. No chemotherapy was given. Dark red thick material was obtained by lung biopsy. This was sterile and showed no organisms on the smear. It consisted of necrotic material, many pus cells, red cells and crystals probably of haemochromogen. The sputum grew salivary organisms only. In spite of penicillin and sulphatriad he continued to be ill and ran a temperature between 99 and 103 degrees. His sputum continued to contain much dark red blood and the neutrophil leucocytosis was maintained. The penicillin dosage was doubled with no effect. Sigmoidoscopy showed no abnormality. Chemotherapy was stopped and the patient still did not improve. He was started

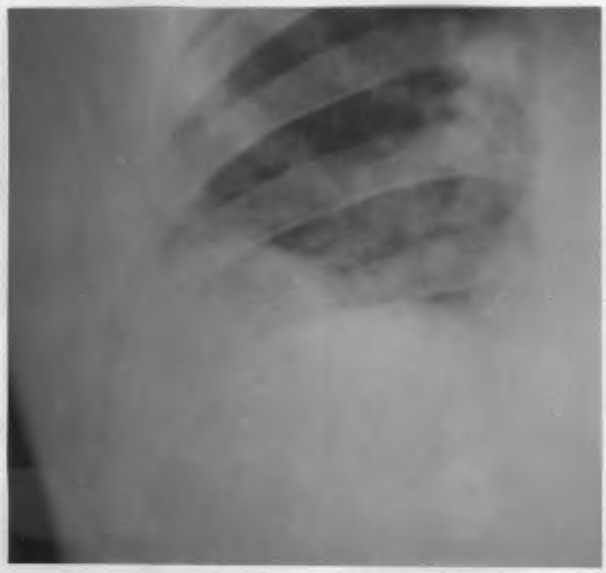


Figure 64. Case 62.

X-ray Chest. PA.

Close up view to show rounded shadow in right costo-phrenic angle.

on emetine and after the third injection his temperature became normal and he remained apyrexial and subsequently made a completely uneventful recovery; the lesion at the right base considerably diminished in size. After the seventh emetine injection another lung biopsy (62-1) yielded cells compatible with normal. If this had been an infected haematoma the biopsy material should not have been sterile and the patient would have responded to chemotherapy. If the haematoma was not infected why had there been this acute episode? The biopsy material closely resembled amoebic pus and the response to emetine was dramatic. Without the information obtained by lung biopsy this case would have been subject to a very wide range of speculation.

BRONCHIECTASIS WITH LUNG ABSCESS.

CASE 44 AND 44-1:

E.R. (C. fem. 18 years) gave a history of pleuritic pain in the left chest, dyspnoea and feverishness for one day. On examination she appeared to be an ordinary pneumonia with a left lower lobe consolidation with a little overlying fluid. There was a high neutrophil leucocytosis. The clinical diagnosis appeared to be confirmed by the X-ray. She responded gradually to chemotherapy. On the fifth day an attempt was made to aspirate the fluid. No fluid was obtained but small particles of tissue found in the local anaesthetic needle were examined. These consisted of densely packed masses of polymorphs possibly with fibrin. The cultures were negative. Five days later an orthodox lung biopsy (44-1) was attempted and at a depth of about 3 cm. thick creamy pus was obtained (about 3ml. were aspirated). This pus was sterile. The penicillin dosage was doubled and over about a month complete resolution gradually took place. Bronchogram showed bronchiectasis of the anterior and posterior basal segments of the left lower lobe. Without lung biopsy one would have accepted this case as a pneumonia with slow resolution secondary to bronchiectasis. The first biopsy probably obtained material from the wall of the abscess and with the second the abscess itself was probably aspirated. One must conclude that this was a case of lung abscess associated with bronchiectasis.

CONGENITAL CYSTIC LUNG.

CASE 27:

N.M. (C. fem. 14 years) presented with cough and haemoptysis and straight X-ray of the chest showed an appearance suggestive of congenital cysts in the right upper lobe.

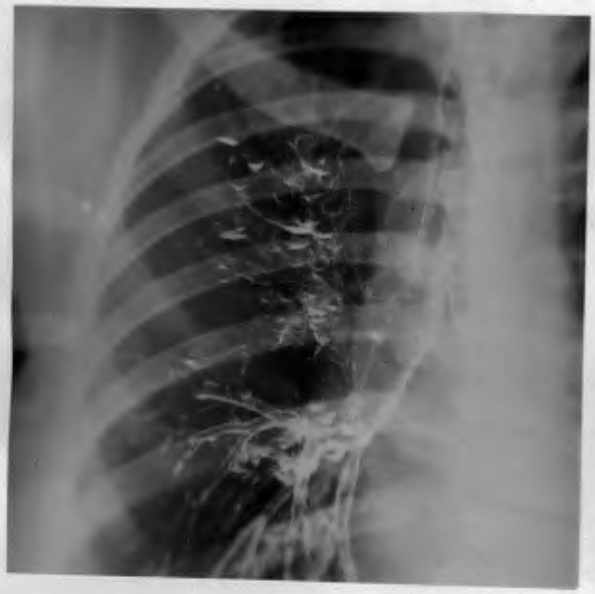


Figure 65. Case 27.
Bronchogram. PA.
Close up view of right upper lobe to show cysts.

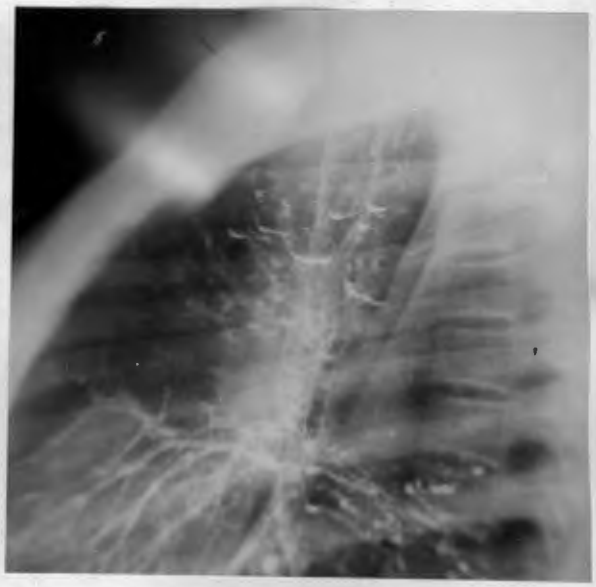


Figure 66. Case 27.
Bronchogram. Lateral
Close up view to show cysts.

She ran a slight pyrexia and the blood showed a slight leucocytosis. She produced only one specimen of sputum from which there was grown a good culture, of Friedlander's bacillus. The possibility of a low grade Friedlander

bacillus infection could not be excluded and she "refused" to produce any more sputum. Lung biopsy was performed and the histology was compatible with a very mild inflammatory condition. The biopsy material was sterile. Bronchogram confirmed the diagnosis of congenital cystic lung or possibly a bronchiectasis sicca. Lung biopsy in this case was very useful to determine if the organism isolated from the sputum had its origin in the lung.

It should be emphasised that the lung biopsy material must be considered together with a clear picture of the clinical state of the patient. It was not very often that the lung biopsy bacteriology or histology alone would give the diagnosis. The chief value of biopsy was when the findings were compatible with one diagnosis and made other diagnoses unlikely. It was seldom that one could state more than this. It must be realised that the diagnostic interpretations of the above cases were based on an experience of only 94 aspirations and that there was little or no literature with which one could compare the results. The histology of the lung biopsy of pulmonary conditions will be placed on a firm basis only after many hundreds of cases have been reported. The above work should be considered very much as a preliminary report.

ASBESTOSIS.

One of the most surprising results of this investigation was the incidental discovery of asbestos bodies in the lungs of four cases. In two of these (Cases 23 and 38) the asbestos bodies were very scanty but in the other two cases they were numerous (Cases 34 and 41). In none of these cases was there any history of contact with asbestos. Three of the cases (23, 38 and 41) were admitted with acute pneumococcal lobar pneumonia and resolution took place perfectly normally. Case 34 had widespread pulmonary tuberculosis. These patients apparently did not have "asbestosis". This was defined by Merewether as a specific occupational disease of the lungs caused by the inhalation of asbestos dust and characterised by the progressive replacement of the essential active functioning tissue of the lung by inactive non-functioning fibrous or scar tissue. Lanza (1938) emphasised that the presence of asbestos bodies in the lung signified exposure to asbestos dust but could not be depended upon for a diagnosis of asbestosis. Asbestos is used for many purposes, especially for roofing, and these patients probably were occasionally exposed to the asbestos dust. The asbestos bodies were shown very well in the biopsy material and lung biopsy should be a valuable aid in the diagnosis of suspected asbestosis. In neither of the two cases where sputum was available (Cases 38 and 41) were asbestos bodies found in ordinary sputum smears.

Asbestos bodies are illustrated in Figures 67 to 76.

In some cases phagocytosis by macrophages was taking place.

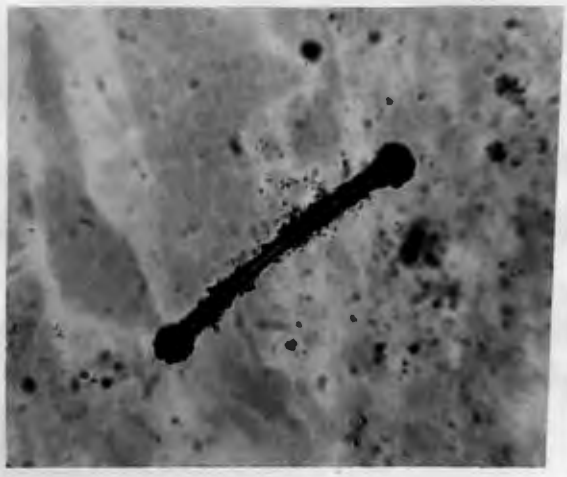


Figure 67. Case 23.
Asbestos Body
Oil Immersion.

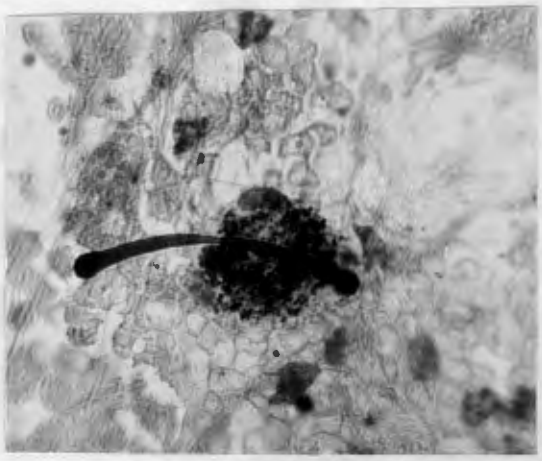


Figure 68. Case 34.
Asbestos Body being ingested by a macrophage.
Oil Immersion.

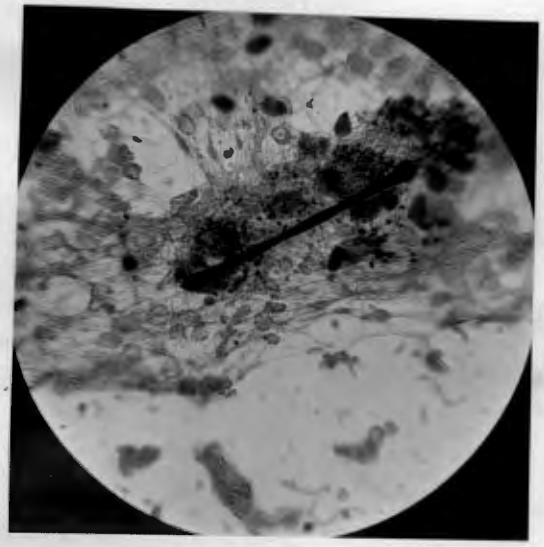


Figure 69. Case 34.
Asbestos Body and a group of macrophages.
Oil Immersion.

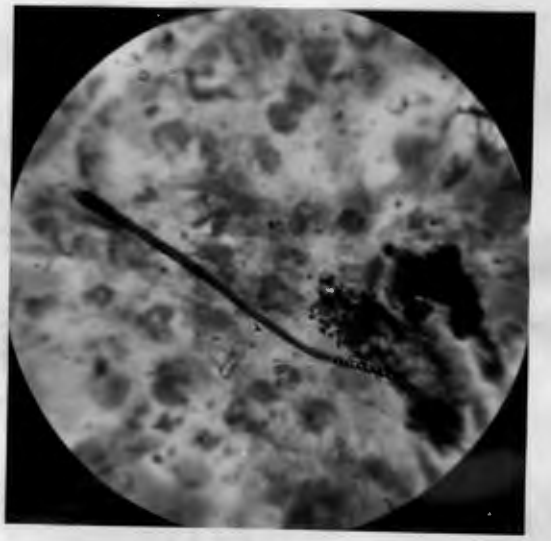


Figure 70. Case 34.
Asbestos Body.
Oil Immersion.

ASBESTOS BODIES WITHIN DUST CELLS.

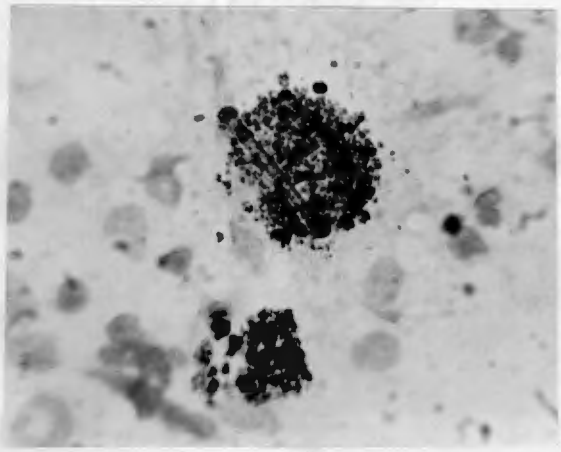


Figure 71. Case 38.
Oil Immersion.

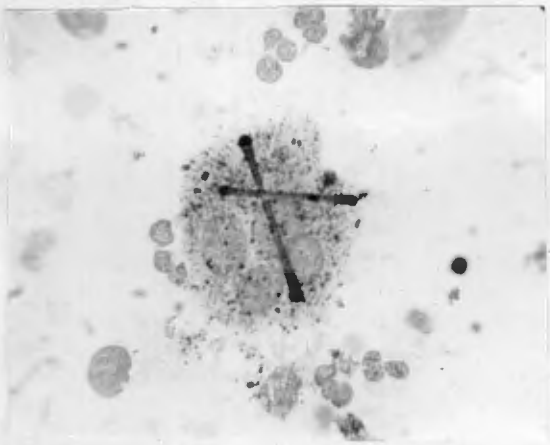


Figure 72. Case 41.
Oil Immersion.

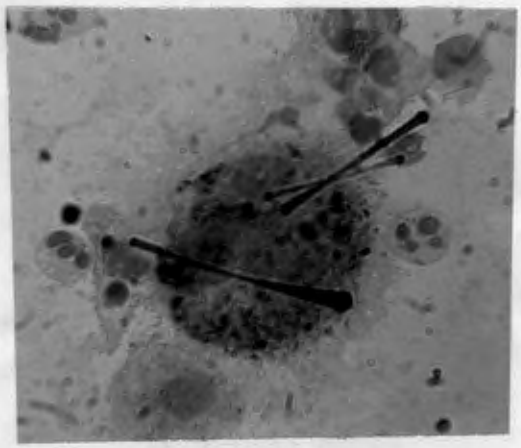


Figure 73. Case 41.
Oil Immersion.

ASBESTOS BODIES.

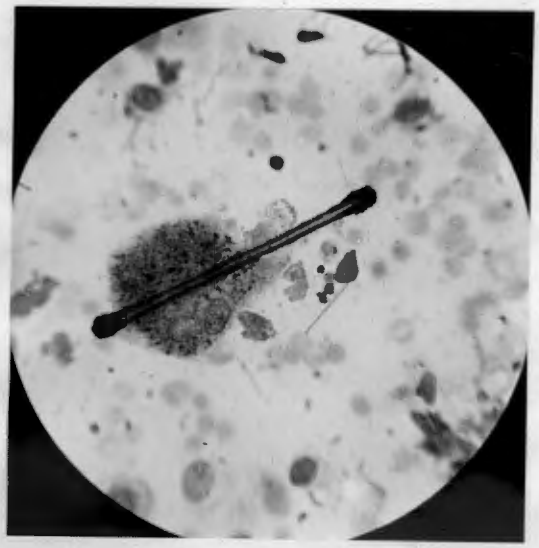


Figure 74. Case 41.
Oil Immersion.

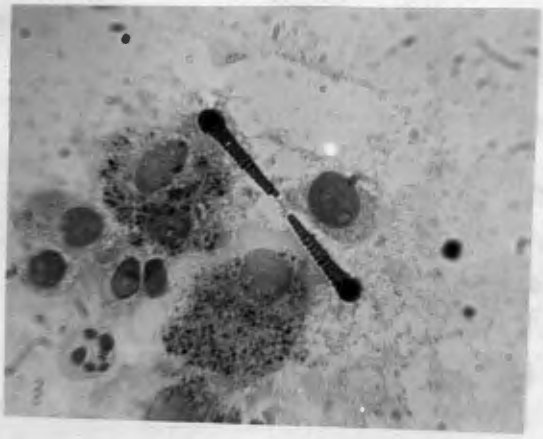


Figure 75. Case 41.
Oil Immersion.

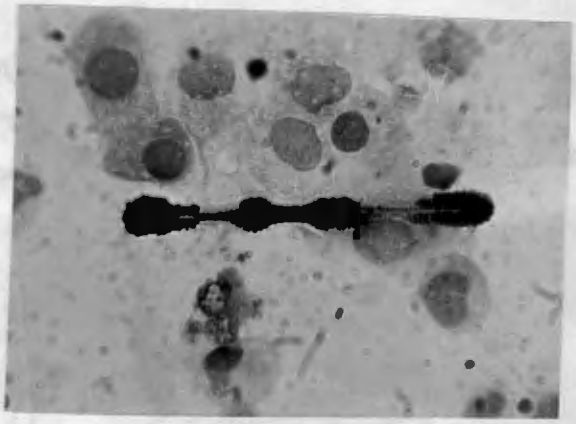


Figure 76. Case 41.
Oil Immersion.

SECTION IV

THE PATHOGENESIS OF THE NORMAL RESOLUTION OF ACUTE LOBAR PNEUMONIA.

THE PATHOGENESIS OF THE NORMAL RESOLUTION OF ACUTE LOBAR PNEUMONIA.

A REVIEW OF THE LITERATURE.

The classical description of the etiology and pathogenesis of lobar pneumonia may be found in any textbook of pathology. The two or three printed pages gives little indication of the years of patient research, the numerous animal experiments, the examination of human autopsy material and the endless speculations on the origins of certain of the cells that take part in the inflammatory reaction. In this era of antibiotics lobar pneumonia is cured in most cases with relative ease and interest in the pathology of this condition has waned. There has been a little work done on the pathology of pneumonia induced in animals which were then treated with sulphonamides but, to my knowledge, there is nothing at all known about the changes in the lung which occur when an artificial crisis is induced with penicillin. The difficulty is that patients no longer die of pneumonia and autopsy material is not available. The present report deals with the results obtained by lung biopsy of living patients at different stages of their illness during chemotherapy and treatment with antibiotics.

Pneumonia, as a clinical entity, was recognised in

ancient times by Hippocrates (470-370 B.C.) and his successors but it was grouped with many other acute pulmonary conditions under the term "peripneumony". However bacteria, which appeared to be pneumococci, were found in the consolidated portions of lungs of Egyptian mummies thousands of years old.

The differentiation between pleurisy and pneumonia was apparently first made in 1700 by De Kanilfeld and soon after by Valsalva and Morgagni. Auenbrügger (1761) introduced the technic of percussion in the clinical study of pneumonia and Laennec, after developing the art of auscultation, was able to differentiate pneumonia from pleurisy by clinical methods.

Boerhaave (1728) was credited as being the first to separate lobar pneumonia from other forms. The first accurate descriptions of the pathological changes found in the lungs were made by Laennec (1819), Cruveilhier (1829) and Rokitansky (1842). Seiffert (1837) introduced the term "bronchopneumonia" and Rokitansky recognized the difference between this form and the form now known as lobar pneumonia.

The pneumococcus "blushed unseen" until Sternberg (1880) injected some of his saliva under the skin of a rabbit and found that a fatal septicaemia ensued, the blood containing great numbers of oval micrococci. His paper published in 1881, was accompanied by a photomicrograph showing capsu-

lated diplococci. About the same time Pasteur did a similar experiment with similar results. Talamon (1883) isolated the pneumococcus from material obtained by lung puncture in cases of lobar pneumonia and concluded that pneumonia was an infectious disease produced by a special microbe of characteristic lanceolate form. The pneumococcus was destined to become one of the most thoroughly investigated organisms. It was classified by Dochez into four big groups and in 1929 Cooper separated Group IV into 29 different types.

Lung puncture was used not infrequently to obtain the causal organism (Patella 1888, Tchistovitch 1904, Eyre 1910, Rosenow 1911,Lister 1916, Clough 1917, Netter 1918, Nuzum et al. 1918, Thomas and Parker 1920, Glynn and Digby 1923). After a refined concentrated antiserum was made possible by the work of Felton (1924), Biopsy played an important part in obtaining rapidly pure cultures of the organisms especially in cases without sputum (Stewart 1930, Alston and Stewart 1930, Cruikshank 1931, Shibley and Rogers 1932, Sappington and Favorite 1936). From 1936 onwards no paper could be traced which dealt with lung biopsy in lobar pneumonia.

THE PATHOGENESIS OF LOBAR PNEUMONIA:

This was to a large extent worked out on experimental animals - dogs, monkeys, rabbits, guinea pigs, rats and

mice have all played their part.

Experimental lobar pneumonia was produced for the first time in dogs by Lamar and Meltzer in 1912. This was done by intubation of the pharynx and insufflation of the lung with the organisms. In a very careful and basic investigation Blake and Cecil (1920) used monkeys as their experimental animal. A broth culture of pneumococci was introduced through a needle which had been inserted between the tracheal cartilages just below the larynx. Spraying of the nose and throat with the culture and subcutaneous and intravenous injections did not cause pneumonia. The evidence was conclusive that lobar pneumonia was bronchogenic not haematogenous in origin. They showed the pneumococcus to be definitely the specific cause of lobar pneumonia. Their theory that the pneumococci spread through the lung by way of the perivascular, peribronchial and septal tissue, and the lymphatics was subsequently to be proved incorrect. Detailed descriptions were given of the histology of the various stages of engorgement, red and grey hepatisation and resolution but the macrophage reaction was not stressed.

Gaskell (1927) did a series of experiments on rabbits into which he introduced the pneumococcal culture via a catheter through a tracheotomy. The importance of his work was that as the infecting dose was increased there resulted

a progressively more extensive lesion, namely broncho-pneumonia, lobular pneumonia, lobar pneumonia, lobar pneumonia plus septicaemia and finally septicaemia only.

The work of Blake and Cecil was confirmed on dogs by Terrell, Robertson and Goggeshall (1933). They emphasized the part played by the "macrophage reaction" in resolution. During the stages of red and grey hepatisation the alveoli were filled with polymorphs and only very occasional macrophages were present. The onset of resolution was characterised by the macrophage reaction. Early in resolution the macrophages were few in number but actively engulfed polymorphs, red cells and pneumococci. Toward the end of the process they were practically the only cells seen in the exudate.

Reimann (1938) described the initial process spreading by direct extension from alveolus to alveolus through the pores of Kohn, by way of the lymphatics and blood vessels, and through the bronchioles via the infected oedema fluid and exudate. However, it was only in 1942 that Loosli in his experiments on dogs and monkeys proved that the method of spread was almost the same as Reimann had postulated. He showed that the inflammatory process was primarily intra-alveolar and intrabronchial. The pneumococci spread within the air spaces as a result of the dissemination of the infected oedema fluid directly from alveolus to alveolus

through the pores of Kohn and from bronchiole to bronchiole as a result of repeated aspiration during breathing and coughing. Gravity also appeared to play an important part in the direction of spread of the infection within the lobes. The organisms spread to the interstitial tissue secondarily from the alveolar spaces. Once in the interstitial tissues they appeared to be the important source of infection producing bacteraemia but were not important in the mechanism by which consolidation was produced. The spread of organisms to the interstitial tissues bore no relation to the extent or intensity of the consolidation.

The mechanism of the crisis has been the source of very considerable speculation and it is not the purpose of this paper to review the innumerable theories that have been propounded. Blake and Cecil (1920) quoted Neufeld and Haendel, Cole and his co-workers, Blake, and others as attributing recovery in part to the development of humoral antibodies and these antibodies were shown to appear at or about the time of the crisis. Lord (1919) suggested that recovery was due to local biochemical changes in the course of which the acid death-point of the pneumococcus was reached. Gaskell (1927) considered that there was an increasing liberation of endotoxin from destroyed pneumococci up to the fifth day and the crisis was due to the final neutralisation of endotoxin by the defences of the body two days later. Reimann (1938) summarised the various theories:

(1) Neutralisation of toxins - but the existence of a circulating toxin in pneumonia has never been demonstrated.
(2) Loss of virulence or sudden death of pneumococci probably due to the accumulation of protective substances - but the lung biopsy studies of Patella (1888), Tchistovitch (1904), Rosenow (1911) and Thomas and Parker (1920) showed that positive cultures might be obtained during the critical fall in temperature and even days after the crisis whilst negative cultures were not infrequent before the crisis occurred. In addition Reimann stated that at the crisis the blood did not always possess pneumococcicidal properties.
(3) The crisis represented a form of anaphylactic or allergic reaction - this theory was difficult to prove or disprove.
(4) Microbic dissociation - where there was a change from virulent capsulated to non-virulent non-capsulated forms; but the non-capsulated "S" and "R" forms were but rarely encountered at any time during the disease or in convalescence and unchanged virulent forms might be present in the blood stream and lung (see Patella, etc. as above) even after the crisis.

One must conclude that the mechanism of the crisis is not understood. A possible modern source of enquiry may be along the lines of Selye's "adaption" where endocrine reactions play a major role.

The mechanism of the initial acute stages and the

theories of the crisis have been briefly reviewed for the sake of completeness. The concern of this paper is with the process of resolution.

All authors are now agreed that the macrophages play a major role in bringing about resolution. As early as 1900 Pratt described the occurrence of macrophages in the late stages of pneumonia. Mallory (1920) observed the appearance of "endothelial leukocytes" in large numbers in the stage of resolution. Loeschcke (1931) described macrophages as replacing the polymorphs of the exudate in the late stages of pneumonia and assigned to them the function of the removal of fibrin. Fried (1934) called attention to the prominence of the macrophages in the resolution of lobar pneumonia and he also described the progressive mobilisation of these cells in experimental allergic inflammation of the lungs.

Robertson and Uhley (1936) made a very accurate and painstaking study of ninety separate lobe lesions in forty autopsy cases of human lobar pneumonia. They were particularly interested in the changes that occurred in the macrophage system. The age of the lesion was determined from the day of onset of the condition and from repeated X-rays. Cultures from the lungs showed that the series was representative of all four groups of pneumococci.

They demonstrated that the macrophages gradually

replaced the polymorphs, the total number of cells composing the exudate diminished, the fibrin disappeared progressively and open spaces appeared in the air sacs. No difference in the cellular response was detected between the various types of pneumococcal pneumonia.

The appearance of the macrophage reaction was not confined to any one stage but in lesions up to the fourth day the reaction was relatively slight in degree and occurred in a smaller percentage of the lesions than after this period. Until the stage when some of the lesions began to show a well marked macrophage reaction (fifth day) the intra-alveolar exudate was predominantly polymorph in nature. Even after the fifth day the great majority of the lesions showed this same cellular picture, and it was not until the tenth day that the macrophage became the predominant cell of the exudate. In no case was resolution observed in the absence of the macrophage reaction.

In all six cases dying at intervals of six days to two months following recovery from lobar pneumonia there was a pronounced macrophage reaction.

Pneumococci were present in large numbers in the great majority of the lesions up to the seventh day. From the fifth day onwards a certain percentage of the lesions contained few pneumococci; after the ninth day only one case out of eleven showed many organisms and in the other ten cases

pneumococci were few or absent.

During the first 24 hours of the evolving inflammatory process the pneumococci were, for the most part, free in the oedema fluid. After this stage they were observed to be principally within the phagocytic cells. As the macrophage reaction developed there was a corresponding diminution in the number of pneumococci. Disappearance of the pneumococci occurred only when the macrophage reaction was well advanced.

Sections showed that the macrophages were capable of engulfing and digesting large numbers of organisms. The most active phagocytosis was observed where macrophages were first appearing in heavily infected regions. Scores of pneumococci could be counted not infrequently within a single cell. In regions where the macrophages were the predominant cells usually few or no intracellular pneumococci could be detected. The macrophages showed an effective intracellular digestive power which was in sharp contrast to that shown by many of the surrounding polymorphs. The latter cells containing well preserved pneumococci were frequently observed in the immediate neighbourhood of macrophages filled with partially digested forms. The number of polymorphs within the macrophages could account for the disappearance of a considerable portion of these cells from the exudate. The leucocytes and their contained pneumococci appeared to be destroyed effectively and rapidly by the macrophages. No evidence of extracellular destruction of pneumococci

could be detected.

The finding of clear zones surrounding macrophages distributed in fibrin masses suggested that they exerted some kind of lytic action on the fibrin.

In the pneumonias due to other organisms (streptococci, staphylococci, gonococci) the macrophage reaction appeared in its well developed form in the older lesions and was accompanied by resolution and a diminution in the number of microorganisms present.

The macrophage reaction preceded and always accompanied resolution and was thus closely associated with healing of the lesion.

Neither in their studies of canine pneumonia nor in the human disease was it possible to discover a constant relationship between the appearance of circulatory immune substances and the development of the macrophage reaction in the lung lesion. They concluded that if immune substances were necessary for the adequate functioning of the macrophages, either they were present in the blood in concentrations too low for their methods of detection or they were produced locally in the lung. Their difficulty was solved by the investigations of Wood and his co-workers. Phagocytosis by cells was investigated on various tissue and artificial surfaces. The conclusions were that both polymorphs and macrophages, when given access to a suitable surface, will

phagocytose virulent pneumococci without the aid of an intermediary antibody or any other tissue factor; the body tissues afforded surfaces suitable for the efficient operation of phagocytic cells in this non-antibody reaction. They showed that the cells phagocytose the bacteria by trapping them against the tissue surfaces and between the individual phagodytes themselves. They termed this process "surface phagocytosis". (Wood, Smith and Watson 1946, Wood 1946, Wood 1947).

Robertson and Loosli (1938) and Robertson and Coggeshall (1938) went on to study the macrophage reaction in the pulmonary lesions of dogs with experimental pneumococcal lobar pneumonia. Hadfield and Garrod (1942,1947) placed much emphasis on their work in their discussions on the pathogenesis of resolution of lobar pneumonia in "Recent Advances in Pathology". These investigators were able to confirm fully the autopsy work of Robertson and Uhley. In addition they found that the macrophage system in its inception was by no means uniformly distributed throughout the pulmonary lesion but was characterised initially by numerous more or less isolated foci which coalesced and spread to form larger areas. It also appeared that resistance to experimental reinfection depended largely on the continued presence of these cells in the lung, and was strictly local. It was found that an inoculum that had

no effect on a previously affected lung would produce a second attack of pneumonia if introduced on the other side. There appeared to be both a local cellular resistance and also a humoral immunity which seemed to act independently of one another. This was illustrated by further dog experiments showing that death might result from bacteraemia in spite of an adequate macrophage reaction and consequent clearing of the lung; conversely the macrophage reaction might fail to develop and the dogs died of lung infection but without blood stream invasion.

Robertson (1938) showed that one attack of pneumonia conferred on an animal heightened resistance to another attack. The basis of this heightened immunity appeared to consist principally in a marked acceleration of the macrophage reaction in the inflammatory lesion. After recovery a high degree of local immunity could be demonstrated in the involved lobes but this persisted only as long as the macrophages were present in the alveoli. In vitro experiments with macrophage and polymorph suspensions showed that the macrophages took up pneumococci promptly and digested them so rapidly that sometimes within an hour or two all the pneumococci had melted away within the cells; the polymorphs acted much more slowly, often taking many hours to accomplish the same result, and unless the concentration of opsonins was sufficiently high complete digestion did not occur.

Reimann (1938) came to the conclusion that it was not known just how the exudate in the consolidated lung was removed. Pneumococci possessed enzymes capable of digesting carbohydrates, esters and proteins but they probably played no part in the process of resolution. It was most reasonable to presume that the bulk of the exudate was removed by phagocytic macrophages or was autolysed or dissolved by enzymes liberated in situ either by the substance itself, by the alveolar cells, or by the macrophages. Macrophages definitely were capable of ingesting fibrin as Geever et al. (1951) reported autopsy examinations of some "atypical inflammatory reactions" in which macrophages were seen ladened with fibrin fragments.

On the basis of these investigations it may be assumed that the macrophage plays an important part in resolution. There is no doubt that macrophages are present in the lung but what is their origin? This problem has vexed pathologists for fifty years. Innumerable papers have been written on the subject and only a few of the more important and relevant observations will be reviewed.

Briscoe (1908) used guinea pigs for his experiments and concluded that the alveoli were lined by epithelial cells, and that the smaller cells increasing in size, ultimately came to form larger ones. The latter, while living, were liable to be detached from their seat of

origin and formed the free macrophages. Permar (1920) quoted Slavjansky (1869) as having had similar ideas to Briscoe. He also described the work of Haythorn (1913) who demonstrated that the cells constituting the lining of the lung alveoli in man were not concerned with phagocytosis; Haythorn believed that the phagocytic cell was a wandering cell, of endothelial type, and suggested that its possible origin was from the endothelial lining cells of the blood and lymph channels. Haythorn was supported by Mavrogordato (1918). Permar's vital stain experiments with rabbits and guinea pigs suggested that the macrophages arose from proliferation of the endothelial cells lining the blood capillaries of the alveolar walls, whence the newly formed cells migrated directly into the alveolar spaces by passing between the cells lining the alveolus. After phagocytosis the cells slowly returned to the interstitial tissues of the lung, wandered up gradually into the terminal lymphatics and so along these channels to the bronchial lymph node and finally to the lymph nodes at the hilus of the lung. The cells did not arise from lymphatics, and alveolar epithelial cells did not have any phagocytic properties. Permar continued his work and in 1923 reported that the macrophages in experimentally induced rabbit pneumonia had their origin also from the proliferation of capillary endothelium. Foot (1927) in a careful review of the subject presented arguements for and against the various theories of epithelial

origin, monocytic origin, histiocytic origin, vascular endothelium origin and lymphocytic origin. From his own work on rabbits and human autopsy material he concluded that the most likely origin of the pulmonary dust cell was from the blood stream, and more specifically from the monocytes in the blood. Gay (1931) showed graphically the possible interrelationships between macrophages and lymphocytes, monocytes, tissue histiocytes, capillary endothelium and fibroblasts and he quoted the chief proponents of each theory. No definite conclusions were reached. Terrell, Robertson and Coggeshall (1933) held the theory that the macrophage had its origin from the cells of the alveolar wall. These cells swelled up and on reaching a certain size became detached from their fellows and wandered into the exudate as actively phagocytic cells. Fried (1934) was in favour of the alveolar epithelium hypothesis and quoted as his supporters Aschoff, Bloom, Seeman, Marchand, Maximow, Carlton, Cappell, Lang, Pagel, Policard, Huguenin, Tchistovitch and Chiodi. Certainly this was an impressive list. He felt that the point of dispute was whether these cells were endodermal (Aschoff and his school) or mesodermal (Maximow, Lang, Bloom, Policard and Fried). Robertson and Uhley (1936) stated that they knew of no conclusive evidence on the origin of the macrophages. They made the important observation that it would seem that macrophages might be mobilized from areas outside the immediate alveolar unit. For example in some cases with an

obvious macrophage reaction there was no reaction of the septa and occasionally nests of a macrophage type of cell was found in areas of lymphoid tissue near blood vessels or bronchi. However, large mononuclears of the macrophage type had been only rarely observed in the blood vessels of the resolving lung.

After a perusal of this very confusing and conflicting literature one can only hope that Loosli (1942) has said the last word on the subject. He showed in dogs that during the course of pneumococcal pneumonia the exudate changed from one consisting mainly of polymorphs to one of large macrophages. The polymorphs entered the exudate principally from the alveolar capillaries and small blood vessels . Lymphocytes and monocytes of the blood entered the exudate in the early stages of the disease along with the polymorphs. At first they were inconspicuous but in the older lesions the haematogenous mononuclear cells increased in numbers in the exudate and at the same time underwent morphological changes. The haematogenous mononuclear exudate cells continued to migrate from the blood vessels throughout the period of consolidation. After they had entered the exudate, it soon became impossible to separate them into groups as typical lymphocytes and monocytes; they began to enlarge, assumed many sizes and shapes and became transformed into the large mononuclear cells which gradually assumed the appearance and phagocytic properties

of typical macrophages. Cells representing all transitional stages in the development of lymphocytes into monocytes and monocytes into small macrophages could be seen in the exudate. The hypertrophy and transformation of lymphocytes into monocytes and monocytes into macrophages were more or less complete by the time the local cells began to be conspicuous on the alveolar walls. The swelling and proliferation of the septal cells and other cellular constituents of the alveolar walls could be interpreted as a result of the mild toxic injury due to the soluble products of the pneumococci growing in the exudate; alteration of the environment of the cells as a result of consolidation probably also played a part. They found no evidence for the origin of macrophages from the alveolar epithelial cells, fixed histiocytes, the local connective tissue of the septal, bronchial, blood vessel or pleural walls, or from the endothelial lining of the alveolar capillaries.

It is comforting to think that if this theory of origin is correct then the inflammatory cell response in the lung falls into line with the cellular response to inflammation in all other parts of the body. It is this very fact that makes the work of Loosli so acceptable. Maximow, Bloom, Taliaferro and co-workers, Kolouch, and others found that, in inflammation in general, the blood leucocytes constituted the chief source of the cells which appeared

in the involved area. The macrophages, which eventually replaced the polymorphs, were derived principally from the haematogenous mononuclear cells (lymphocytes and monocytes) after they had entered the exudate. The inflammatory process in the lungs differed from that of ordinary inflammation elsewhere only in that the cellular exudate entered spaces not normally occupied by cells. Menkin (1940), in describing inflammation in general, referred to the macrophages as scavengers which engaged actively in engulfing and digesting polymorphs, red cells and various necrotic material resulting from the acute inflammation. In the polymorph there was an intracellular enzyme (leucoprotease) which acted in a slightly alkaline or neutral medium and in the macrophage an enzyme (lymphoprotease) which caused active digestion of protein in a weakly acid medium. The underlying mechanism involved in the cellular sequence depended on the production of a local acidosis in the inflamed area. The correlation between the pH and the cytological picture suggested that the hydrogen ion concentration was the factor conditioning the cellular pattern of the exudate. The mechanism of local acidosis in inflammation was referable to a local depletion of the alkali reserve. This, in turn, appeared to be due to a disturbance in the intermediary carbohydrate metabolism in the form of increased glycogenolysis which favoured the production of a true lactic acid acidosis. It has still to be proved that these same biochemical changes also occur in the lung.

Although it has been shown that the inflammatory process in lobar pneumonia is not divided into definite static phases, four stages are usually described - engorgement, rdd hepatisation, grey hepatisation and resolution. It will be necessary, for convenience, to use these terms in this paper and thus the description of Boyd (1938), as an example of what is generally accepted, is given. Other textbooks on pathology differ but little from that of Boyd. During the stage of engorgement the capillaries in the alveolar walls are intensely congested, and large numbers of pneumococci lie in a fluid exudate. During red hepatisation the alveoli become filled with fibrin and well preserved polymorphonuclear leucocytes. During grey hepatisation degeneration and softening of the exudate takes place. The various constituents of the exudate have lost their freshness, the nuclei of the polymorphs become blurred and indistinct, the red blood cells have vanished or appear as mere ghosts, and the threads of fibrin are clumped together into amorphous masses. Macrophages appear in the exudate and in the stage of resolution the exudate consists of little more than disintegrating nuclei, granular debris, and mononuclear phagocytes. Differences of opinion lie in where grey hepatisation ends and resolution begins.

Most of the work on the pathogenesis of lobar pneu-

monia has been done on animals or on human autopsy material. Gaskell (1927) ruefully admitted that the opportunity seldom arose to make a complete pathological examination of the earlier or later stages. The clinical condition when such an opportunity did arise, was so different from that of the same stage of an uncomplicated lobar pneumonia that the criticism could always be made that the conditions found were not comparable in the two cases. Robertson and Uhley (1936) also felt this difficulty for they stated: "but as to whether the cellular changes occurring in the consolidated lung during recovery from the disease are identical with those observed in the resolving lung at postmortem, our study provides no data".

Curphey (1935) seems to have clarified the position and Robertson and Uhley (1936) and Robertson (1938) quoted his work: "Curphey has bridged the gap between our experimental observations and the postmortem studies by means of biopsies performed on the lungs of patients during the course of lobar pneumonia. He showed that the cellular reactions which we have observed in the resolving lung after death occur during recovery." Unfortunately only an abstract was available on Curphey's investigations and as this was so pertinent to the present investigation it is quoted in full:

"Biopsy sections of the lungs of patients suffering from lobar pneumonia were obtained from a series of recovered cases

at different stages of their disease as well as from cases at postmortem in which autopsy was not permitted. The object - to determine whether the histiogenesis of this process differed in recovered cases from that usually seen in postmortem studies. From the material available certain definite changes can be noted in the pericapillary histiocytes in the early stages of the disease which would suggest that these cells play a definite defensive role. Certain interesting changes are similarly noted in the alveolar capillaries". In the discussion that followed the question of empyema was raised and Curphey replied that the incidence was no greater in the biopsied group. He felt that the pathology of the recovery from lobar pneumonia could not be studied on the autopsy table. This abstract revealed very little but one must accept the statement of Robertson, who probably attended the reading of the paper at the American Association of Pathologists and Bacteriologists, that Curphey confirmed in living patients the conclusions drawn from experimental and autopsy material.

A great amount of work has clarified the pathogenesis of lobar pneumonia which runs its course uninterrupted by specific therapy; but <u>what happens in the lung when the pneumococci are destroyed, not by the body processes alone, but with the help of sulphonamides or penicillin</u>? This fascinating problem seems to have intrigued few investigators

and the only papers one was able to find on the subject were by Wood and Irons (1946) and Wood, McLeod and Irons (1946). Experimental pneumococcal pneumonia was produced in albino rats by the intrabronchial inoculation of Type I pneumococci suspended in mucin. Sulphapyridine was started six hours after the inoculation (250 mg. orally and then 125 mg. every 12 hours). During the first 18 hours the drug apparently had little effect but at the end of this time the pneumococci in the oedema zone began to show striking changes in their morphology, indicating bacteriostasis. Forty-two hours after the start of therapy the oedema zone had disappeared, the pneumonia had ceased to spread, and the pneumococci at the margin of the lesion were being phagocytosed by polymorphs. At 66 hours macrophages were numerous and seemed to be taking an active part in destroying the bacteria. By the fourth day no pneumococci were seen and after a week there remained only macrophages in the rapidly clearing alveoli. Using leucopenic irradiated rats in similar experiments they showed that polymorphs did not occur in the exudate and instead macrophages appeared and actively phagocytosed the pneumococci. In a very ingenious series of experiments it was proved that phagocytosis was related neither to natural nor acquired type-specific opsonins in the blood serum and this led on to the theory of "surface phagocytosis".

The present work developed into an investigation of

those changes that occurred in the lung after the administration of penicillin and sulphonamides in living human patients with acute pneumococcal lobar pneumonia.

LUNG BIOPSY STUDIES OF HUMAN PATIENTS DURING THE NORMAL RESOLUTION OF ACUTE LOBAR PNEUMONIA TREATED WITH SULPHONAMIDES AND PENICILLIN.

It is felt that at this stage it is necessary to define what is meant by the terms acute and chronic lobar pneumonia. By acute lobar pneumonia is meant one which runs an uncomplicated course to complete clinical and radiological resolution within thirty days of the commencement of adequate chemotherapy or antibiotic therapy or both. A chronic pneumonia is one which presents in a similar manner to an acute pneumonia and appears at first to respond like the acute case except that the temperature is frequently more persistent; although the patient's general condition is excellent clinical or radiological signs of consolidation remain for many weeks and even months but eventually complete resolution does occur without any serious residua. The definition of chronic pneumonia will further be clarified under the section on this subject. A few cases will fall just over the 30 day limit of the acute pneumonia, for example, slight radiological signs might eventually clear about the 35th day. These cases are probably best included in the acute group. It will be shown that all cases are

simply gradations of the same process and it is of little importance into which group these intermediate cases fall.

Twenty seven lung biopsies were done on twenty one cases of acute lobar pneumonia. As will be seen from Table 11 the shortest duration of the illness after chemotherapy was 12 days and the longest 31 days. An exception was Case 50 with a duration of 43 days. This was included in the series because he was a classical acute pneumonia, radiological signs continuing probably because of the accumulation of fluid after the biopsy had induced a pneumothorax. This case will be remembered as the one where the pneumothorax occurred because the point of the biopsy needle was in the pleural cavity and not in the lung when the stylette was withdrawn. In Case 9 it was uncertain when radiological resolution took place as he left hospital before the last X-ray could be taken. However, clinical resolution was complete after 14 days and an X-ray taken 13 days after the beginning of chemotherapy showed resolution to be well advanced. It was felt reasonable to include him in the acute series. In Case 56 the time of the onset of symptoms was uncertain as the patient was mentally deficient and had little idea of how long he had been ill. In Case 60 again the duration was uncertain as the patient refused to stay longer in hospital but clinical resolution had occurred after 9 days and X-ray only four days after admission had shown marked resolution. In Case 48 it was known that

Table 11.

To Show Duration of Illness from Onset to Clinical and Radiological Resolution.

Case No.	Duration from onset of symptoms till clinical resolution.	Duration from onset of symptoms till radiological resolution.	Duration from onset of chemotherapy till clinical resolution.	Duration from onset of chemotherapy till radiological resolution.
	Days	Days	Days	Days
4	19	19	12	12
9	16	?	14	?
23	13	23	8	18
26	27	33	20	26
28	27	30	23	26
33	25	34	18	27
38	23	26	18	21
41	16	25	14	23
42	16	17	11	12
45	16	18	13	15
48	15	18	Uncertain	Uncertain

Table 11. (Continued)

Case No.	Duration from onset of symptoms till clinical resolution.	Duration from onset of symptoms till radiological resolution.	Duration from onset of chemotherapy till clinical resolution.	Duration from onset of chemotherapy till radiological resolution.
	Days	Days	Days	Days
50	18	46	15	43
51	22	22	14	14
54	13	23	12	22
55	23	35	18	31
56	Uncertain	Uncertain	8	14
57	17	34	13	30
60	13	Uncertain	9	Uncertain
67	10	24	5	19
71	35	35	29	29
72	31	35	25	29

Table 12.

To Show the Relationship Between Lung Biopsy Findings and Duration of Illness from Time of Onset of Symptoms.

Time from Onset of Symptoms. Days.	Case No.	Chemotherapy.	Sputum Culture	Biopsy Culture	Biopsy Histology.
1	-	-	-	-	-
2	9	Nil	No Sputum	Pos.	Polymorphs. Pneumococci numerous. Red hepatisation.
3	41	2 days. (P and S)	Neg.	Neg.	Macrophages and polymorphs in equal numbers. Pneumococci not seen. Early resolution.
3	50	Nil	Pos.	Pos.	Polymorphs. Pneumococci fairly frequent. Red hepatisation.
4	26	1 day (S)	-	Neg.	Polymorphs. Pneumococci very scanty. Red hepatisation.
4	28	6 hours (P)	No Sputum	Neg.	Polymorphs. Pneumococci not seen. Red hepatisation.
4	45	1 day (S)	-	Neg.	Polymorphs. No pneumococci seen. Red hepatisation.

Table 12. (continued)

Time from Onset of Symptoms. Days.	Case No.	Chemotherapy.	Sputum Culture	Biopsy Culture	Biopsy Histology.
4	48	?duration (P and S)	Neg.	Neg.	Polymorphs, few macrophages No pneumococci seen. Early resolution.
4	57	6 hours (S)	Pos.	Pos.	Polymorphs. Pneumococci fairly frequent. Red hepatisation.
4	60	12 hours (S)	Neg.	Neg.	Polymorphs, few macrophages No pneumococci seen. Late red hepatisation.
5	23	Nil.	-	Pos.	Polymorphs. Pneumococci very scanty. Red hepatisation.
5	42	Nil.	Neg.	Pos.	Polymorphs. Pneumococci very scanty. Red hepatisation.
6	54	5 days (S and P)	Neg.	Neg.	Polymorphs and macrophages in equal numbers. No pneumococci seen. Early resolution.
6	67	Nil.	Neg.	Pos.	Polymorphs, few macrophages Pneumococci very scanty. Late red hepatisation.
6	71	Nil.	Pos.	Pos.	Polymorphs, few macrophages Fairly frequent pneumococci Late red hepatisation.

Table 12. (continued).

Time from Onset of Symptoms. Days.	Case No.	Chemotherapy.	Sputum Culture	Biopsy Culture	Biopsy Histology.
6	72	Nil.	Pos.	Pos.	Polymorphs. Numerous pneumococci. Red hepatisation.
7	4	90 mins. (P and S)	Neg.	Neg.	Polymorphs. Scanty pneumococci. Red hepatisation.
7	33	Nil.	Pos.	Pos.	Polymorphs, few macrophages. Pneumococci scanty. Late red hepatisation.
7	57-1	3 days (P and S)	Neg.	Neg.	Macrophages. No pneumococci. Advanced resolution.
7	60-1	3 days (P and S)	Neg.	Neg.	Macrophages, few polymorphs. No pneumococci. Fairly advanced resolution.
8	55	4 days (P and S)	Neg.	Neg.	Macrophages. No pneumococci. Advanced resolution.
9	38	4 days (P and S)	Neg.	Neg.	Macrophages, few polymorphs. No pneumococci. Fairly advanced resolution.
9	45-1	6 days (P and S)	Neg.	Neg.	Macrophages. No pneumococci. Advanced resolution.
10	51	2 days (P and S)	Neg.	Neg.	Macrophages. No pneumococci. Advanced resolution.

Table 12. (continued)

Time from Onset of Symptoms. Days	Case No.	Chemo-therapy.	Sputum Culture	Biopsy Culture	Biopsy Histology.
11	71-1	5 days (P and S)	Neg.	Neg.	Macrophages. No pneumococci Advanced resolution.
12	72-1	6 days (P and S)	Neg.	Neg.	Macrophages. No pneumococci Advanced resolution.

Two of the biopsies (56 and 56-1) are not included because the time from onset of symptoms was very uncertain.

Table 13.

To Show the Relationship Between Lung Biopsy Findings and Duration of Illness from time of Beginning Chemotherapy.

Time from Onset of Chemo-therapy Days	Case No.	Chemo-Therapy	Sputum Culture	Biopsy Culture	Biopsy Histology.
0	9	Nil	No Sputum	Pos.	Polymorphs. Pneumococci numerous. Red hepatisation.
0	23	Nil	-	Pos.	Polymorphs. Pneumococci very scanty. Red hepatisation.

Table 13. (continued)

Time from Onset of Chemo-therapy Days	Case No.	Chemo-therapy	Sputum Culture	Biopsy Culture	Biopsy Histology
0	33	Nil	Pos.	Pos.	Polymorphs, few macrophages. Pneumococci scanty Late red hepatisation.
0	42	Nil	Neg.	Pos.	Polymorphs. Pneumococci very scanty. Red hepatisation.
0	50	Nil	Pos.	Pos.	Polymorphs. Pneumococci fairly frequent. Red hepatisation.
0	67	Nil	Neg.	Pos.	Polymorphs, few macrophages. Pneumococci very scanty. Late red hepatisation.
0	71	Nil	Pos.	Pos.	Polymorphs, few macrophages. Fairly frequent pneumococci. Late red hepatisation.
0	72	Nil	Pos.	Pos.	Polymorphs. Pneumococci numerous. Red hepatisation.
0 - 1	4	90 mins. (P and S)	Neg.	Neg.	Polymorphs. Scanty pneumococci. Red hepatisation.
0 -1	57	6 hours (S)	Pos.	Pos.	Polymorphs. Pneumococci fairly frequent. Red hepatisation,

Table 13. (continued)

Time from Onset of Chemo-therapy Days	Case No.	Chemo-Therapy	Sputum Culture	Biopsy Culture	Biopsy Histology
0 - 1	28	6 hours (P)	No Sputum	Neg.	Polymorphs. No pneumococci seen. Red hepatisation.
0 - 1	60	12 hours (S)	Neg.	Neg.	Polymorphs, few macro-phages. No pneumococci seen. Late red hepatisation.
0 - 1	56	12 hours (P and S)	Neg.	Neg.	Polymorphs, few macro-phages. No pneumococci seen. Late red hepatisation.
1	26	1 day (S)	-	Neg.	Polymorphs. Pneumococci very scanty. Red hepatisation.
1	45	1 day (S)	-	Neg.	Polymorphs. No pneumococci seen. Red hepatisation.
2	41	2 days (P and S)	Neg.	Neg.	Macrophages and polymorphs in equal numbers. Pneumo-cocci not seen. Early resolution.
2	51	2 days (P and S)	Neg.	Neg.	Macrophages. No pneumo-cocci. Advanced resolution.
3	57-1	3 days (P and S)	Neg.	Neg.	Macrophages. No pneumo-cocci. Advanced resolution.
3	60-1	3 days (P and S)	Neg.	Neg.	Macrophages, few polymorphs No pneumococci. Fairly well advanced resolution.

Table 13. (continued)

Time from Onset of Chemo-therapy Days	Case No.	Chemo-therapy	Sputum Culture	Biopsy Culture	Biopsy Histology
4	38	4 days (P and S)	Neg.	Neg.	Macrophages, few polymorphs. No pneumococci. Fairly well advanced resolution.
4	55	4 days (P and S)	Neg.	Neg.	Macrophages. No pneumococci. Advanced resolution.
5	54	5 days (P and S)	Neg.	Neg.	Polymorphs and macrophages in equal numbers. No pneumococci seen. Early resolution.
5	56-1	5 days (P and S)	Neg.	Neg.	Macrophages. No pneumococci. Fairly well advanced resolution.
5	71-1	5 days (P and S)	Neg.	Neg.	Macrophages. No pneumococci Advanced resolution.
6	45-1	6 days (P and S)	Neg.	Neg.	Macrophages. No pneumococci. Advanced resolution.
6	72-1	6 days (P and S)	Neg.	Neg.	Macrophages. No pneumococci. Advanced resolution.

One case (Case 48) is not included because it was uncertain when chemotherapy commenced.

the patient had had penicillin and sulphonamide before admission but it was uncertain for how long. However the duration of his illness from the onset of symptoms to radiological resolution was 18 days so he could easily be included in the class of acute pneumonias. It must be realised that one cannot vouch for the absolute accuracy of certain durations given as the patients were often poor or inaccurate observers, and sometimes spoke a language which was difficult or impossible to understand. In addition, at the time when most of these cases were done the X-ray department was under-staffed, under-equipped and over-worked and it was impossible to ask them to do very frequent X-rays. In some cases the sputum culture was not recorded because there was no sputum being produced by the patient.

BACTERIOLOGICAL FINDINGS:

These are shown in Tables 12 and 13 (where P indicates penicillin and S sulphonamide therapy). Table 13 probably illustrates the bacteriological findings most clearly. It will be noted that in all the cases which had received no treatment positive cultures of pneumococci were obtained. In all these cases pneumococci were seen on the smear stained by Gram's method. Pneumococci were recorddd as numerous, fairly frequent (easily found), scanty (where they were found but they had to be searched for) and very scanty (where only one or two diplococci were found after a pro-

longed search). On the whole pneumococci were scanty but it was doubtful whether one should draw any conclusions from the number found on the biopsy smear. The pneumococci were usually lying free in the exudate but in some cases had been ingested by polymorphs. In two patients (Cases 42 and 67) pneumococci were cultured from the biopsy material but not from sputum which was plated out at the same time.

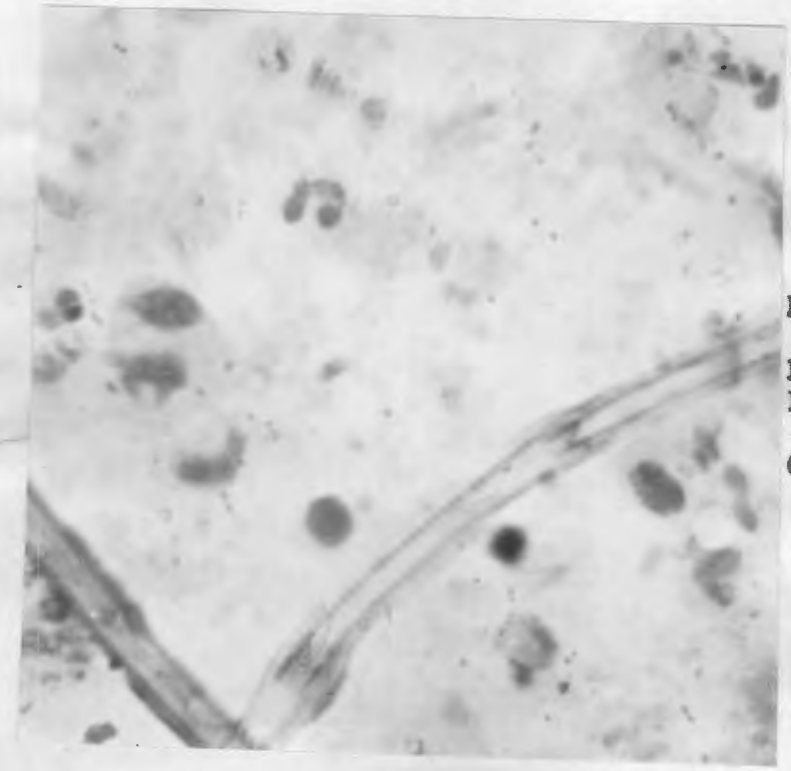


Figure 77. Case 9.

Pneumococci in the Exudate.

Oil Immersion.

Of great interest were the <u>results of cultures done shortly after the beginning of chemotherapy</u>. Case 4 had been treated probably very inadequately with sulphadiazine some days before admission. He was given on admission penicillin 400,000 units and two tablets of sulphatriad and biopsy was

performed about 90 minutes later. Although pneumococci were seen the cultures were negative. If the original sulphadiazine could be discarded one might assume that within two hours of the giving of penicillin bacteriostasis had occurred. The actual presence of pneumococci made it almost certain that the original sulphadiazine had had little affect; in addition the patient was still seriously ill.

Case 57 had had four tablets of sulphonamide six hours before biopsy and it was not surprising to obtain positive cultures. In contrast Case 28 had had 400,000 units of penicillin 6 hours before biopsy and the culture was negative and no pneumococci were seen. Case 60 had taken two tablets of sulphonamide four hourly for the 12 hours before biopsy and both sputum and biopsy were negative and no pneumococci were seen on the smear. Similarly Case 56 showed negative findings 12 hours after the commencement of penicillin and sulphatriad (he had received 800,000 units of penicillin and four tablets of sulphatriad during this period). Two patients (Cases 26 and 45) who had had sulphonamides for about a day before biopsy showed negative results. In no case who had had chemotherapy (either sulphonamides or penicillin or both) for a day or more were pneumococci cultured from the sputum or the biopsy material.

It might be argued that those cases that were negative

shortly after the beginning of chemotherapy were not really cases of pneumococcal pneumonia but were, for example virus pneumonia. A consideration of the case histories will show that they were all clinically and radiologically classical pneumococcal lobar pneumonias and that there was a high neutrophil leucocytosis in all these cases. In addition their response to chemotherapy was as expected for a pneumococcal lobar pneumonia. In several cases where serial biopsies were done cultures of pneumococci were obtained from the first punctures but not from subsequent punctures which were done at varying intervals after the beginning of chemotherapy. (The term chemotherapy is used to embrace both sulphonamide and antibiotic therapy). In no case was a sputum culture positive without the biopsy culture also being positive.

Certain conclusions may be drawn from the results:

(1) Providing that no chemotherapy has been given, positive cultures of pneumococci will be obtained from cases of lobar pneumonia by means of lung biopsy, at least during the first seven days of the illness (the seventh day was the latest that any untreated case entered hospital in this series).

(2) One injection of penicillin (400,000 units) will possibly cause bacteriostasis within two hours.

(3) One injection of penicillin (400,000 units) will probably cause bacteriostasis within six hours.

(4) Four tablets of sulphonamide will probably not effect the pneumonia within six hours.

(5) Sulphonamide in adequate dosages will probably cause bacteriostasis within 12 hours.

(6) There is little doubt that after a patient has been on chemotherapy (either sulphonamide or penicillin) for over 24 hours the lung will be sterile as far as can be ascertained by lung biopsy cultures. It is probably a complete waste of time to ask for sputum cultures after the patient has been on chemotherapy for 12 - 24 hours.

Although this is a very small series and represent cases of pneumonia over a definite period in a definite institution, the results are clear cut and bear out what one would have expected from purely theoretical considerations.

HISTOLOGICAL FINDINGS:

These are summarised in Tables 12 and 13. In all cases adequate material for examination was obtained. Fibrin is not mentioned in the tables as it was present in all cases. The type of cell which was by far the most numerous is indicated simply by, for example, "polymorphs". Where cells are mentioned as "few" this means that a fair number were seen but in no way rivalled the number of the predominant cell. For the sake of brevity and relevance no mention is made of the many other cells seen in the smears, for example, alveolar cells, bronchial and bronchiolar epithelium and interstitial tissue. Although there are not a large number of cases in this series they fall into a definite pattern.

From Table 12 it will be seen that irrespective of how long the patient had been ill before the lung biopsy, if adequate chemotherapy had been given, resolution had commenced. It will be noted that all patients entered hospital within eight days of becoming ill. On admission they were started on penicillin and sulphatriad and there were no cases in this series of the acute stage of illness after the seventh day without chemotherapy. The one patient admitted on the eighth day (Case 51) was biopsied only after chemotherapy had been given in hospital for two days.

Table 13 shows the relationship between the histological

findings in the lung and the duration of chemotherapy.

All untreated cases showed the histiological picture of red hepatisation. This was well demonstrated in Cases 3, 9, 23, 42, 50 and 72. (See Figures 78 to 83). The slides showed large masses of fibrin associated with innumerable well preserved polymorphs. Macrophages of all types were present but scanty; small macrophages were the most frequently seen type. Very occasionally a polymorph, in the process of being digested, was seen within a small macrophage. Not very infrequent "transitional cells" were seen. The term "transitional cells" is used to describe those cells from which probably the macrophages arise, namely, lymphocytes and monocytes and transitional forms between lymphocytes and monocytes and monocytes and small macrophages.

Those cases which showed an early macrophage response associated with a polymorph response and positive cultures (Cases 33, 67 and 71) were all admitted after having had symptoms for six or seven days; these cases were approaching the "natural crisis" and showed "late red hepatisation".

The cases which had been treated for a day or less (Cases 4, 57, 28, 60, 26, 45), irrespective of whether the lung was sterile or not, still showed the picture of red hepatisation. Case 56 showed a fair number of macrophages

but the duration of illness was uncertain and he might well have been near the time of the normal crisis.

RED HEPATISATION.

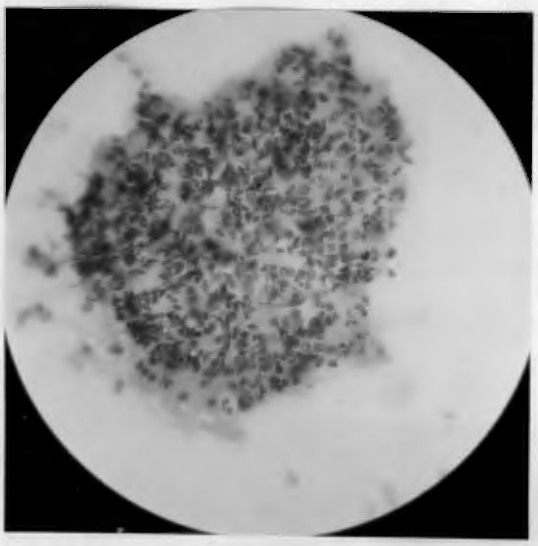


Figure 78. Case 3.

Polymorphs and Fibrin.

High Power.

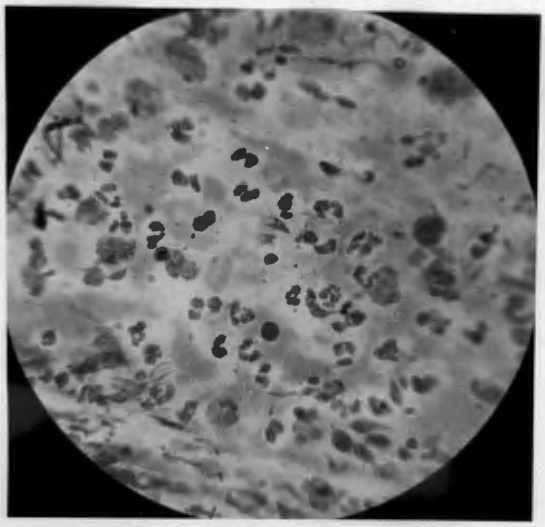


Figure 79. Case 9.

Polymorphs. Fibrin is not well demonstrated. (Leishman stain).

Oil Immersion.

RED HEPATISATION.

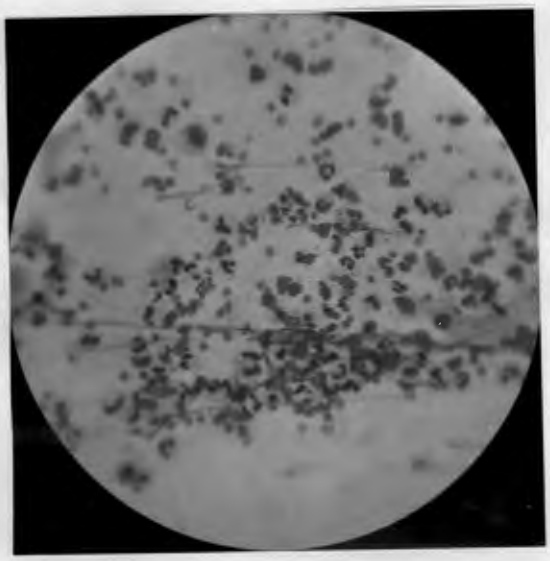


Figure 80. Case 50.

Polymorphs and Fibrin.

High Power.

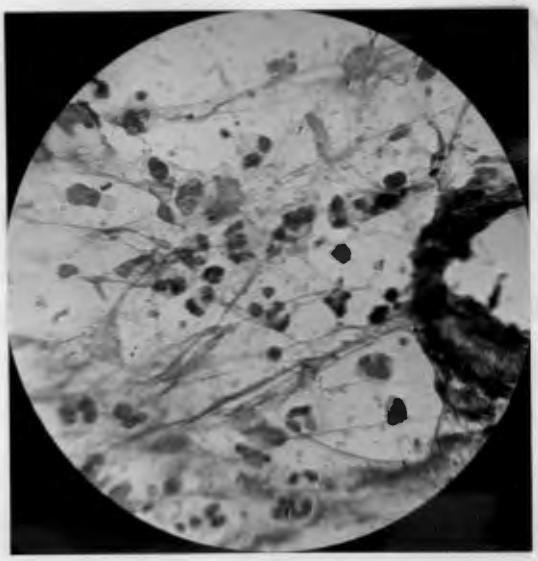


Figure 81. Case 50.

Polymorphs and Fibrin.

Oil Immersion.

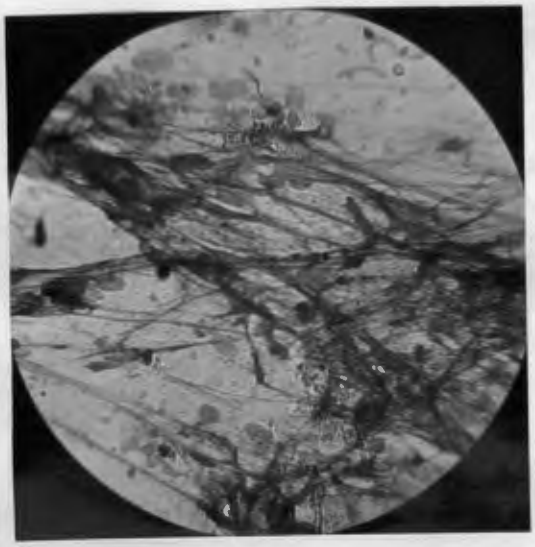


Figure 82. Case 42

Fibrin.

Oil Immersion.

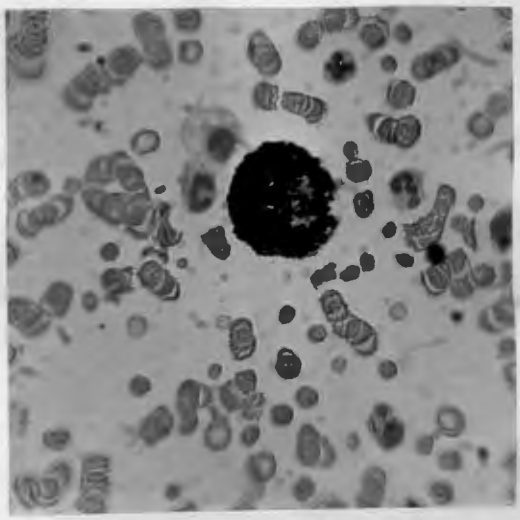


Figure 83. Case 23.

Dust Cell and Small Macrophage. These are infrequent in red hepatisation.

Oil Immersion.

After adequate chemotherapy for two days the macrophage reaction was found to have begun and the picture was that of early resolution. This was well illustrated in Case 41. (See Figures 84 to 87).

There were large masses of fibrin associated with polymorphs and small macrophages in about equal numbers. Most of the polymorphs were well preserved but many were smaller than normal and showed signs of degeneration. Macrophages of all types had ingested polymorphs and many contained two partly digested cells. Transitional cells were frequent.

EARLY RESOLUTION.

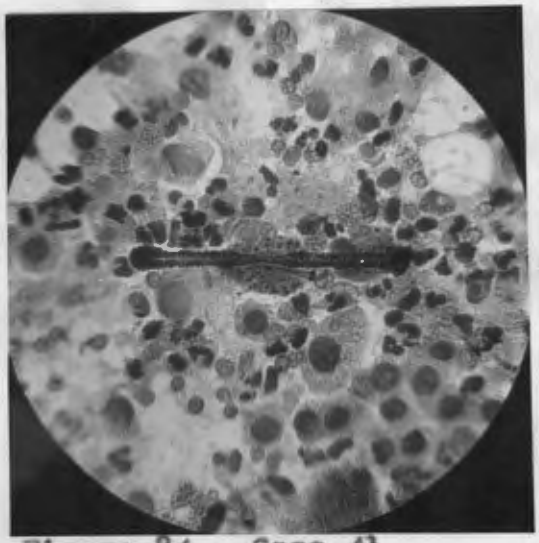


Figure 84. Case 41.

Polymorphs and Small Macrophages. Asbestos bodies also present.

Oil Immersion.

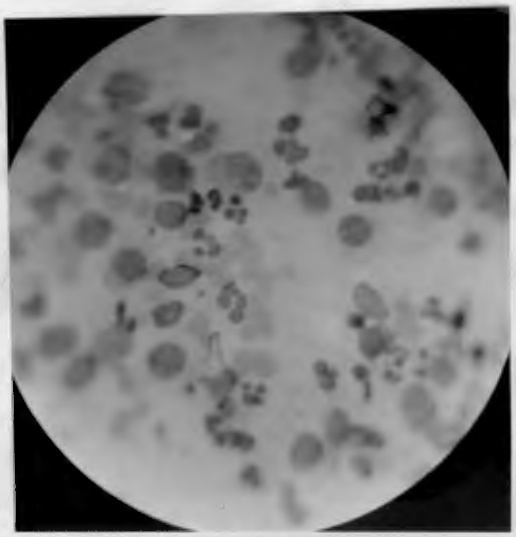


Figure 85. Case 41.

Polymorphs and Small Macrophages.

Oil Immersion.

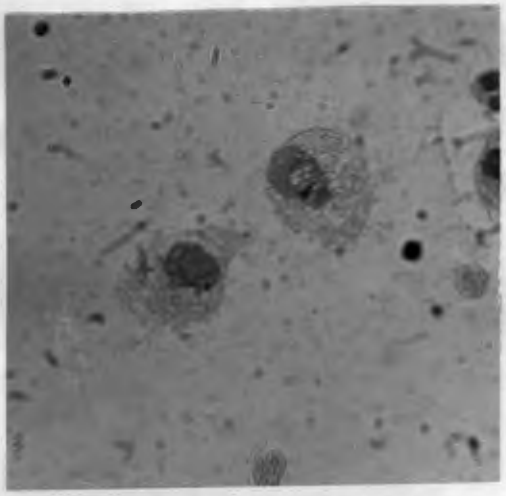


Figure 86. Case 41.

Classical small macrophages of resolution.

Oil Immersion.

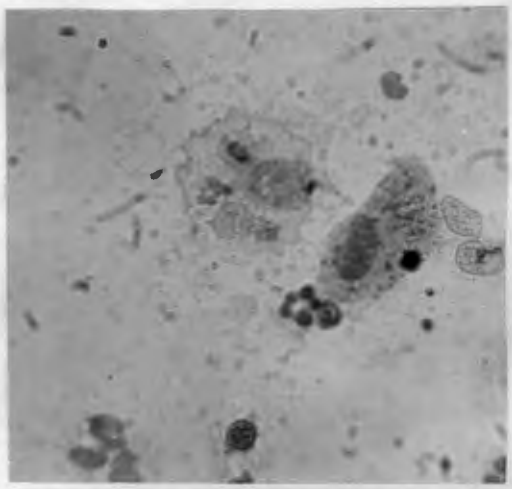
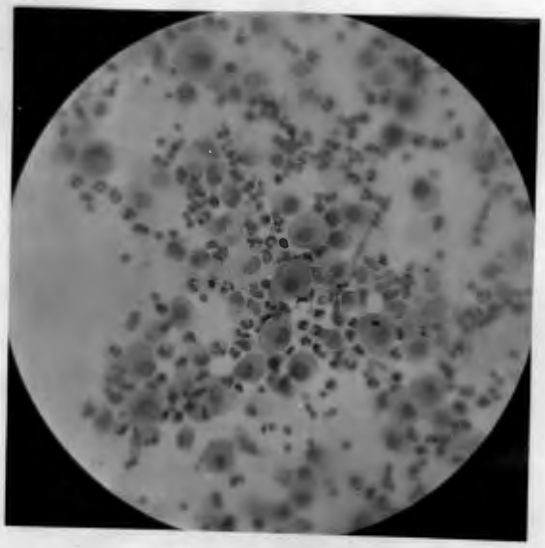


Figure 87. Case 41.

Macrophage which has ingested three polymorphs and a red cell. Next to it is a small dust cell.

Oil Immersion.

Case 54 showed only early resolution (see Figure 88) after five days of chemotherapy but for three of these days he had been on only sulphonamides; for the latter two days he had received penicillin in addition. Sulphonamides certainly took longer to sterilise the lung than penicillin and there was a slower clinical and probably also a slower cellular response. He had been admitted very ill, toxic and pyrexial inspite of the sulphonamide and had really been on effective chemotherapy for only two days when biopsy was done.



EARLY RESOLUTION

Figure 88. Case 54.

Numerous Polymorphs but Small Macrophages fairly frequent.

High Power.

Finally <u>after three or more days of therapy</u> resolution was well established. <u>Fairly well advanced resolution</u> was shown by Cases 60-1, 38 and 56-1. (See Figures 89 to 92). There were still large masses of fibrin with numerous cells. The majority of the cells were small macrophages but polymorphs were not uncommon. Often a small macrophage was seen to contain a still recognisable partly digested polymorph. Transitional cells were frequent.

FAIRLY WELL ADVANCED RESOLUTION.

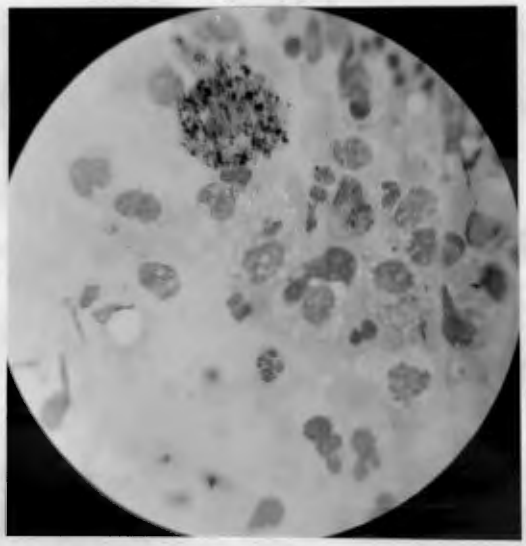


Figure 89. Case 38.

Many Small Macrophages but Polymorphs still present.

Oil Immersion.

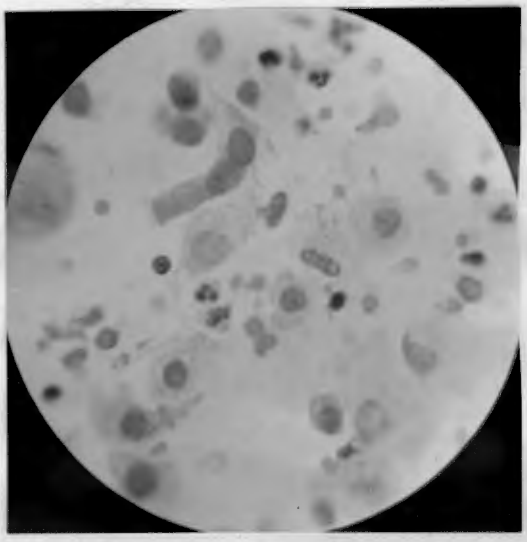


Figure 90. Case 60 - 1.

Many Small Macrophages but Polymorphs still present.

Oil Immersion.

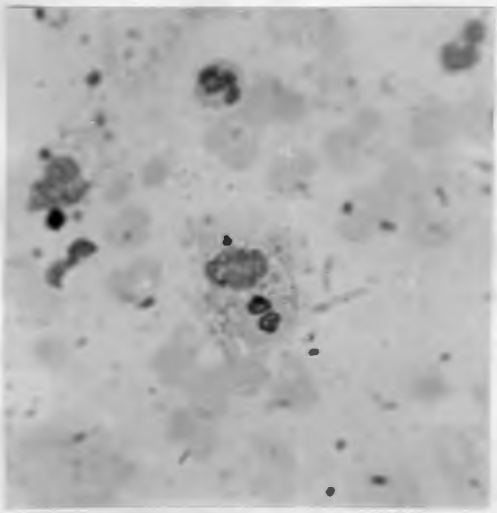


Figure 91. Case 38.

Polymorph within a Small Macrophage.

Oil Immersion.

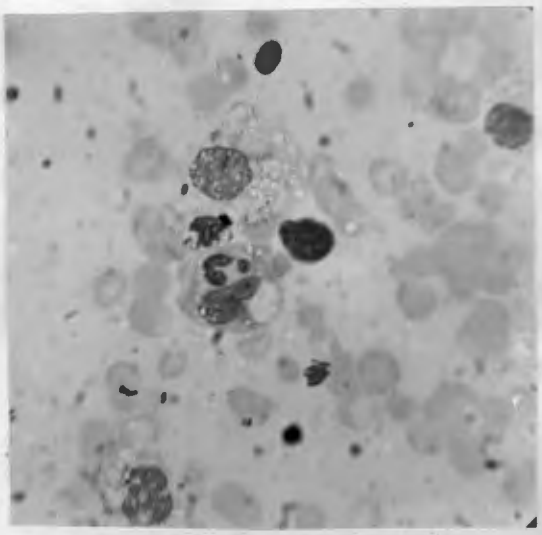


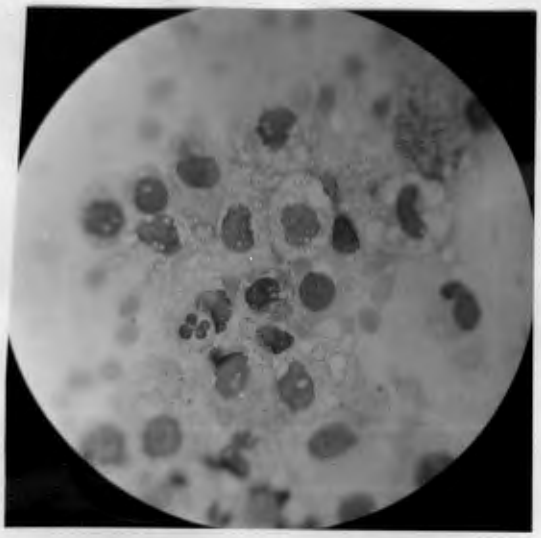
Figure 92. Case 38.

Polymorph within a Small Macrophage.

Oil Immersion.

Advanced resolution was well illustrated by Cases 57-1, 71-1, 45-1 and 72-1. The fibrin was considerably less in amount and in some areas appeared to be becoming granular (see Figure 95). Small macrophages were very numerous and many transitional cells were present. Polymorphs were scanty and mostly well preserved. Very rarely, a polymorph was seen within a macrophage.

Case 51, who had received chemotherapy for only two days, showed advanced resolution; she had been admitted on the eighth day of her illness and had probably already had a commencing macrophage response even before the onset of treatment. (See Figures 93 and 94).



ADVANCED RESOLUTION.
Figure 93. Case 51.
Numerous Small Macrophages.
Oil Immersion.

ADVANCED RESOLUTION.

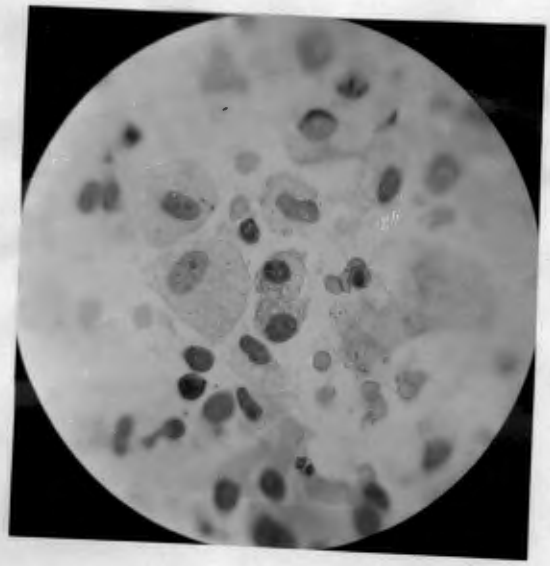


Figure 94. Case 51.

Many Small Macrophages.

Oil Immersion.

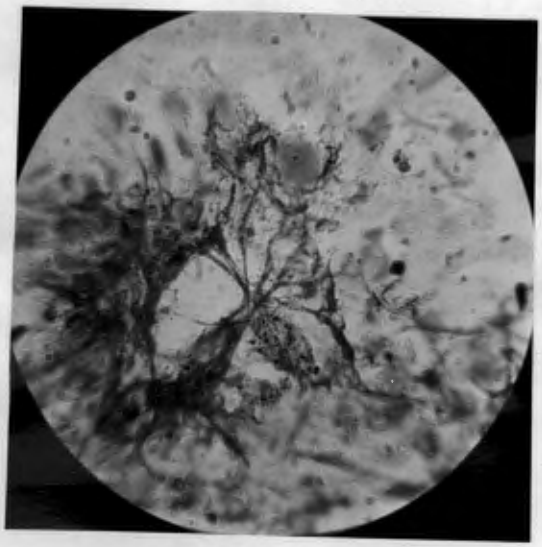


Figure 95. Case 72-1.

Fibrin beginning to show signs of degeneration.

Oil Immersion.

CONCLUSIONS:

From a consideration of these cases one was able to arrive at a dynamic conception of the cellular responses in acute lobar pneumonia. By the time that a patient presented himself at hospital with definite symptoms his lung was in the stage of red hepatisation. The alveoli were filled with a fibrinous exudate in which were numerous well preserved polymorphs. Pneumococci were present and were being ingested by these phagocytes. Macrophages were always present in the normal lung but as red hepatisation progressed especially the small type were found in increasing numbers. Polymorphs occasionally became degenerate and were taken up by these scavengers. As the time for the "normal" crisis approached macrophages increased in numbers. It was at this stage or a day or two before that the patient consulted a doctor and received sulphonamide, penicillin or both. The pneumococci were destroyed within twenty four hours of the commencement of chemotherapy, probably by means of bacteriostasis in the case of sulphonamide and by lysis in the case of penicillin. An artificial crisis had now been induced. Red hepatisation was cut short. Macrophages appeared in the lung in greater and greater numbers. These cells rapidly ingested the polymorphs which now had no function because the organisms they had come to combat had been destroyed. More and more macrophages accumulated in the lung and finally most of the polymorphs had been removed.

The work was done mainly by the small macrophages. Finally the fibrin was taken up by the macrophages which in turn left the lung and were probably destroyed in the reticulo-endothelial system. In this way the inflammatory exudate was removed and the lung returned to normal. It would appear that with chemotherapy the stage of grey hepatisation has ceased to exist.

Case 45 illustrates the change from red hepatisation to resolution. Figure 96 shows red hepatisation which was present on admission. Figures 97 to 99 show the macrophage response and advanced resolution after six days of penicillin and sulphonamide therapy.

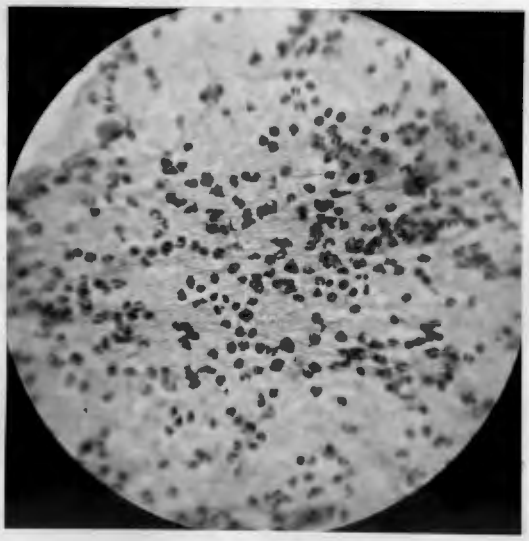


Figure 96. Case 45.
Numerous polymorphs and Fibrin.
High Power.

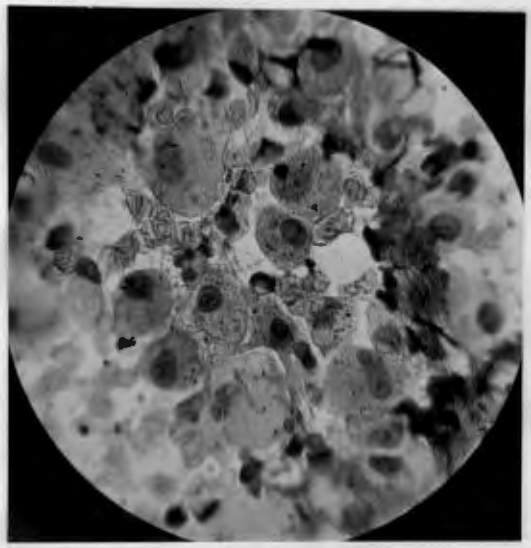


Figure 97. Case 45-1.
Numerous macrophages and Fibrin.
Oil Immersion.

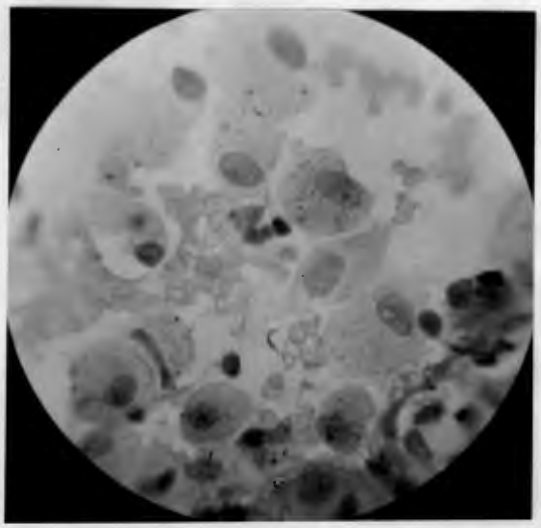


Figure 98. Case 45-1.
Numerous Macrophages.
Oil Immersion.

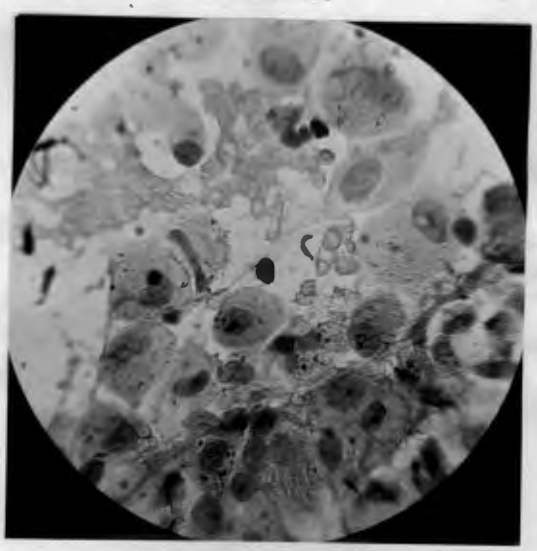


Figure 99. Case 45-1.
Numerous Macrophages and Fibrin. Oil Immersion.

Of particular interest was the light that was thrown on the probable origin of the macrophages. At all stages cells were seen that resembled the lymphocytes or monocytes normally found in the blood. In addition there were cells which were difficult to place in any particular class and these appeared to be transitional cells, that is cells which were in the process of being converted from lymphocytes to monocytes and from monocytes to small macrophages. It was of interest that these transitional cells were least frequent during the stage of red hepatisation, most numerous during early resolution and frequent but not very numerous during advanced resolution. This fitted in well with the theory that mobilisation of these cells was at its height during early resolution when the macrophages were beginning to accumulate. It was felt that the present work to some extent confirmed Loosli's theories of 1942. There was no evidence of any increase of the alveolar histiocytes during the stage of resolution.

The cell changes, described in the human cases in this series, were very similar to those that occurred in experimental pneumonia in rats treated with sulphonamide. (Wood and Irons 1946; Wood, McLeod and Irons 1946).

TRANSITIONAL CELLS.

Figures 100 to 105 show many of the intermediate stages between small lymphocytes and small macrophages. All these microphotographs were taken under oil immersion in a small area of one of the slides of Case 38 (which showed fairly well advanced resolution).

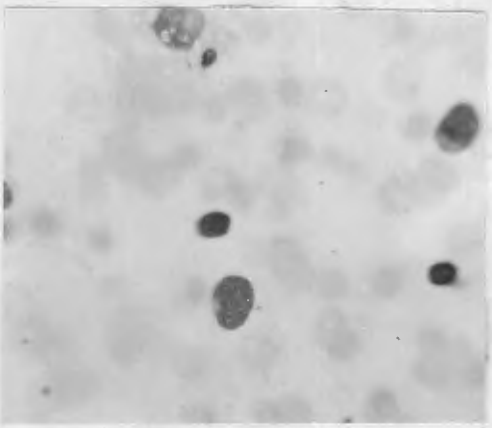


Figure 100.

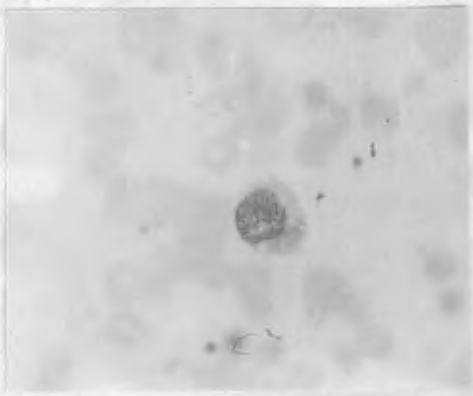


Figure 101.

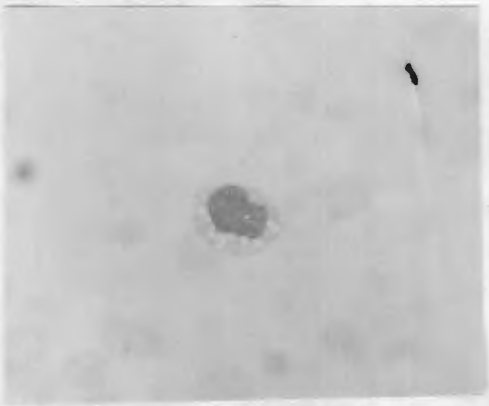


Figure 102.

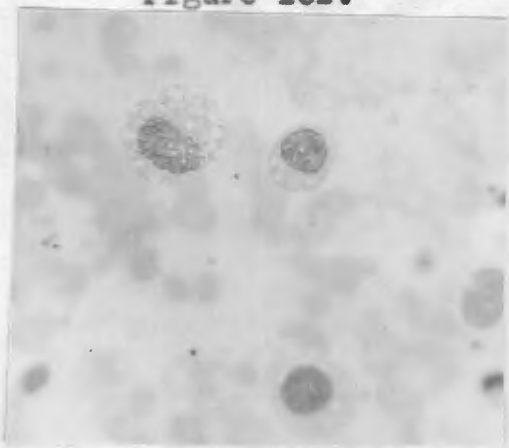


Figure 103.

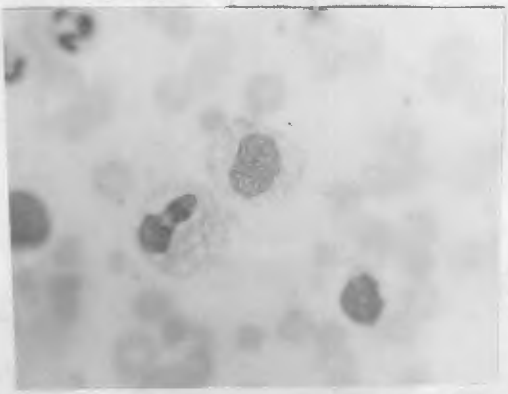


Figure 104.

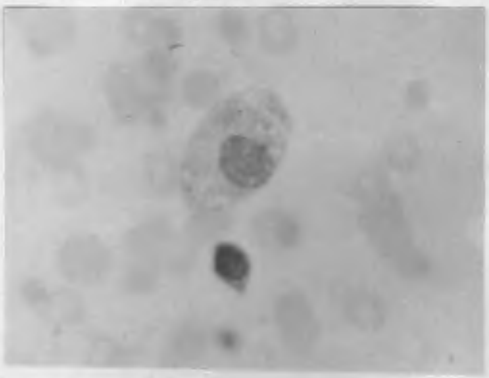


Figure 105.

As can be seen from Table 3, Group III, five biopsies were done on the right upper lobe and middle lobe areas, six on the right lower lobe, three on the left upper lobe and twelve on the left lower lobe. Thus it was unlikely that the changes described were confined to lobar pneumonia affecting any one particular lobe. Serial biopsies were done on several cases to avoid the criticism that, for example, if Case A showed red hepatisation before chemotherapy, and on the fourth day after chemotherapy Case B showed resolution then it was not necessarily true that on the fourth day Case A would also have shown resolution. In the six cases in which two serial biopsies were done on each (Cases 45, 56, 57, 60, 71 and 72) the alteration in the same patient from red hepatisation to resolution were exactly as expected.

It is well known that one part of a lung might be in one stage of consolidation whereas another portion quite nearby might be in quite a different pathological state. By lung biopsy one obtained material from only one area of the lung. The needle was always inserted into that part of the lung where the physical signs were the most obvious and thus biopsies were obtained from those areas where presumably the most marked processes were occurring. Here again the value of serial biopsies always through the same area was demonstrated - these showed the sequence of changes which have been described. Thus although the changes in different parts

of the lung may be different at any one time, for every individual area it may be assumed that the sequence is always the same.

It must be remembered that these results have been obtained over a definite period of time, in a definite hospital with coloured and native patients; there is no guarentee that were cases investigated at another time, in another hospital with a different class and race of patient the results would necessarily be identical. However, these observations show a very definite pattern and confirm the results which one would have expected on purely theoretical grounds.

There appeared to be no difference in the pathological findings in the Coloured and Native patients.

As a clinician, rather than a pathologist, I was particularly interested in trying to relate the general condition of the patient and the physical signs in the chest to the underlying pathological process and to see if one could predict from physical signs the pathological state of the underlying lung. The physical findings as related to the stage of the pathology are set out in Table 14. It will be seen that physical signs gave little indication of what was actually going on in the lung. All cases showed some diminished movement of the affected side (not set out in the

Table 14.

To Show the Relationhhip Between Physical Signs and Underlying Pathology.

T - Toxic; ST - Slightly Toxic; NT - Not Toxic; P - Pyrexial; A - Apyrexial; L - Leucocytosis; Percussion: D - Dull; SD - Slightly Dull; R - Resonant; VF and VR: I - Increased; N - Normal; D - Diminished; Breath Sounds: B - Bronchial and V - Vesicular; Crepitations: M - Medium; F - Fine; FM - Few Medium and FF - Few Fine.

Case No.	General Condition	Per-cussion	VF	VR	Breath Sounds	Crepi-tations	Biopsy Pathology.
9	T P L	D	I	I	B	-	Red hepatisation
23	T P L	D	I	I	B	-	Red hepatisation
42	NT P L	SD	N	N	V	M	Red Hepatisation
50	T P L	D	D	D	B	FF	Red hepatisation
72	T P L	D	I	I	B	M	Red hepatisation
4	T P L	D	I	I	V	M	Red hepatisation
57	T P L	D	I	I	B	FM	Red hepatisation
28	T P L	D	I	I	B	M	Red hepatisation

Table 14. (continued)

Case No.	General Condition	Per-cussion	VF	VR	Breath Sounds	Crepi-tations	Biopsy Pathology
26	T P L	D	I	I	V	M	Red hepatisation
45	T P L	D	I	I	B	-	Red hepatisation
33	T P L	D	I	I	B	M	Late red hepatisation
67	T P	D	I	I	V	-	Late red hepatisation
71	T P L	D	I	I	V	M	Late red hepatisation
60	NT P L	D	D	D	B	FF	Late red hepatisation
56	T P	D	I	I	B	-	Late red hepatisation
41	T P	D	I	I	V	M	Early resolution
54	ST A	D	I	I	B	FF	Early resolution
60-1	NT A	R	I	I	V	-	Fair resolution
56-1	NT A	D	I	I	B	FF	Fair resolution

Table 14. (continued)

Case No.	General Condition	Per-cussion	VF	VR	Breath Sounds	Crepi-tations	Biopsy Pathology
38	ST P	D	I	I	B	M	Fair resolution
51	NT A	D	I	I	B	M	Advanced resolution
57-1	NT A	SD	I	I	V	FM	Advanced resolution
71-1	NT A	SD	N	I	V	M	Advanced resolution
45-1	NT A	D	N	I	B	-	Advanced resolution
72-1	NT A	D	I	I	B	M	Advanced resolution.

table) and most cases were relatively dull to percussion irrespective of whether the lesion was active or resolving. Similar comments may be made in respect to alterations in vocal fremitus and vocal resonance. Breath sound were often bronchial in spite of the presence of the cellular changes of advanced resolution. Crepitations were also of little help as they were found associated with red hepatisation as well as with advanced resolution; crepitations were also absent in some of the cases of both groups. Taking the individual case one occasionally did find diminished dullness, or the appearance of or increase in the number of crepitations as the lesion resolved. Probably the most valuable guide was the general clinical condition of the patient. If he became non-toxic and apyrexial and actually expressed a feeling of well being then one could usually correctly predict that resolution was progressing satisfactorily. It must be emphasised that the clinician's ability to assess the general condition of his patient was the important point in deciding the progress of the case; the local physical signs were of much less importance. The period that has been under discussion was that critical first five or six days after the onset of chemotherapy. It seemed hardly necessary to state that the physical signs were important in determining when the lung had returned to normal or near normal.

This investigation was carried out over a period of about 18 months and the cases were not drawn from any definite epidemic of lobar pneumonia.

The importance of alterations in the nature of the sputum both macroscopically and microscopically will be considered in some future communication.

SECTION V.

THE PATHOGENESIS OF THE RESOLUTION OF CHRONIC LOBAR PNEUMONIA.

THE PATHOGENESIS OF THE RESOLUTION OF CHRONIC LOBAR PNEUMONIA.

It is necessary to make quite clear what is meant in this investigation by the term "chronic lobar pneumonia". A chronic lobar pneumonia is one which presents just as an ordinary acute lobar pneumonia, and appears to respond at first in a similar manner but clinical or radiological signs of consolidation persist for many weeks or even months in spite of the excellent general condition of the patient. The consolidation eventually completely resolves without any serious residua. It is important that after the acute stage is over these patients look and feel well and are usually apyrexial. The only abnormalities are the physical or radiological signs of consolidation. In all fairness one should really call this condition by the unwieldy term: "lobar pneumonia with slow or delayed resolution".

REVIEW OF THE LITERATURE.

Although chronic lobar pneumonia must have not infrequently been observed in hospitals and in private practice very little has been written on the subject, and it is often not described in the standard textbooks. However, a few papers have been written specifically about this condition.

Weinstein and Goodman (1934) described unresolved

pneumonia as found in those patients, who though much improved or essentially clinically well, continued to exhibit abnormal physical signs or substantial changes on X-ray for more than two weeks after the termination of the acute phase of the illness. Their paper dealt mainly with the etiological role of syphilis.

Holmes (1936) was emphatic that the term unresolved pneumonia could be correctly applied only to those cases in which there was delayed resolution. Crisis or lysis was incomplete; the temperature, pulse rate and respiratory rate did not return to normal within the usual period and signs of consolidation persisted unduly. The main purpose of his report was to distinguish this condition from other goups which were often incorrectly referred to as unresolved pneumonia:

(1) Creeping pneumonia where resolution in one lobe was followed by involvement of another lobe with thus a protracted course and irregular pyrexia.
(2) Post-pneumonic pyrexia due to the complications of pneumonia - empyema, pericarditis, pulmonary abscess, bronchiectasis, phlebitis, arthritis, otitis media, pyaemic abscesses in soft parts and septicaemia.
(3) Some cases originally wrongly diagnosed as lobar pneumonia - bronchopneumonia superimposed on a chronic pulmonary affection such as tuberculosis or bronchiectasis

or related to pulmonary neoplasm.

His definition was quite similar to the one in use in the present paper and his group of true unresolved pneumonia probably corresponded to chronic lobar pneumonia.

Robertson and Uhley (1936) in their postmortem study of lobar pneumonia posed the question of what happened in those cases where parts of the lung remained consolidated for varying periods of time after the patient had made a clinical recovery. Unfortunately their material did not include any of these cases of chronic pneumonia.

Reimann (1938) attempted to distinguish between delayed resolution and unresolved pneumonia. By delayed resolution he implied merely the persistence of signs of consolidation; unresolved pneumonia denoted the persistence of the disease.

Holinger (1938) stated: "True unresolved pneumonia is a definite clinical entity in which resolution is delayed several weeks or even months following the crisis. It occurs in about 2 to 3 per cent of all lobar pneumonias". He described three cases of pulmonary atelectasis during the course of upper respiratory infections which simulated unresolved pneumonia. The main theme of his paper was the value of early bronchoscopic aspiration in these cases of atelectasis.

A few papers have been written on entities called chronic

pneumonia in infants, chronic benign pneumonitis, chronic exudative and indurative pneumonia, chronic pneumonitis, unresolved pneumonia and chronic pulmonary catarrh. The conditions described were quite different from chronic lobar pneumonia. Textbooks of pathology usually did not mention the condition and even Coope (1948) used carnification synonymously with unresolved pneumonia. Boyd (1938) put forward the conception of a race between resolution and fibrosis. A delay in resolution gave the fibroblasts time to invade the exudate with carnification as the end result. Muir (1941) used the term "chronic interstitial pneumonia" and carnification synonymously.

It is necessary to review briefly some of those conditions called chronic pneumonia to show how much confusion there is in this subject.

Sanderson (1936) described six cases of infants with chronic pneumonia, some of a lobar distribution with enlarged tracheobronchial nodes but persistently negative tuberculin tests. These cases took eight to ten months to fully resolve. He suggested that these might have been oil aspiration pneumonias. A similar series of nine infants (mostly under five months) was described by Greenwald et al. (1936). These babies presented with anorexia and failure to gain weight. Some cases showed signs of consolidation but others did not. X-ray revealed either a homogeneous

consolidation involving all or part of a lobe or a diffuse patchy coalescent lesion similar to a bronchopneumonia. Enlarged hilar glands were present in some cases. Mantoux tests were always negative. The course was benign, the physical signs and X-ray appearances persisting for months to even four years. He suggested that these might also be cases of oil aspiration pneumonia.

Under the heading of "chronic exudative and indurative pneumonia" Hirsch and Russel (1945) described a bilateral pulmonary infiltration due to inhalation of shellac used in the making of furniture. Schneider (1948) described a series of cases of "chronic benign pneumonitis" which were almost certainly oil aspiration pneumonias. An asymptomatic basal or upper lobe pneumonitis was discovered by routine X-rays of persons habitually taking mineral oil and especially in those cases where the gag reflex was reduced or absent.

Waddell et al. (1949) performed lobectomies and pneumonectomies on cases of a chronic pulmonary condition. The histology was that of a marked fibrosis with unusual deposits of cholesterol and cholesterol esters contained in large mononuclear cells. The etiology was uncertain. The condition was termed a "chronic pneumonitis".

Hamilton (1938) conceived chronic pulmonary catarrh as being a bronchopneumonia which ran a chronic course to the full picture of bronchiectasis. Similar ideas were held by Grier

(1944) whose cases of unresolved pneumonia were actually cases of bronchopneumonia with an underlying bronchiectasis.

A number of investigators have described series of cases as chronic or unresolved pneumonia in which some of the cases have been obvious "true" chronic pneumonias and others a variety of other pulmonary conditions.

Thatcher (1913) set a time limit of seventeen days after which a pneumonia was considered to be unresolved. In only three of his 34 cases could the term chronic pneumonia be truly applied. The other cases were conditions such as empyema and lung abscess. Similarly an analysis of Pickhardt's fifty two cases diagnosed as unresolved pneumonia revealed only six which really fell into this class. About 36.5 per cent were frankly surgical conditions such as suppurative pleurisy, abscess, neoplasm and foreign bodies (Pickhardt 1928).

In a discussion on pneumonia thought to be prolonged by the presence of coexisting syphilis, Head and Seabloom (1919) described three cases of which two were patients with bilateral bronchopneumonia. The third case was probably a chronic lobar pneumonia. On a similar theme of syphilis as an etiological factor in the causation of chronic pneumonia, Youmans and Kampmeier (1927) recorded 31 cases but only two of these corresponded to true chronic pneumonia. The others were cases of abscess, empyema, bronchiectasis and carnification

Scadding (1939) produced one of the few comprehensive papers on chronic pneumonia. He defined chronic pneumonia as a chronic inflammation of the lung in which exudation into the pulmonary alveoli was the primary process, with organisation leading to fibrosis or suppuration leading to abscess formation as possible secondary processes, resolution being possible at any stage with more or less residual fibrosis. This was a very wide definition and embraced a great variety of conditions. These included chronic diffuse bronchopneumonias and chronic suppurative pneumonias of uncertain etiology both with and without abscess formation. These types were not included in the present series. However, a chronic circumscribed non-suppurative pneumonia was described and said to be the usual type of delayed resolution of acute pneumonia. Radiologically complete clearing of opacities might be delayed as long as 85 days. The consolidation appeared to remain in a quiescent state and finally complete resolution did occur without organisation or suppuration. There was no doubt that this condition was exactly the same as the chronic lobar pneumonia that has been defined in this present paper. In addition he described a similar condition of subacute or chronic consolidation, capable of complete resolution, but the onset was insidious or with only mild symptoms. An example was given of a fifty six year old man with delayed resolution for "several weeks" which then slowly cleared over about six months.

Collins (1947), writing from Australia, defined unresolved pneumonia as the clinical condition resulting from delayed resolution of lobar pneumonia and comprised delayed resolution without toxaemia or secondarily chronic inflammation. The state of unresolved pneumonia lasted several weeks to several months, when resolution took place. So far one agreed with his definition. He then went on to state that occasionally organization of the exudate took place leading to pulmonary fibrosis. He described two types of chronic pneumonia:

(1) The temperature fell by crisis or responded rapidly to chemotherapy but the chest signs of dullness, bronchial breathing or diminished breath sounds, and râles persisted. These signs disappeared "at the onset of resolution". This type was rare.

(2) The temperature fell by lysis and the local signs remained and were accompanied by slight irregular fever, occasional sweats and a rapid pulse rate. X-ray confirmed the diagnosis and empyema, especially of the interlobar type was frequently mistaken for or masked by the unresolved pneumonia. Frequently small empyemata or pulmonary abscesses accompanied the unresolved pneumonia and were found to resolve together with the consolidation. Occasionally the condition terminated in fibrosis which was frequently accompanied by permanent collapse of the affected area.

His first group obviously corresponded to chronic lobar pneumonia.

Rajaram (1946), writing in "The Antiseptic", distinguished chronic pneumonia from the sequelae of pneumonia. In rather picturesque language he described in chronic pneumonia the kaleidoscopic pathological picture of congestion, varying stages of resolution with perhaps foci of suppuration all in one and "is something akin to winter and summer painted in one landscape simultaneously". In the sequelae of pneumonia there was "a monotonous pathological picture of either fibrosis or a static interstitial inflammation or a delay in the last phase of the pneumonic lung, that is, late resolution". It will be shown that his last phrase comes very close to the truth about chronic pneumonia although he included it in his description of the sequelae. He divided chronic pneumonias into several groups:

(1) Chronic non-suppurative cases where there "is the usual type of pneumonia which sometimes runs into a couple of months with a delay in the phase of consolidation and resolution and the lung clearing up without any gross fibrosis." This possibly corresponded with chronic lobar pneumonia.

(2) Chronic suppurative pneumonia similar to the above but with suppurative changes without actual abscess formation (compare Scadding 1939).

(3) Chronic suppurative pneumonia with abscess formation.

Five of the cases in his first group resolved within

10 days to six weeks with sulphonamide or penicillin therapy. His plea was that these cases should not be confused with cases of tuberculosis.

Most authors had something to say about the etiology of the delayed resolution in the true cases of chronic lobar pneumonia.

The theory that the presence of coexisting syphilis delayed resolution was easy to understand, flourished and died hard. Head and Seabloom (1919) described their three cases (two bronchopneumonia and one lobar pneumonia) who after six weeks still showed dullness and crepitations on physical examination, and the presence of consolidation was confirmed by X-ray. In all three the Wassermann reaction was strongly positive. Arsphenamin 0.4 Gm. was given weekly intravenously and within three weeks the physical signs had completely cleared in all cases. Protagonists of the "syphilis theory" were Fitz-Hugh (1924), Kampmeier and Youmans (1927) and Kampmeier (1932). As, already stated, the cases of Youmans and Kampmeier were not convincing from the point of view of being cases of chronic pneumonia. Their explanatinn of the delayed resolution was that syphilis caused an upsetting of the delicate balance of physico-chemical forces concerned with resolution and resulted in non-specific failure of resolution with or without compli-

cations. Treatment of the syphilis early in the course of the pneumonia would prevent these complications. Weinstein and Goodman (1934) in a very convincing paper disposed of the "syphilis hypothesis". In a series of 509 cases of pneumonia seen at the John Hopkins Hospital, forty five were chronic lobar pneumonias. Of these 45 cases fifteen had syphilis and thirty had not. Of the 139 cases in the entire series with syphilis 10.7 per cent showed some retarded resolution as compared with 8.1 per cent of the 370 non-syphilitic cases. They showed that the clinical course of lobar pneumonia was not perceptibly different in patients with and without syphilis. A classical crisis occurred with the same frequency in the two groups. The mortality rates were the same. Antisyphilitic therapy appeared to have no effect on the resolution of the chronic cases. They quoted Lieven (1931) as also disagreeing with the "syphilis theory".

A large series of 1469 cases of pneumococcic pneumonia treated at the Los Angeles County Hospital from 1934 to 1938 was analysed by Moom et al. in 1940. These were divided into two more or less equal groups - the one group had some concomitant pathology and the other not. The commonest associated conditions were pneumonia twice or more in the past with or without bronchiectasis, frequent colds with or without sore throats, asthma with or without chronic cough, pulmonary tuberculosis, recubrent pleurisy, arteriosclerotic heart disease, syphilis, alcoholism, recent loss of weight,

obesity, and pregnancy. The difference in outcome of the two groups was not impressive. Where there was a concomitant condition there was a somewhat higher death rate, a lower optimum outcome rate and a suggestively lower complication rate. In the large group of syphilitic cases the incidence of complications was not impressively greater nor were they febrile longer than the control group. Unfortunately chronic pneumonia was not specifically dealt with but probably had there been one of these very varied concomitant conditions constantly associated with prolonged consolidation this would have been emphasised. However, Holmes (1936) felt that circumstances which contributed to chronic pneumonia were debility from any cause, valvular heart disease, cardio-vascular sclerosis and senility. Reimann (1938) commented on the possible failure of autolytic enzymes to function, and mentioned the "syphilis theory"; he concluded that any complicating illness or condition might delay the normal process of resolution and even severe anthracosis was said to delay resolution. Collins (1947) reluctantly admitted that the exact etiology was unknown but stated that in a large proportion of cases there was a constitutional debilitating factor. He quoted the theory of Meakins that there was local pulmonary collapse, associated with massive pulmonary collapse at the height of the illness (compare Holinger 1938).

Gleichman, Leder and Zahn (1949) investigated 52 cases

of delayed resolution. They stated that the term chronic pneumonia was a useful clinical expression but that no specific pathological entity existed. Delayed resolution was said to include a number of different pathological conditions. An arbitrary time limit of 30 days was set for complete resolution. They found a cause for the delay in almost every case and divided the etiology into three large groups:

(1) Bacteriological and chemical factors - 16 cases - Friedlander's bacillus, pneumococcus Type III, streptococcus, staphylococcus, P.tularensis, tuberculosis, anaerobic organisms of the oropharynx, viruses of primary atypical pneumonia and ornithosis, fungi, aspiration of food or gastric contents, oil aspiration, septic embolism.

(2) Factors influencing bronchial drainage - 22 cases - upper respiratory obstruction (vocal cord paralysis, pharyngeal paralysis); bronchial obstruction of an endo-bronchial type (tumour, foreign body, tuberculosis, non-specific stenosis) or an extra-bronchial type (aneurysm, mediastinal tumour, hilar node enlargement); impaired ciliary action in chronic bronchitis, bronchiectasis, bronchial asthma, arrested pulmonary tuberculosis; impaired pulmonary mobility in pulmonary fibrosis and emphysema, pneumoconiosis, chest trauma, paralysis of diaphragm or intercostal muscles.

(3) Intrinsic complications of the pneumonic process -

12 cases - pleural effusion, empyema, lobar or segmental atelectasis, lung abscess.

(4) Undiagnosed. - 2 cases.

It will be obvious from a consideration of this list that few of their patients were true cases of chronic lobar pneumonia. One was tempted to speculate that the only cases which might have been chronic pneumonias were the last two in the undiagnosed group.

From the pathological point of view Robertson and Uhley (1936) make an excellent suggestion. They said that it was possible that the evolution of the process was inhibited at some point prior to the stage of removal of the exudate, but not before the effective control of the invading organisms had been accomplished.

Of great interest was the case of chronic pneumonia which was subjected to lung biopsy by Horder in 1909. The patient was a man of 20 years, and consolidation with pyrexia and leucocytosis (the case was unusual in these respects) had persisted for 23 days. At this stage lung biopsy was performed and the material was sterile. The temperature settled soon after this and the general condition was excellent but when the patient left hospital in "good health" the lung was still "solid". This case was recorded as a negative lung puncture but these findings will be

seen to fit in with the results of the present investigation. No other cases of lung biopsies used for diagnostic purposes in true chronic pneumonias could be traced.

In conclusion, it would appear that few cases of chronic lobar pneumonia have been recorded although no doubt they occurred not infrequently in practice. The presence of concomitant pathology might play a part in delaying resolution but there was no striking evidence to support such a proposition. It must be acknowledged that both the etiology and pathology of chronic lobar pneumonia was unknown.

The treatments suggested for chronic pneumonia were very unimpressive. At first much store was placed on treatment of any coexisting syphilis but this was proved of little importance (Weinstein and Goodman 1934). Rajarem (1946) obtained satisfactory results with sulphonamide or penicillin but his cases were poorly described and from the very nature of the definition of chronic pneumonia the important point was that it did not respond completely to chemotherapy. General measures in the form of breathing exercises, tonics, sunshine, ultra-violet radiation and diathermy to the affected lung were suggested by Holmes (1936). Collins (1947) kept his patients in bed while gross physical or radiographic signs persisted and chemotherapy was given if pyrexia was present. Diathermy to the chest was said to be helpful. Patients were given vitamins, any

anaemia was treated and nursing care was emphasised. These vague therapeutic measures were the result of ignorance of the underlying pathology.

The only startling therapeutic suggestion has come from Colby (1909) who reported twelve cases in which he performed puncture of the lung as a therapeutic measure. He obtained "good results" and there were no complications. His original paper was published in the Journal of the Tennessee Medical Association which unfortunately was not to be obtained from any of the South African libraries nor from the available sources in Britain.

LUNG BIOPSY STUDIES OF LIVING PATIENTS WITH CHRONIC LOBAR PNEUMONIA.

In this series twenty biopsies were done on thirteen patients. The results are summarised in Tables 15 and 16 (pages 252, 253). A brief description of each case with the lung biopsy findings will be of some value to show the general pattern of the series.

CASE 6:

J.W. (C. male 31 years) commenced his illness with a dry cough four days before admission, followed two days later by cold shivers and feverishness with subsequent delirium, in which state he was admitted. He was very ill, dyspnoeic, pyrexial (101 degrees); over the right upper lobe dullness, bronchial breathing and medium crepitations; X-ray confirmed the massive right upper lobar consolidation. His general condition responded well to chemotherapy and on the fourth day lung biopsy showed the picture of fairly advanced resolution with sterile cultures. For about the next six weeks he continued to run an intermittent or remittent temperature to about 100 degrees and there was little change in the physical signs locally although X-ray showed slight resolution. Biopsy at this stage was again sterile and showed much fibrin and many macrophages. Although his temperature had been gradually settling to a lower level he was started on streptomycin and a few days later he

became apyrexial. His physical signs quite rapidly diminished but X-ray showed still quite considerable consolidation. He was discharged and an outpatient check X-ray approximately two and a half months after his original admission showed further resolution but the lung had not yet returned to normal. It must be emphasised that although the patient remained pyrexial for over 6 weeks and had signs of consolidation, after the first week of the acute stage, he felt perfectly well.

Concomitant pathology was a hypochromic anaemia of uncertain origin. He was a fairly heavy drinker and smoker.

CASE 19:

J.D. (C. male 36 years) was admitted with a history of left sided pleuritic pain, dyspnoea, cough with slight bloody sputum, fever and sweating for four days. He was very ill, dyspnoeic, apyrexial; no cardiomegaly but mitral stenosis and mild aortic regurgitation; over the left lower lobe dullness, medium crepitations and harsh vesicular breathing; leucocyte count 12,000 with 88 per cent neutrophils. X-ray confirmed the left lower lobar pneumonia. On chemotherapy he rapidly improved and was pyrexial with a temperature of 99 degrees only on the second and third days. His physical signs remained unaltered although the X-ray showed some resolution. Lung biopsy about three weeks after admission was sterile and showed a little fibrin with small macrophages

(and some larger ones) which were not very numerous. The picture was that of advanced resolution. Over the next three weeks resolution gradually became complete. Bronchogram was normal.

J.D. was of particular interest because a year previously he had been in Somerset Hospital with a classical right upper and middle lobe pneumonia which had followed almost an identical chronic course. Concomitant pathology was the rheumatic heart, fairly heavy drinking and smoking, and a positive serology for syphilis.

CASE 24:

N.A. (C. male 40 years) was admitted after six days of feverishness, shivering, dyspnoea, left sided pleuritic pain and a cough with greenish sputum. He was very toxic, pyrexial (101.5 degrees) and dyspnoeic; over the left lower lobe there was dullness and increased vocal fremitus and resonance with bronchial breathing; leucocytes 30,500 with 97 per cent neutrophils. X-ray showed a left lower lobar consolidation. Pneumococci were grown from both the lung biopsy material (which showed classical red hepatisation) and the sputum. Chemotherapy caused his temperature to fall by crisis and within six days there were many crepitations heard and the breath sounds were vesicular. Penicillin was discontinued on the seventh day and three days later he again became pyrexial with peaks to

over 101 degrees for about five days. X-ray showed a fair amount of resolution. He was started on penicillin again but insisted on going home. He was given sulphonamide to take with him. He returned to the outpatient department about two weeks later feeling fit but X-ray showed no further resolution. Unfortunately no local physical examination was done. He did not return for further examinations. This case has been included in the chronic group because 29 days after the commencement of chemotherapy X-ray showed a more or less static consolidation which seemed unlikely to resolve for at least some days if not weeks.

Factors which might have contributed to this slow resolution were the removal of a gastric ulcer by gastrectomy five months previously, and insufficient bed rest during his attack of pneumonia. In addition there were old areas of fibrosis at both apices.

CASE 29:

I.S. (C. male 46 years) complained of left sided pleuritic pain, blood stained sputum, feverishness and cold shivers for ten days. He was not very ill, slightly pyrexial (99 degrees) and slightly dyspnoeic; over the left lower lobe there was dullness, increased vocal fremitus and resonance, bronchial breathing and medium crepitations but at the extreme base it was stony dull and the bronchial

breathing was distant; leucocytes 25,100 with 87 per cent neutrophils. X-ray showed a left lower lobe consolidation with a small effusion and slight pneumonic changes in the right middle lobe. In spite of chemotherapy he ran a temperature in the region of 100 degrees for eight days. After the first week about 10 c.c. of sterile exudate were aspirated from his chest. The patient felt perfectly fit and gradually the fluid became absorbed and the consolidation began to resolve. About three weeks after admission there was still considerable consolidation and lung biopsy (which was sterile) showed large masses of fibrin with fewer small macrophages than were usually found in normal resolution. Clearing continued at a slow pace and on discharge (about six weeks after admission) there were only signs of what was probably thickened pleura. No bronchogram was done because of iodine sensitivity.

The only adverse factors were that he had been treated for venereal disease in the past.

CASE 31:

F.B. (C. female 23 years) gave a slightly different history from the other cases. Her illness commenced two weeks before admission with a dry cough, right sided pleuritic pain and headache. After a week only the cough persisted but she became feverish and sweated a lot especially at night. She was not very ill but her temperature was 100.2 degrees and

over the right lower lobe there was increased vocal fremitus and resonance, dullness, bronchial breathing and fine and medium crepitations; leucocyte count 8,100 with 76 per cent neutrophils. X-ray showed a right basal consolidation with effusion and a left perihilar consolidation. An attempt at lung biopsy resulted in a small pneumothorax. In spite of penicillin she continued to be pyrexial (in the region of 100 degrees) for about two weeks. At the time when she first became apyrexial X-rays showed some resolution of the right basal lesion but now a small left basal effusion was present. She remained feeling perfectly well. About two weeks later there was diminished movement, dullness and decreased air entry at the right base and lung biopsy was done. The material was sterile and histologically showed only scanty small macrophages, lymphocytes and sheets of non-ciliated bronchiolar epithelial cells, a picture which was quite compatible with normal. Gradually the fluid was reabsorbed until only bilateral basal pleural thickening remained - she had been in hospital for 45 days. Throughout her course a fan shaped infiltration of the left upper and middle zones had remained unchanged. Numerous gastric juice examinations for tubercle had been negative and the E.S.R. was normal.

This case showed many peculiar features and was included in this series more for the sake of completeness and because it was possibly the type of chronic pneumonia with

insidious onset described by Scadding. This case may have been a virus pneumonia. Lung biopsy gave no useful information.

CASE 35:

D.M. (N. male 51 years) complained of pleuritic pain in the left chest for two days, and cough with mucoid sputum and dyspnoea for one day. He was not very ill, apyrexial and the only abnormal signs were medium crepitations over the left lower lobe; leucocyte count 17,500 with 60 per cent neutrophils. He was started on chemotherapy but ran an intermittent pyrexia for four days (up to 100 degrees) and during this time he coughed up occasionally blood stained sputum. Five days after admission there was dullness and bronchial breathing in addition to the crepitations. X-ray about a week later (for the first time) showed consolidation of the posterior part of the left upper lobe and the upper part of the lower lobe. About three weeks after admission his physical signs were unchanged and lung biopsy was performed. The material was sterile, contained a little fibrin with numerous macrophages some of which were of the larger variety. The picture was that of advanced resolution. About seven weeks after admission there was improvement in the physical signs and X-ray appearance. He then slowly resolved and a final bronchogram showed no pathology.

The only contributing factors to the slow resolution

might have been a small area of fibrosis in the left upper lobe (probably old healed tubercle) and a slight anaemia.

CASE 37:

C.S. (C. female 50 years) complained of left sided pleuritic pain, dyspnoea and cough with mucopurulent sputum for two weeks. She was thin, dirty and neglected with sores on the perineum and buttocks; dyspnoeic and ill; temperature 100 degrees; there were crepitations and bronchial breathing over the left lower lobe; leucocyte count 21,000 with 75 per cent neutrophils. She was started on chemotherapy and for four days had a temperature at the highest 101.5 degrees; for the subsequent three weeks she occasionally ran a peak to 99 degrees. About a week after admission there was bronchial breathing over the left midzone posteriorly and medium crepitations at the base. Lung biopsy was done first into the former and 15 minutes later into the latter area. All cultures were sterile. The biopsy from the area of bronchial breathing showed masses of fibrin and many small macrophages with a few polymorphs thus indicating fairly advanced resolution; from the area of crepitations was obtained no fibrin and only a fair number of small macrophages, transitional cells and alveolar cells indicating probably very advanced resolution. This was gratifying in being exactly what was predicted. Four days later X-ray showed consolidation of the left lung involving the upper

lobe and the upper part of the lower lobe. After being a month and a half in hospital there was no bronchial breathing but occasional crepitations remained and the X-ray showed some resolution. About a week later the crepitations were no longer heard. Some consolidation persisted but she was finally discharged having been in hospital about three months.

Her very poor neglected condition may have played a part in producing the very chronic course.

CASE 53:

D.J. (C. male 32 years) apparently had had a right sided pleuritic pain with cough and mucoid sputum for one day but his history was completely unreliable. He was ill and dyspnoeic with a high temperature; over the right middle and lower lobes was dullness, increased vocal fremitus and resonance with bronchial breathing and crepitations; white cell count 17,000 with 89 per cent neutrophils. His temperature fell by crisis after chemotherapy was started, but for 12 days it remained at a lower level varying from normal to 100 or 101 degrees. X-ray showed consolidation of the right middle and lower lobes. On the third hospital day his sputum contained rusty areas and he was still ill with the same physical signs except that the breathing was vesicular (leucocyte count 22,500). Lung biopsy was done and the material was sterile. The slides showed large masses

of fibrin with fairly numerous polymorphs but not as many as were usually seen in red hepatisation; many areas of fibrin contained no cells at all. The day after biopsy he began to improve and four days later he was much better but with his physical signs unaltered. Lung biopsy was repeated and the sterile material obtained showed fibrin and blood, and polymorphs in proportion to the blood present. It was not impossible that only blood was obtained and that the fibrin had come from the blood itself. No pulmonary tissue appeared to be present. After about two weeks in hospital the physical signs were unchanged but after about three weeks the physical signs altered to resonance with few crepitations and by the 24th day the chest was clear clinically. However X-ray resolution was not complete till the end of two months.

There was nothing in his history to account for the chronic course of the pneumonia.

CASE 58:

S.P. (C. male 47 years) commenced his illness six days before admission with right sided pleuritic pain, dyspnoea and feverishness. For four days he had had a dry cough and for two days he had been delirious. He was ill with a temperature of 99.5 degrees; there was dullness and bronchial breathing over the right lower lobe. X-ray showed right middle and lower lobe consolidation. Chemotherapy was started and the

patient's general condition improved but he continued with an intermittent pyrexia up to 99-100 degrees for over a month. Two weeks after admission the physical signs were unchanged and the patient felt perfectly well but X-ray showed no change in the consolidation and in addition there was now a small pleural effusion. Three weeks after admission lung biopsy was attempted but the material obtained was hepatic in origin. Two days later crepitations were heard in addition to the bronchial breathing. Another lung biopsy was attempted but because of the presence of fluid no material was obtained. However fluid was aspirated and proved to be a sterile exudate containing both polymorphs and lymphocytes. The patient remained in status quo and about two weeks later 240 c.c. and 45 c.c. of sterile exudate were removed on different occasions. Four days after the last aspiration the physical signs were unaltered except that crepitations were no longer heard and lung biopsy was again done. The material was sterile and showed small areas of fibrin with fairly numerous small macrophages and transitional cells but there were some macrophages of the larger variety. Polymorphs were scanty. The picture was that of very advanced resolution. A week later crepitations were again heard. Two weeks after this the physical signs were unaltered. The patient was given 10 c.c. of Calgluquine daily intravenously for seven days. By the end of this time the chest was normal on examination and X-ray showed almost complete resolution. The previous X-ray taken three weeks before

the last one had shown no change. The whole process had taken 70 days from the onset of chemotherapy.

An attack of "bronchitis" where he "coughed a lot" had occurred ten years previously and he was in the habit of consuming much alcohol. Again there was the persistent temperature and the accumulation of a small effusion.

CASE 63:

B.N. (N. male 52 years) complained of right sided pleuritic pain, cough with bloody sputum, dyspnoea and feverishness for ten days. He had taken sulphonamide tablets four hourly for 5 days without improvement. He was very ill, dyspnoeic and pyrexial (101.5 degrees); sputum rusty; over right lower lobe dullness, decreased vocal fremitus and resonance, bronchial breathing, and a few crepitations; leucocyte count 9,000 with 71 per cent neutrophils. Chemotherapy was started and although the temperature responded by crisis there continued a slight intermittent pyrexia of 99.5 degrees for a further 10 days. X-ray showed consolidation of both lower and upper lobes on the right side and a small effusion. Two weeks after admission the breath sounds were vesicular but otherwise the signs were unchanged. The patient felt perfectly well. Five weeks after admission X-ray showed only slight resolution and there was dullness and fairly numerous crepitations persisting at the right base. Lung biopsy was done and the material was sterile. No fibrin

was seen but there were a fair number of small macrophages and also some of the larger ones. The picture was that of very advanced resolution. About a week later the physical and radiological signs had returned to normal. Resolution had taken 52 days.

In addition to his pneumonia this patient had osteosclerosis, an anaemia refractory to all haematinics, and grossly disordered liver functions.

CASE 65:

J.M. (C. male 38 years) was admitted complaining of right sided pleuritic pain, cough with mucopurulent sputum and feverishness for seven days. He had had clubbing of the fingers and toes for as long as he could remember. He was very ill, dyspnoeic, temperature 103 degrees; over the right upper lobe increased vocal fremitus and resonance, dullness, bronchial breathing and numerous medium crepitations; right lower lobe the same findings but no bronchial breathing; white cell count 9,850 with 90 percent neutrophils. His temperature responded to chemotherapy by crisis but continued to fluctuate between 99 and 101 degrees for six days and then between normal and 100 degrees for a further 5 days. X-ray showed massive consolidation of almost the whole of the right lung. His general condition rapidly improved but his physical signs remained unaltered. About 10 days after admission the physical signs and X-ray were exactly the same as on admission but he was perfectly "fit".

Lung biopsy was performed and the material was sterile. The slides showed large masses of fibrin much of which was relatively acellular. Small macrophages were numerous and transitional cells frequent. Polymorphs were seen in small numbers. Apart from the excessive fibrin this was the picture of fairly advanced resolution. It was felt that this was a case which one could predict would fall into the chronic group. Two days after biopsy he was given a course of Calgluquine. By the end of the course the physical signs had changed and harsh vesicular breathing with increased vocal resonance and fremitus were the only abnormal findings. X-ray showed a fair degree of resolution as compared with the X-ray taken immediately before the course of injections. For two weeks after stopping the Calgluquine he remained in status quo both from the clinical and X-ray point of view. Then over a further 10 days he progressed to complete resolution. Bronchogram could not be done because of iodine sensitivity.

For five years every six months he had had an attack of "bronchitis". He was also quite a heavy wine drinker. His nutritional state was fair.

CASE 69:

S.G. (C. male 38 years) complained of right sided pleuritic pain with mucopurulent sputum for four days. He did not look very ill in spite of a temperature of 102 degrees; over the

right upper lobe dullness, increased vocal fremitus and resonance with numerous medium crepitations and bronchial breathing; leucocyte count 16,000 with 85 per cent neutrophils. X-ray showed a right upper lobe consolidation. Lung biopsy material and sputum cultures both grew pneumococci. The histology was that of a classical red hepatisation. He was started on chemotherapy and his temperature fell by crisis to normal the next day and he remained apyrexial from then onwards. Resolution appeared to be rapid and four days after admission there was only increased vocal fremitus and resonance with medium and fine crepitations; X-ray showed definite resolution. A second lung biopsy was sterile and the histology showed a classical advanced resolution with a fair amount of fibrin and numerous small macrophages. Within two weeks there were no abnormal physical signs and X-ray showed still further resolution. From then onwards radiological resolution proceeded slowly and a third biopsy was done about a month after admission. This was sterile and showed scanty fibrin with a fair number of small macrophages and a few larger ones, the picture of very advanced resolution. Complete X-ray resolution was only completed by the 46th day in hospital. No bronchogram could be done because of iodine sensitivity. He had had an attack of "pleurisy" seven years previously, drank a fair amount and had no fixed place of abode.

CASE 70:

J.W. (C. male 31 years) complained of right sided pleuritic pain, dry cough, feverishness and dyspnoea for four days. A doctor had given him an intramuscular injection 10 hours before admission. He was ill, dyspnoeic and pyrexial (102.5 degrees); over the right chest dullness, increased vocal fremitus and resonance, bronchial breathing and medium crepitations especially over the upper lobe anteriorly and over the whole chest posteriorly; sputum rusty; leucocyte count on day after admission 6,000 with 89 per cent polymorphs. Lung biopsy of right lower lobe soon after admission grew no pneumococci (nor did the sputum) but showed small areas of fibrin with numerous polymorphs many of which were in a state of early degeneration; small macrophages were not uncommon and many had ingested polymorphs; transitional cells were not frequent. The picture was that of late red hepatisation going on to grey hepatisation. His temperature responded by crisis on the third day but intermittent temperatures up to about a 100 degrees continued for about two weeks and there were occasional peaks to 99 degrees for a further week. X-ray showed consolidation of most of the right lung. Five days after admission he was much improved generally but the physical signs were little different and the sputum was still rusty; in addition extensive herpes febrilis of the nose and right ear appeared. Another lung biopsy was performed and was again

sterile but now showed no fibrin and a fair number of macrophages many larger than those in normal resolution. X-ray showed the consolidation to be unchanged. Physical signs quite rapidly improved and by the eighth day the chief signs were dullness, increased vocal fremitus and resonance and harsh vesicular breathing over the right lower lobe. A few days later crepitations again appeared. About three weeks after admission X-ray showed a small basal effusion but the X-ray appearance of the consolidation was little changed. A sterile exudate (100 c.c.) was aspirated. By the fourth week there was only dullness and diminished air entry at the right base and X-ray showed some resolution but the effusion was still present.

After 35 days there was only a little dullness at the right base and after 46 days the X-ray showed complete resolution with a little pleural thickening in the right costo-phrenic angle. A bronchogram showed very slight dilatation of the bronchus to the posterior basal segment of the right lower lobe.

Factors contributing to the slow resolution might have been operations on the kidneys for renal calculi and an obscure co-existing neurological condition. This was the only case of chronic pneumonia where a bronchogram had showed very slight dilatation.

Table 15.

To Show Duration of Illness from Onset to Clinical and Radiological Resolution.

Case No.	Duration from onset of symptoms till clinical resolution.	Duration from onset of symptoms till radiological resolution.	Duration from onset of chemotherapy till clinical resolution.	Duration from onset of chemotherapy till radiological resolution.
	Days.	Days.	Days.	Days.
6	64	77 plus	60	73 plus
19	49	49	45	45
24	?35 plus	35 plus	?29 plus	29 plus
29	53	53	43	43
31	59	59	45	45
35	69	69	67	67
37	62	103 plus	48	89 plus
53	25	66	24	65
58	76	76	70	70
63	57	57	52	52
65	52	52	45	45
69	18	50	14	46
70	39	50	35	46

Table 16.

To Show The Relationship Between Lung Biopsy Findings And Duration Of Illness From Time Of Onset Of Symptoms And Beginning Of Chemotherapy.

Case No.	Time from onset of symptoms. Days.	Time from beginning of chemo-therapy. Days.	Sputum culture.	Biopsy culture.	Biopsy Histology
24	6	0	Pos.	Pos.	Polymorphs. Pneumococci numerous. Red hepatisation.
69	4	0	Pos.	Pos.	Polymorphs. Pneumococci scanty. Red hepatisation.
70	4	10 hrs. (P)	Neg.	Neg.	Polymorphs. No Pneumococci. Few macrophages. Late red hepatisation.
53	?3	2	Strept.	Neg.	Polymorphs. Much fibrin. Red hepatisation
6	7	3	Neg.	Neg.	Macrophages, few polymorphs. Fairly advanced resolution.

Table 16. (continued).

Case No.	Time from onset of symptoms. Days.	Time from beginning of chemo-therapy. Days.	Sputum culture.	Biopsy culture.	Biopsy Histology.
69-1	8	4	Neg.	Neg.	Macrophages. Advanced resol-ution.
70-1	9	5	Neg.	Neg.	Macrophages. Advanced resolu-tion.
37	20	6	None.	Neg.	Macrophages, few polymorphs. Fairly advanced resolution.
37-1	20	6	None.	Neg.	Macrophages. Very advanced resolution.
53-1	?7	6	Strept.	Neg.	Fibrin, scanty polymorphs. ? blood only.
6-1	15	11	Neg.	Neg.	Macrophages. Advanced resolu-tion.
65	18	11	Staph.	Neg.	Much fibrin, macrophages, few polymorphs. Fairly advanced resolution.

Table 16. (continued).

Case No.	Time from onset of symptoms. Days.	Time from beginning of chemo-therapy. Days.	Sputum culture.	Biopsy culture	Biopsy Histology.
35	20	18	Neg.	Neg.	Macrophages. Very advanced resolution.
29	34	24	Strept.	Neg.	Macrophages. Very advanced resolution.
19	30	26	-	Neg.	Macrophages. Very advanced resolution.
31	43	29	None	Neg.	Lymphocytes, bronchiolar epith-elial cells. Normal.
69-2	37	33	Neg.	Neg.	Macrophages. Very advanced resolution.
58-2	48	42	None	Neg.	Macrophages. Very advanced resolution.
63	49	44	Neg.	Neg.	Macrophages. Very advanced resolution.

Biopsy 58-1 is not included in this table as no material was obtained.
Biopsy 58 contained liver cells.

Table 15 shows the duration of the illness from the onset of symptoms and from the onset of chemotherapy to clinical and radiological resolution.

It will be noted that the shortest time that elapsed between the onset of chemotherapy and complete radiological resolution was 43 days (excluding Case 24 where the ultimate duration was unknown). A comparison between Table 11 and Table 15 will show that the patients could be placed clearly into acute or chronic groups; there were no cases in the intermediate group.

BACTERIOLOGICAL ASPECTS:

Table 16 shows that the lung was sterile in all cases which had received chemotherapy. Cases 24 and 69 were the only ones from which pneumococci were identified but these were also the cases which had not received chemotherapy before the biopsy was performed. It was of great interest that

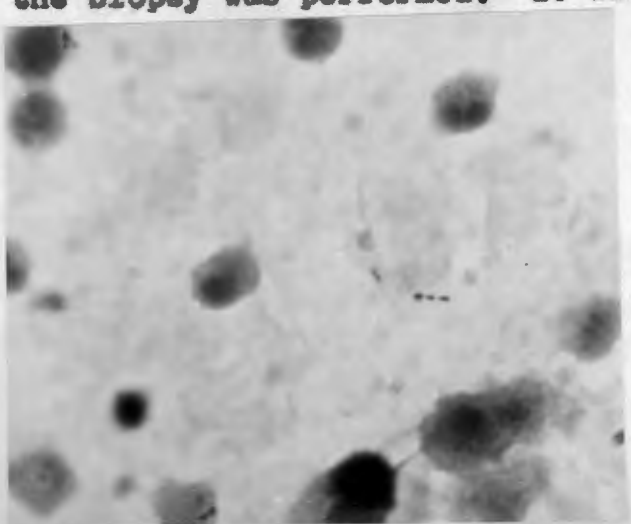


Figure 106. Case 24. Pneumococci. Oil Immersion.

even in cases which were still pyrexial and where the signs of consolidation were marked the lung biopsy material was sterile. In those cases where a significant organism was grown from the sputum - beta-haemolytic streptococci in Cases 53, 53-1, and 29 and a coagulase positive staphylococcus aureus in Case 65 - the biopsy material was sterile. This was a very important finding as many cases of chronic pneumonia, on the evidence of organisms cultured from the sputum, have been attributed to a persisting infection. One was convinced from this investigation that in these cases sputum cultures gave results which should be interpreted with considerable caution.

The conclusion was that the delayed resolution in cases of chronic lobar pneumonia was not due to a persistence of an infecting organism resistant to chemotherapy. It was very unlikely that these cases were of virus origin and this aspect will be more fully discussed under the section dealing with the clinical features.

HISTOLOGICAL ASPECTS:

Table 16 is arranged in order to show the pathological changes which occurred at various times after the onset of chemotherapy.

Cases 24 and 69 illustrated that chronic pneumonia cases apparently commenced with red hepatisation like the acute cases (see Figure 124). The histological picture in these

cases was identical with that seen in the acute pneumonias - there were masses of fibrin with innumerable well preserved polymorphs and infrequent small macrophages and transitional cells; only very occasionally were polymorphs seen within macrophages.

Case 70 showed a slightly later stage of red hepatisation and was on the border of the normal grey hepatisation - there were smaller areas of fibrin with very numerous polymorphs many of which showed early degenerative changes; small macrophages were not uncommon and in many cases had ingested the effete polymorphs; it was of interest that in this case transitional cells were not frequent. After five days of chemotherapy the normal picture of advanced resolution was present (see Figures 107-110).

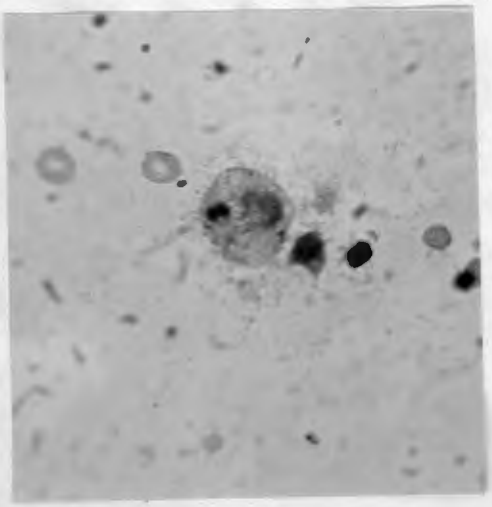


Figure 107. Case 70.

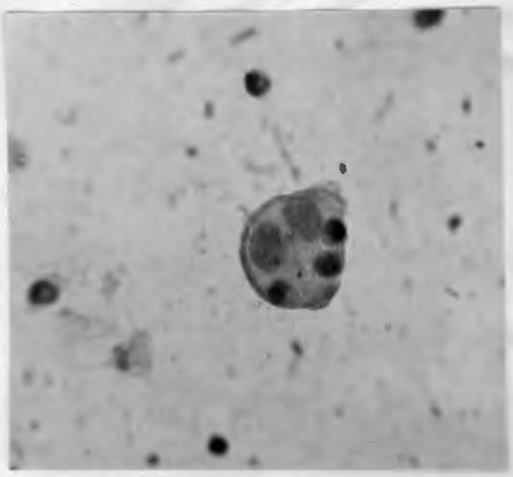
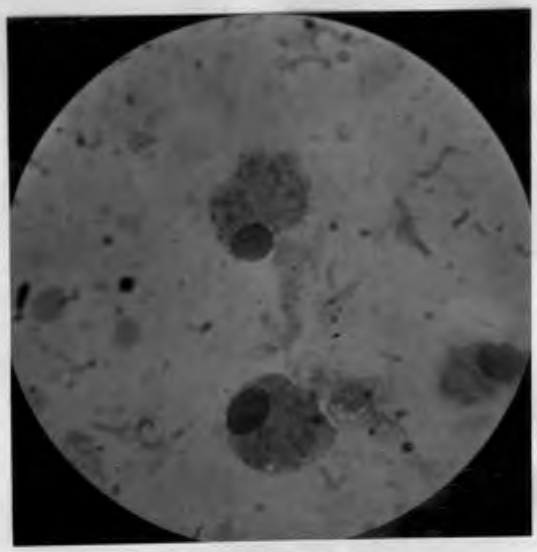


Figure 108. Case 70.

Macrophages containing polymorphs in late red hepatisation or early grey hepatisation.

Oil Immersion.



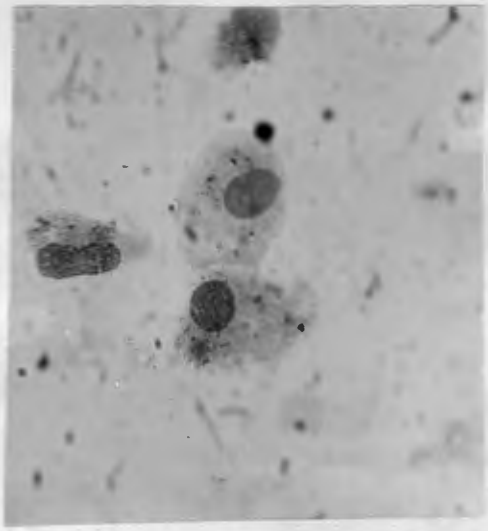


Figure 109. Case 70-1. Figure 110. Case 70-1.
Small macrophages of advanced resolution. (After five days of penicillin and sulphonamide therapy) Oil Immersion.

Case 53 showed certain unusual features; after two days of chemotherapy the cells present were still polymorphs in masses of fibrin and there appeared to be almost no macrophage response (see Figure 111). Unfortunately the second biopsy, done four days later, showed no obvious pulmonary tissue. The masses of fibrin in this biopsy could have come from the blood present. If the material was truly from the lung then there was again the picture of masses of fibrin with almost no cell response.

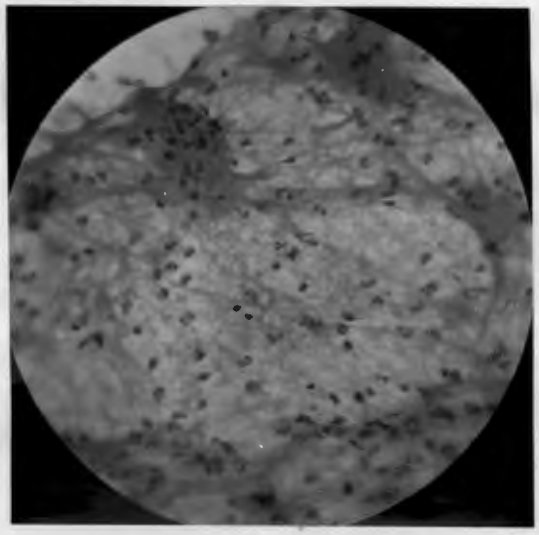


Figure 111. Case 53.

Much fibrin with not very numerous polymorphs.

Oil Immersion.

The remainder of the cases were done four days or more after the onset of chemotherapy and showed various stages of resolution. In most of these cases there were varying amounts of fibrin and numerous macrophages (see Figures 112 to 114). In those cases where the cells were fewer than normal it was difficult to determine whether this was due to less material being actually obtained or due to a truly poor cell response. There were certain striking features about the macrophages. The numerous small macrophages found in normal cases during resolution were present in cases biopsied during the first six days after the onset of chemotherapy. (See Figure 113). In the cases of longer duration one noticed that in addition to the small macrophages there were a fair number of larger cells which differed from the classical dust cell; these "macrophages of chronic pneumonia" were about twice the size of the small macrophages but were otherwise similar; there was a single nucleus, very vacuolated cytoplasm and very scanty or absent ingested particles (see Figures 117 to 120). These were probably simply older forms of the small macrophages. These large macrophages were present in small numbers during normal resolution; but as the duration of resolution became prolonged, they were found more frequently. The number of transitional cells varied considerably in the late cases from fairly numerous to infrequent. There appeared to be no direct correlation between the number of

transitional cells and the duration of the pneumonia. All the cases biopsied more than 18 days after the onset of chemotherapy showed a similar histological picture; macrophages and fibrin were present irrespective of the duration of the pneumonia (see Figures 115 and 116).

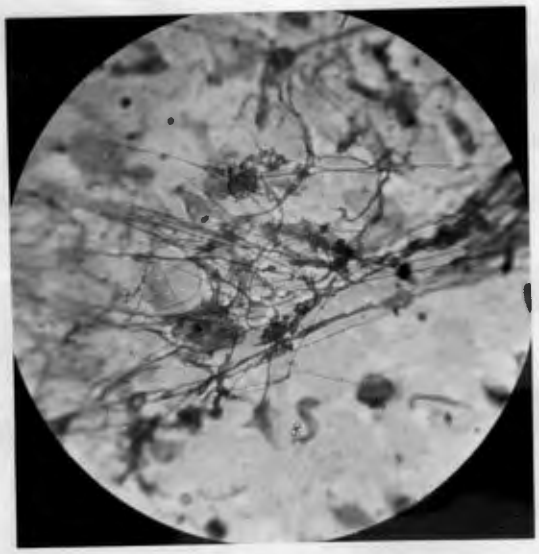


Figure 112. Case 37. Relatively acellular fibrin. (Six days after the beginning of chemotherapy. Oil Immersion.

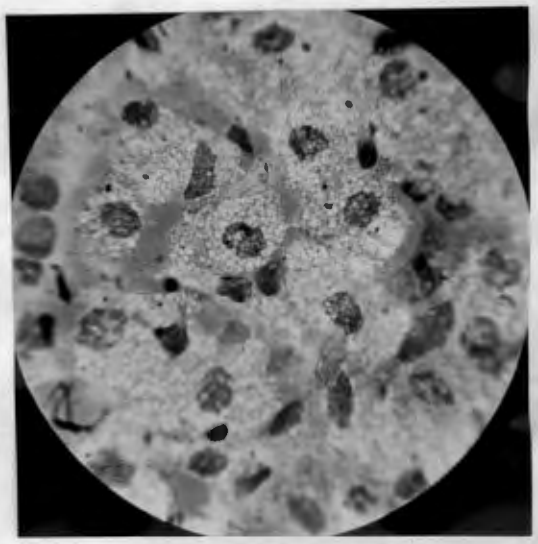


Figure 113. Case 37. Numerous small macrophages and occasional polymorphs. (Six days after the beginning of chemotherapy). Oil Immersion.

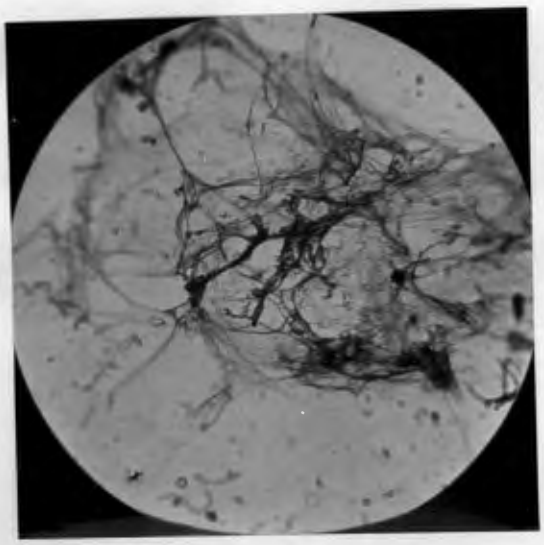


Figure 114. Case 6-1. Relatively acellular fibrin. (Eleven days after the beginning of chemotherapy). Oil Immersion.

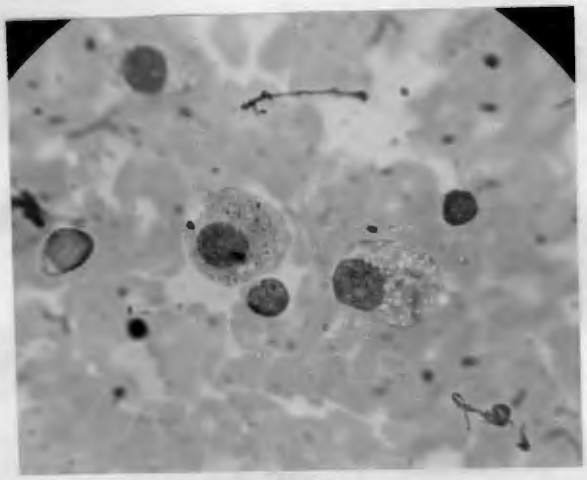


Figure 115. Case 35.

Small macrophages and transitional cells of resolution. (Eighteen days after the beginning of chemotherapy.

Oil Immersion.

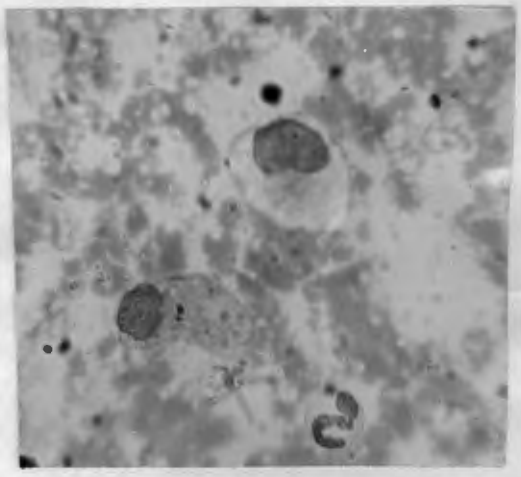


Figure 116. Case 58-2.

Small macrophages of resolution. (Forty two days after the beginning of chemotherapy).

Oil Immersion.

CHRONIC PNEUMONIA MACROPHAGES.

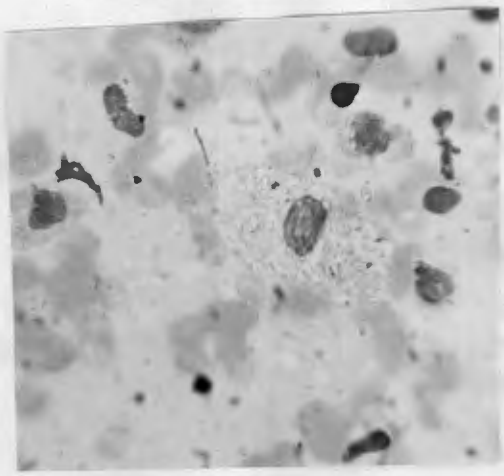


Figure 117. Case 35.

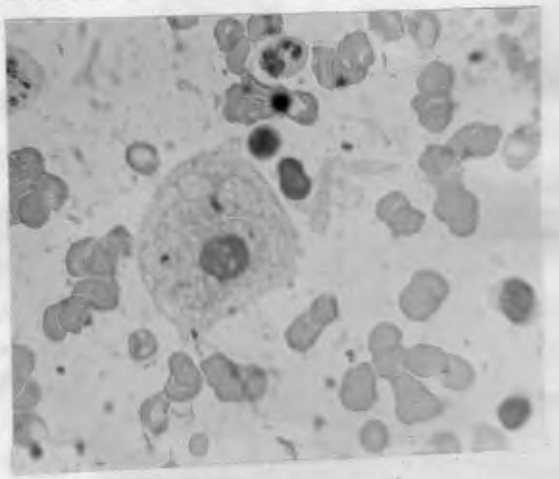


Figure 118. Case 35.

(Eighteen days after the beginning of chemotherapy).

Oil Immersion.

CHRONIC PNEUMONIA MACROPHAGES.

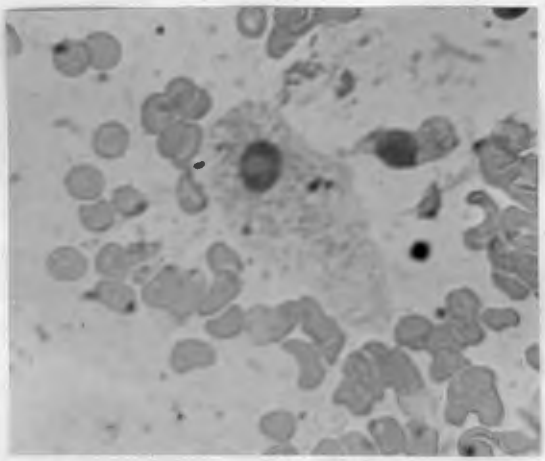


Figure 119. Case 35.

(Eighteen days after the beginning of chemotherapy).

Oil Immersion.

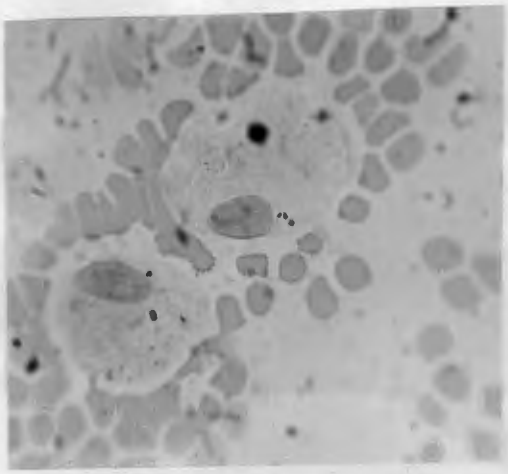


Figure 120. Case 58-2.

(Forty two days after the beginning of chemotherapy.
Oil Immersion.

One or two cases deserved special mention. Case 65 was striking in that very large masses of fibrin were seen often with few associated cells; there were many macrophages and not infrequent polymorphs (see Figures 121 to 123). This picture in the normal case could have passed for fairly advanced resolution (if one was able to ignore some of the fibrin); normally fairly advanced resolution was expected about three or four days after the onset of chemotherapy but this stage was seen in Case 65 eleven days after the beginning of treatment. It would appear obvious that there had been a retardation of the progress of resolution.

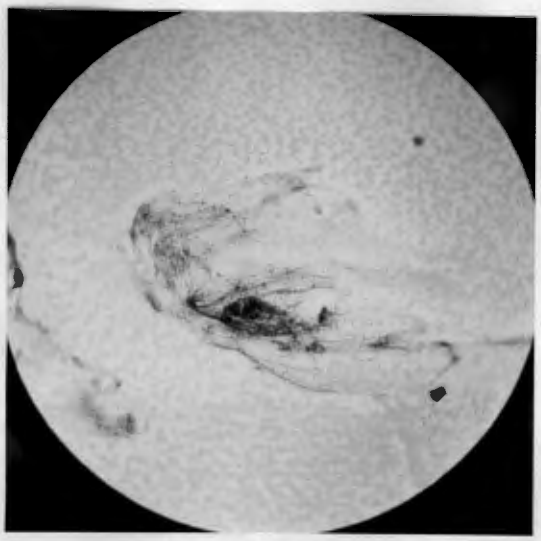


Figure 121. Case 65.

Relatively acellular fibrin.

Low Power.

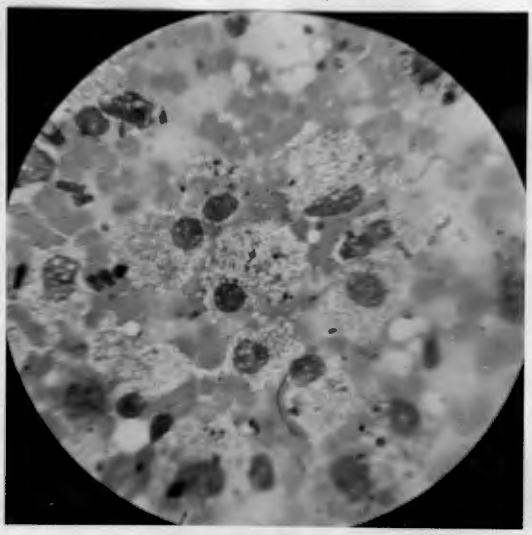


Figure 122. Case 65.

Many small macrophages with occasional polymorphs.

Oil Immersion.

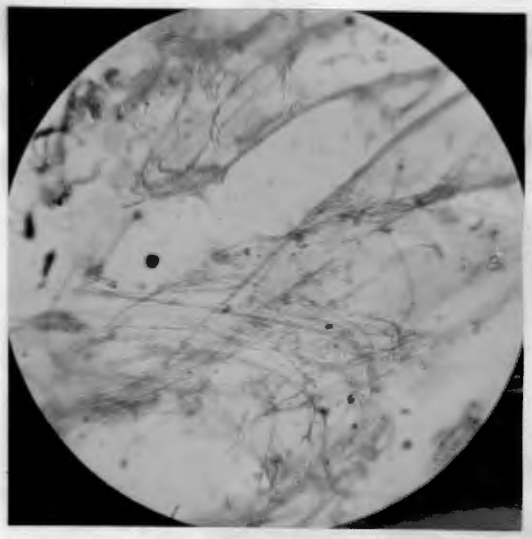


Figure 123. Case 65.

Relatively acellular fibrin.

Oil Immersion.

Case 31 was an unusual case clinically and the biopsy material obtained 29 days after the beginning of chemotherapy was compatible with normal. It was possible that the lung had completely resolved and that the X-ray appearance and physical signs at the right base were due simply to residual thickened pleura.

Case 37 was different in that it was the only case in the whole series where two lung biopsies were done on the same side within 15 minutes of each other. In this patient the lower part of the left lung should have been in advanced resolution whereas the more recently involved upper part should have been in an earlier state of resolution. It was an unique opportunity to demonstrate two parts of the same lung in different phases of resolution in the living patient. The lung biopsies were performed without any complications and the histology was exactly as expected, the lower part of the lung showing advanced resolution and the upper part fairly advanced resolution.

Case 69 was followed through all the stages by means of three biopsies. (See Figures 124 to 126). The first biopsy done before chemotherapy showed classical red hepatisation and pneumococci were cultured from the material. The next biopsy, four days later, indicated that resolution

was apparently proceeding normally. The final biopsy done on the thirty third day showed scanty granular fibrin, small macrophages and large "chronic pneumonia" macrophages indicating very advanced resolution. In this case the delay in the stage of resolution was clearly demonstrated.

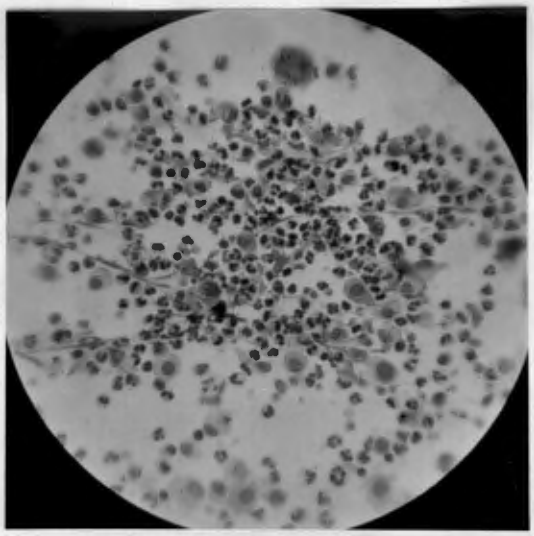


Figure 124. Case 69.

Red hepatisation with fibrin and numerous polymorphs. (No chemotherapy).

High Power.

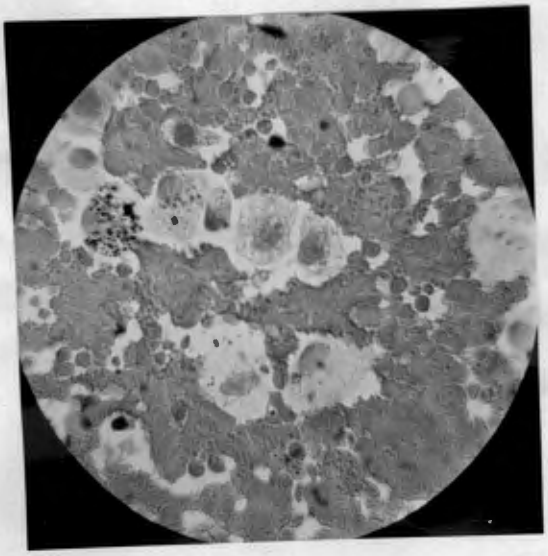


Figure 125. Case 69.

Advanced resolution with many small macrophages. (After four days chemotherapy).

Oil Immersion.

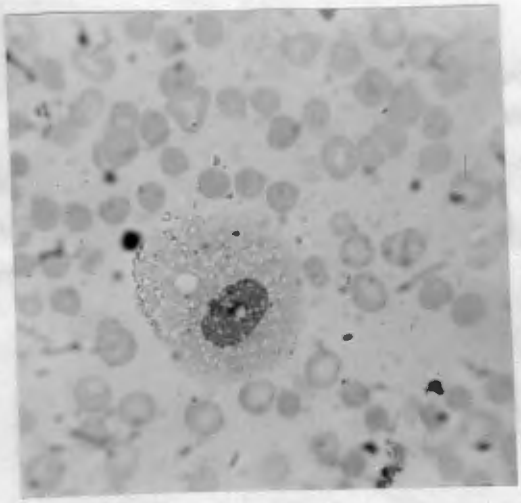


Figure 126. Case 69.

"Chronic Pneumonia Macrophage".
(Thirty three days after the beginning of chemotherapy).

Oil Immersion.

INTERPRETATION OF RESULTS:

From these cases the pattern of the pathogenesis of chronic lobar pneumonia emerged. Invasion by pneumococci occurred and the lung responded in a normal manner with a fibrinous exudate into the alveoli and a normal or sometimes reduced polymorph response. The patient was seen by the doctor with his lung in the stage of red hepatisation. Chemotherapy was given and the organisms were destroyed. Resolution then began to take place; the macrophage reaction might be apparently normal or it might be somewhat delayed. Finally almost the only cells present were macrophages and resolution should have proceeded normally. However for certain reasons (which will be discussed later) the fibrin was not removed, the macrophages became older and new ones entered the lung; the number of transitional cells did not indicate that "reinforcements" were called for urgently. The process remained an indolent one of macrophages and fibrin in status quo, or, it was more likely that the process of resolution continued slowly at a very low level until final clearing resulted. The function of the macrophages was to remove the fibrin. The evidence for this has been discussed (Robertson and Uhley 1936, Reimann 1938, Menkin 1940, Geever et al. 1951).

CLINICAL FEATURES:

An attempt was made to fit these thirteen cases into a definite clinical group without taking into consideration the duration of the illness.

All the cases were of the 30 to 55 year age period. Case 31 who was 23 years of age was the only exception and it was uncertain whether she was really a case of chronic lobar pneumonia. The age groups are shown in Table 17. It was possibly important that there were no cases in the younger age groups. Eleven cases were male and two female; eleven were coloured and two native. It would need a very large series to determine the importance of this sexual and racial predominance. The age groups of the 21 acute lobar pneumonia cases are compared in Table 17 and shows how the majority of these cases are in the under 30 year old group. There were seventeen males and four females; fifteen coloured cases, five natives and one Moslem. From such a small series one cannot draw any justifiable conclusions.

In the chronic group in eight cases the right lung was the most affected and in five cases the left lung. In the acute group the distributions were nine and twelve respectively. A much larger series is necessary to test the significance of these variations.

Table 17.

To Show the Relationship Between the Age Incidence of Cases of Acute and Chronic Pneumonia.

Age	Acute Pneumonia	Chronic Pneumonia
Years	No. of Cases	No. of Cases.
10 - 19	2	0
20 - 29	14	1
30 - 39	2	6
40 - 49	3	3
50 - 59	0	3
Total	21	13

The type of onset was acute and severe with pyrexia in nine of the chronic cases, moderately acute in two cases and rather mild in two cases. Nine cases had marked temperature on admission whilst four had only a slight pyrexia or were apyrexial. All the acute cases had a sudden severe onset and all were admitted with high or moderately high temperatures.

The leucocyte counts of ten of the chronic cases were available shortly after admission - in six there was a high neutrophil leucocytosis, in one a low neutrophil leucocytosis (12,000) and in three the count was under 10,000 but in these the neutrophil percentage varied from 76 per cent to 90 per cent. The leucocyte count of Case 70 was done about 12 hours after admission and was 6000 with 89 per cent neutrophils. In the acute cases there were sixteen with a high neutrophil leucocytosis, four with a low leucocytosis and one with a count of 6,950 with 76 per cent neutrophils (Case 41).

In both groups the response to chemotherapy was striking and rapid from the general point of view. Within a very few days the patients were considerably improved, and usually felt quite well within a week.

However, there was a considerable difference between

the way in which the temperature responded. In the chronic group only four cases were apyrexial within five days and of these two were admitted only slightly pyrexial and one had at a later stage a pyrexial "relapse". The remaining nine cases, although the high temperature fell by crisis, continued with slight intermittent or remittent pyrexias for from eight to thirty days; the general condition remained good. In almost all the acute cases the temperature came down by crisis and remained down; in two cases there was a pyrexia for 15 and 17 days respectively. A very difficult problem was the persistence of these small peaks of temperature when chemotherapy has been adequate and lung biopsy had shown the lung to be sterile. One could find no obvious explanation for the pyrexia.

In five of the chronic cases a small associated pleural effusion occurred which was shown, in the cases aspirated, to be sterile. However in the acute group there were seven similar cases. Case 50 of the acute series was of particular interest from this respect. Lung biopsy was performed soon after admission. The needle was inserted, the stylette removed, the syringe attached, and suction applied. A little opalescent fluid and air entered the syringe. It was obvious that the needle point had been in a small effusion in the pleural cavity. The fluid was expelled into a sterile test tube for culture and the needle was reinserted deeply and a lung biopsy performed. The fluid was sterile and from

the biopsy material pneumococci were cultured. This indicated that even before chemotherapy was started these small effusions associated with lobar pneumonia were probably reactive in nature and not small empyemata. The cause of these effusions was very uncertain as they might develop even whilst the patient was on chemotherapy. Certainly there was no difference in the biopsy findings in those that did and those that did not develop effusions. In the chronic cases there seemed little relationship between the pressure of an effusion and the duration of the pyrexia after the beginning of chemotherapy. However two of the cases which remained pyrexial for 30 days and 21 days (Cases 58 and 70 respectively) both had effusions which could be aspirated. Cases 6 and 37 which were pyrexial for 42 days and 25 days respectively did not have any associated exudate. In both the cases of acute pneumonia with prolonged pyrexia a small exudate had been present. There might possibly be some connection between the presence of effusion and prolongation of the temperature.

The presence of concomitant pathology as a possible cause of delayed resolution was a very difficult subject. In two of the chronic cases the Wassermann reaction was positive and five of the acute cases were also positive. All cases received penicillin which was considered good treatment for syphilis; thus if syphilis was an important

underlying cause there should have been no cases of chronic pneumonia because of syphilis. In almost every case whether acute or chronic if one went into the history sufficiently deeply one could find some condition that had occurred in the past which might have been important. Factors such as anaemia, alcoholism, smoking, attacks of bronchitis, previous attacks of pneumonia were all found more frequently in the chronic group but it must be remembered that this was also the older age group where one would normally expect such factors to be more prevalent. Striking examples of concomitant conditions were Case 63 who had osteosclerosis, severe anaemia and abnormal hepatic functions (he was one of the cases which did not show a leucocytosis) and Case 70 who had had a nephrectomy for renal calculi and whose remaining kidney had been operated on also for stones. (In spite of this his renal functions were quite normal). Did the rheumatic heart of Case 19 play any part? There was no enlargement and no symptoms, signs or history of cardiac failure. It seemed unlikely to have been an important factor. There was the other side of the question. In addition to his pneumonia, Case 41 had numerous asbestos bodies in his lung and also a positive Wassermann reaction; there was no leucocytosis on admission and he developed a small exudate; yet in spite of all this he ran a perfectly normal acute course to complete resolution in 23 days. Case 30 had a coexisting acute nephritis but resolution was normal.

X-ray residua such as thickened pleura or an obliterated costo-phrenic angle were found occasionally in both groups. In two of the chronic cases where bronchograms were done no abnormality of the bronchial tree was detected. In several cases iodine sensitivity prevented a bronchogram from being performed. Case 70, however, showed the branch of the bronchial tree to the posterior basal segment to have a mild degree of dilatation.

It might be argued that the trauma of lung biopsy was a cause of the slow resolution but it will be noted that many of the cases were subjected to lung biopsy for the first time only when they had reached a chronic stage.

An important aspect was whether these cases were truly pneumococcal pneumonias. In two cases the organism was isolated and these require no further discussion. A consideration of the short case reports would suggest that the cases were probably not virus pneumonia - the acute illness, the severe symptoms and signs, in many cases the neutrophil leucocytosis and in others the normal or slightly raised total count but with a very high percentage of neutrophils and the long course but with immediate general response to chemotherapy all combined to give pictures very unlike virus pneumonia; however it is known that in the unusual case virus pneumonia may simulate pneumococcal pneumonia closely. Were these cases due to other bacterial organisms? This

cannot be definitely answered. Robertson and Uhley (1936) showed that pneumonias due to organisms other than the pneumococcus also showed the macrophage reaction. Among the diagnostic cases there was one of chronic broncho-pneumonia (Case 64) which on biopsy showed exactly the same histology as the chronic lobar pneumonias. If some of the cases were due to other organisms it would simply confirm the suspicion that the pathogenesis of chronic pneumonia remains constant irrespective of the infecting organism (this does not include virus pneumonia which would make a most interesting subject for investigation using lung biopsy material for culture experiments and histology).

CONCLUSIONS:

It was extremely difficult to predict whether a pneumonia would become chronic or would undergo normal resolution. If the patient was admitted with only a slightly raised leucocyte count, if he responded generally to chemo-therapy but continued to have a slight intermittent or remittent pyrexia for more than five or six days and developed a small pleural effusion then he might go on to the chronic stage. The local physical signs on admission gave no help whatsoever. It was probable that the presence of concomitant pathology played little part in determining whether the pneumonia would run a chronic course.

Why did some cases of pneumonia take longer to resolve than others? It must be admitted that the same process, pathologically speaking, occurred in both rapid and slow resolution except that in the latter the products of the inflammatory process, mainly the fibrin, was removed more slowly than usual. If one was willing to accept that fibrin remaining in the lung was the main feature of chronic pneumonia, and if one agreed that the macrophages probably played a major role in the removal of fibrin, then by inference chronic pneumonia was due to a defect in the macrophages. This defect might be quantitative or qualitative; either insufficient macrophages were mobilised and fewer macrophages took longer to remove the fibrin, or sufficient macrophages arrived in the lung but were not as efficient in removing the fibrin as normal macrophages and thus the process took longer. No clue to the answer was given by the present investigation except that in some of the chronic cases numerous macrophages were present on the smears. However, this gave little indication of what was really happening in the lung as the number of macrophages seen depended on the amount of material aspirated, the amount of blood present and the thickness of the smear.

Of some interest was the work of Keil and Schissel (1950) who showed by means of pulmonary angiography that, in cases of chronic pneumonia, the vascularity of the part involved was either increased or normal but never diminished. Thus

it was unlikely that a poor blood supply to the affected area played any part in producing slow resolution.

My personal feelings in the matter are that chronic pneumonia is simply a process similar to that occurring in many other pathological conditions. In most diseases one patient will react rapidly and efficiently and with or without the help of the doctor he will rapidly recover; other patients with all the treatment possible will take much longer to return to normal. It appears obvious that some people "react" better than others. The cause of this is very uncertain but recent work on the endocrine system and reaction to stress may be the clue to the final answer. It is of interest in this connection that Menkin (1940) showed that the extirpation of the thyroid in a rabbit decreased phagocytosis which might be increased again by feeding thyroid extract. Be it as it may, the fault is probably in the "soil" not in the "seed". In relationship to the problem of chronic pneumonia one must consider the interesting story of Case 19.

This coloured man was admitted to Somerset Hospital in 1949 with a five day history of pleuritic pain in the right chest, dyspnoea and cough with haemoptysis. X-ray showed pneumonic consolidation of the right upper and middle lobes and the dorsal segment of the lower lobe. Forty days after admission there were still the signs of

bronchial breathing and crepitations over the affected area. His physical signs gradually diminished and the X-ray picture returned to normal about three months after admission. His temperature of 103 degrees on admission had responded to chemo-therapy by crisis and from the fifth day of his illness he had been apyrexial. This patient in 1949 showed a classical chronic lobar pneumonia. About a year later (1950) he was again admitted with an exactly similar history except that the pain was on the left side. Physical signs and X-rays showed a left lower lobar pneumonia. He ran an almost identical course to resolution in 45 days. Here were two different lungs responding to probably the same or similar organisms in almost identical fashion. This case would be an overwhelming arguement in favour of an intrinsically poor reaction capability in respect to pneumonia but unfortunately the patient had a rheumatic heart which could possibly have been the factor in producing the delayed resolution in both lungs. One must, however, state that his heart lesion was symptomless and even the murmurs were not obvious.

The bias of the writer is in favour of the theory that some people will respond to the treatment of pneumococcal pneumonia by rapid resolution and others by slow resolution irrespective of the duration of chemotherapy or the presence of concomitant pathological conditions. The next problem was whether one could select those cases who would go on to

slow resolution using features other than the ordinary unreliable clinical signs already discussed. Does one accept the theories of the somatype protagonists who believe that a certain type of physical build predisposes to certain types of diseases? Possibly one acknowledges their work with reservations. "Somatyping" seemed a new approach to the subject of chronic pneumonias. Would it be possible to state that a certain somatype would show rapid resolution whilst a person of different physical constitution would show slow resolution? To answer this, it would be necessary to somatype all cases of acute and chronic pneumonia and compare the somatypes of each group.

The somatypes were determined by the simple and quick although crude method of Morris and Jacobs (1950). This work was only started towards the end of the present investigation and only a few cases have been done; these are recorded in Table 18. This work is only in its infancy and seven cases of acute and four of chronic pneumonia are recorded. The impression that one gained from these very few cases was that patients who went on to normal resolution tended to be dominant in a particular type, most often mesomorphy; that is they seemed to be "pure" physical types. The chronic cases were rather more a mixture of types, that is an "impure" physical type. It was of interest to examine the apparent exceptions to this rule. In the acute group, Case 55 was a mesoectomorph and took 31 days

Table 18.

To Show the Relationship Between the Somatype and the Type of Pneumonia.

Case No.	Type of Pneumonia	Somatype
54	Acute	1 . 7 . 2. Mesomorph.
55	Acute	1 . 4 . 5. Mesoectomorph.
56	Acute	2 . 6 . 2. Mesomorph.
57	Acute	1 . 7 . 2. Mesomorph.
67	Acute	1 . 7½.1½. Mesomorph.
71	Acute	2½. 6 . 1. Mesomorph.
72	Acute	1 . 3½. 5. Mesoectomorph.
58	Chronic	3 . 5½. 2. Endomesomorph.
65	Chronic	1 . 4 .4½. Mesoectomorph.
69	Chronic	1 . 6 . 2. Mesomorph.
70	Chronic	1 . 6 .2½. Mesomorph.

to completely resolve; similarly resolution in Case 72 (also a mesoectomorph) took 29 days. On the other hand Case 69 of the chronic group (a mesomorph) showed very rapid clinical resolution but the last stages of radiological resolution was delayed; however Case 70 (also a mesomorph) showed delayed resolution for 46 days. Thus the two "exceptions" in the acute group showed "slightly delayed" resolution. This work will be continued and it is hoped that more comprehensive figures will be published in the future.

THERAPEUTIC ASPECTS.

Whatever the ultimate basic reason, it seemed fair to accept that the macrophages did not remove the fibrin as quickly in chronic pneumonia as in acute pneumonia. This fact seemed a sound basis on which to work out a therapeutic approach to the problem of how to make a chronic pneumonia resolve more quickly. There were two ways in which one could approach the problem - either the fibrin must be removed by "artificial means" or the macrophages must be stimulated to take up the fibrin faster and more efficiently.

The means by which fibrin might be removed was suggested in a paper by Jorpes on heparin (1947). He quoted unpublished work by S. Kallner: in some non-virus pneumonias with a protracted course and "resistant to antibiotics" heparin and dicoumarol often had a quite specific effect. In these cases there might be a rise in temperature lasting for weeks, blood stained sputum and diffuse symptoms from the lungs, resistant to sulpha and penicillin therapy. As soon as heparin and dicoumarol were given recovery followed within a few days. Latent thrombi, for example, in the pelvic veins giving pulmonary infarctions, were far more common than suspected in these cases. The anti-coagulant therapy not only treated the lung condition but also protected the patients from recurrent pulmonary embolisms. Jorpes did not

state clearly what he meant by "resistant to sulpha and penicillin therapy" but apart from this the cases certainly seemed to be chronic pneumonias. I wrote to Jorpes to ask for further details on this unpublished work but at the time that this present work was completed no reply had been received.

Only two other papers were of interest in connection with the possible application of anticoagulant therapy to chronic pneumonias. Rigdon and Schrantz (1942) quoted experimental work done by others which showed that heparin had no effect on capillary permeability nor on the phagocytosis of staphylococci by polymorphs. Their own experiments demonstrated that injected Indian ink was quite normally phagocytosed by the reticulo-endothelial cells of rabbits which had been thoroughly heparinised. Boys and Harris (1943) subjected rabbits to irradiation and showed that those that received heparin at the same time reacted with less inflammatory changes in the lungs, and the late changes of pulmonary fibrosis and pleural adhesion formation were diminished. In no way did they suggest that fibrin, when already formed, might be dispersed. They quoted papers in which it was shown that peritoneal adhesions might be prevented by heparinisation.

Here was a possible new approach to therapy. However there were difficulties connected with the use of anticoagulant therapy. First it was difficult to control and we

did not have the laboratory facilities to do frequent clotting and prothrombin times. These tests would also be very time consuming. Secondly heparin was at the time still very expensive and this was also a consideration. This field of treatment was not investigated but it is hoped that at some future date, when work is possible under better conditions, that anticoagulant therapy in pneumonia might be further explored.

A very fascinating idea was to be rather more physiological and to stimulate the macrophages. This was very reminiscent of Bernard Shaw's "The Doctor's Dilemma". It would be very picturesque if one could "butter the fibrin with opsonins" (to slightly misquote Shaw), but there seemed no obvious way of obtaining this effect and Wood's work had shown that phagocytosis occcurred perfectly well in the absence of antibodies. The answer to the stimulation of the macrophages was possibly contained in a small abstract which appeared in the South African Medical Journal in February 1951. A paper by Repetto (1947) was described in which he used intravenously a mixture of quinine and calcium to prevent and treat post-operative pulmonary complications. Repetto quoted many investigators who had described the beneficial actions of quinine and calcium. Quinine was said to affect the pneumococcus, stimulate tonic and antipyretic action, strengthen renal secretion and enhance phagocytosis.

Calcium heightened the resistance against pneumococcal infection, had an action on the heart "resembling digitalis", had a spasmolytic action on the bronchi and repressed their secretion, and enhanced phagocytosis. It was of great interest that quinine and calcium were said to stimulate phagocytosis. Quinine and calcium were readily available in the Sandoz preparation of "Calgluquine". A 10 c.c. ampoule contained 0.6 gm. of quinine gluconate (corresponding to 0.37 gm. of basic anhydrous quinine) in a 10 per cent. solution of "Calcium-Sandoz". In a pamphlet on Calgluquine by Sandoz, it was stated that calcium decreased exudation in pneumonia and hastened the absorption of the exudate already formed. Hamburger (1912) did an extensive investigation into the problem of phagocytosis and showed that the addition of calcium chloride to an in vitro suspension of leucocytes increased the amoeboid movements and the amount of phagocytosis. He considered this to be due to an accelerating action on the enzymatic processes in the cell nucleus. Quinine hydrochloride had an inhibiting effect on phagocytosis. Repetto (1947) quoted work to the contrary. Menkin (1940) commented that calcium ions had the peculiar property of increasing the rate of phagocytosis whilst iodine had an opposite depressant effect.

The use of quinine and calcium in the treatment of pneumonia is not new and it was not infrequently used in the pre-sulphonamide days. There was especially a vast

German literature on the subject. A pamphlet published by Sandoz quoted many large series of cases of both lobar and bronchopneumonia in children, adults and the aged all treated by Calgluquine either intravenously or intramuscularly or both. Barthel (1933), Schoendube (1934), Blackert (1934), Paschke (1936), Raue (1936), Sebian (1936) and Blanc (1936) all obtained similar results, namely that the majority of the cases (especially if treated early) showed rapid disappearance of the fever, improvement in the general condition, rapid resorption of the local process and the course of the disease was appreciably shortened. Similar findings were recorded by Ott (1937). Quinine alone had also been used with good effect and Solis-Cohen (1933) stated that "for over a century the favourable influence of quinine upon the course of pneumonia has been noted by many competent observers, including Corrigan, Gibson, See, Liebermeister, Binz, Aufrecht, Cahn-Bronner, George Wood, Austin Flint, DaCosta, Jacobi, Solomon Solis-Cohen and Kolmer". In a carefully controlled adult series the mortality was 9.6 per cent in the quinine treated cases (1000 cases) as compared with 20 per cent in the untreated controls (2000 cases). Quinine was said to be specifically bactericidal to pneumococci but that part of its effect was probably by stimulating leucocytosis and phagocytosis by the leucocytes. A common result of quinine treatment was a shortening of the duration of the pneumonia. Cahn-Bronner found that in some of his treated cases the physical signs

disappeared rapidly after the administration of quinine. The quinine was given as the dihydrobromide in capsules orally at three hourly intervals and in very ill cases intramuscularly. Maclachlan et al. (1937) reported good effects from the use of a quinine derivative, hydroxyethylapocupreine, in pneumonia.

There have been several papers on Calgluquine used in the prevention and treatment of postoperative pulmonary complications. Both Ulbrich (1936) and Repetto (1947) in large series of cases have shown that, when Calgluquine was given before and after operation, post-operative complications were fewer and less severe; if Calgluquine was started after the complications were established then the mortality was diminished.

The most recent work on Calgluquine has been done by Milanovic (1948) who considered that the course of influenza was shortened by this treatment. To date (1951) the head office of Sandoz in Switzerland had received no reports concerning the combined administration of Calgluquine with sulphonamides or penicillin. (P. Stein, personal communication).

There was, thus, plenty of evidence to support the statement that quinine and calcium had a beneficial action in cases of lobar pneumonia. It was uncertain whether this effect was due to stimulation of the macrophages but Calgluquine seemed worthy of trial. This investigation was

only commenced very late in the series and to date only three cases have been treated - Cases 58, 65 and 64. The former two were cases of chronic lobar pneumonia and the latter a case of chronic bronchopneumonia. Lung biopsy in all cases confirmed the presence of a macrophage reaction. The Calgluquine was given intravenously, 10 c.c. at the rate of 1 c.c. per minute. Injections were given daily for seven days. No toxic manifestations were noted except that after some injections there was a feeling of warmth, occasional slight sweating and very occasionally tinnitus.

Case 58 was a coloured male of 58 years who after being in hospital for 63 days still had the physical signs of dullness, bronchial breathing and medium crepitations at the right base posteriorly. He was started on Calgluquine. On the second day dullness had diminished; on the third day there was no longer any dullness, breathing was vesicular and crepitations fine and much reduced in number; on the fourth day no change; on the fifth day only very occasional crepitations heard; on the day after the last injection there were no longer any abnormal physical signs and X-ray showed almost complete resolution. These astonishing results exceeded even the most enthusiastic expectation. This result was very difficult to assess as one could argue that he would have resolved completely at this time even without Calgluquine. Of much greater significance were the results of the following case.

Case 65 (Coloured male 38 years) showed all the features of a pneumonia which would run a chronic course - he was admitted very ill with a high temperature, extensive consolidation of the right lung, a normal total leucocyte count but with 90 per cent of neutrophils. His general condition was improved by chemotherapy but his temperature continued at a low level for about 11 days. His physical signs remained unchanged and on the 11th day there was still increased vocal fremitus and resonance, relative dullness and bronchial breathing with numerous medium crepitations over the right upper lobe and similar findings over the lower lobe except that the breathing was vesicular. Lung biopsy after 11 days showed that there was retarded resolution of the upper lobe. X-ray was similar to that on admission. Two days later he was started on Calgluquine. On the third day of the course dullness was only slight, vocal fremitus and resonance were still increased, there was only a small area of bronchial breathing, and medium crepitations were as before; on the fifth day the chest was resonant, vocal fremitus and resonance were still increased, vesicular breathing was not as harsh as before and there were neither bronchial breathing nor crepitations. Apart from the vesicular breathing becoming softer there were no other alterations at the end of the seven days. X-ray at the end of the course, as compared with that taken the day before the injection were started, showed a fair degree but not complete

resolution. For the next two weeks there was no change in the physical signs nor in the X-ray appearance but then over the following ten days the patient progressed to complete resolution. Here was a dramatic response which persisted only as long as the injections were continued. When the Calgluquine was stopped resolution appeared to cease and the patients condition remained unaltered for two weeks after the final injection. One felt that these findings might be significant.

A similar occurrence was seen in Case 64 where a bronchopneumonia of the left lower lobe had shown only slight signs of resolution over a period of 37 days. He was given a course of Calgluquine at the end of which there appeared to be some clearing of the consolidation on X-ray (there had been no abnormal physical signs) but some observers did not agree and the plates were lost and thus could not be reviewed. Certainly after the Calgluquine till his death there were no signs of further resolution. If one accepted that clearing did occur then again there was clearing during the period of the injections and this again stopped when the Calgluquine was stopped. This was, of course a much less definite result than Case 65.

This work is being continued. Naturally the next step was to apply this therapy to cases of acute lobar pneumonia to try and obtain more rapid resolution with shortening of the

patient's stay in hospital. Alternate cases are being treated with a course of Calgluquine starting after the first 24 hours. The Calgluquine would then act on a sterile resolving lung on which it should have its maximum effect. The results of this investigation will be published at a later date. With an illness such as lobar pneumonia which varies so considerably in its course from patient to patient, one needs a large series before any conclusions may be drawn as to the efficacy of a new therapeutic agent. The results so far obtained have been both intriguing and hopeful.

SUMMARY.

SUMMARY.

(1) It was considered that aspiration lung biopsy might be of value in determining the pathogenesis of chronic lobar pneumonia. The investigation developed to embrace the pathogenesis of the resolution of acute lobar pneumonia after sulphonamide and penicillin therapy. In addition biopsies were performed on normal lungs and on a number of cases of chest pathology which presented diagnostic problems. Ninety four biopsies were performed on 73 patients.

(2) ASPIRATION LUNG BIOPSY:

(i) Review of the literature. Aspiration lung biopsy had been practiced for about 70 years. The technique was used most frequently for the diagnosis of pulmonary tumours and in the isolation of organisms in cases of pneumonia and lung abscess. The method was also used in the diagnosis of lipoid pneumonia. Godlowski (1949) described the histology of biopsy material obtained from normal lungs.

(ii) The technique used. The technique of lung biopsy as used by other investigators was reviewed. The technique utilised in the present series was then described in detail. The patient was placed in the recumbent position. The tissues of the chest wall, the pleura and the superficial portions of the lung were

infiltrated with local anaesthetic. The biopsy needle with stylette in place was then inserted through a small stab incision in the skin into the lung. The stylette was removed, a 20 c.c. syringe attached and the plunger withdrawn to provide suction. With suction maintained the needle was inserted more deeply and then partly withdrawn. Suction was released and the needle and syringe removed. The material obtained was crushed and smeared onto slides and cultures were made on blood agar, in serum broth and on Lowenstein's medium. The slides were stained by the haematoxylin-eosin, Leishman, Gram and Ziehl Neelsen methods. A special stain to show up fibrin, pneumococci and cells was described.

(iii) Complications and dangers. Reports of other investigators indicated that air embolism and death occurred very rarely; empyema was not a hazard; haemoptysis, a small pneumothorax and slight pain occasionally occurred.

Complications were recorded in 45.8 per cent of the present series of eighty three biopsies on living patients.

The most frequent sequelae was a small haemoptysis (26.5 per cent); occasionally there was a moderate haemoptysis of over a tablespoonful of blood (8.4 per

cent). In no case did the amount of blood lost occasion any anxiety.

Slight pain in the chest occurred in 12 per cent of biopsies and was usually associated with a small insignificant pneumothorax (9.6 per cent of biopsies).

Two cases experienced a transient boute of coughing associated with dyspnoea immediately after the biopsy. Two cases showed a syndrome suggestive of vaso-vagal syncope or possibly air embolism. There was one death probably due to an air embolus. This latter case had widespread tuberculosis and tuberculous meningitis. These were the only cases which gave cause for concern.

Complications were more frequent when an upper rather than a lower lobe was the site of biopsy. The age, sex, and the actual underlying pathology of the patient played little part in determining whether or not complications would follow biopsy.

It was concluded that lung biopsy was a relatively safe procedure but that very rarely death might occur.

In four cases the biopsy material contained liver cells, and in one case (done after death) cells from the spleen were present.

(3) LUNG BIOPSY OF THE NORMAL LUNG:

(i) Thirteen biopsies were performed on patients with normal lungs (three after death).

(ii) The cultures of the biopsy material were sterile.

(iii) Histologically all or some of the following elements were demonstrated: red cells and white cells from the pulmonary vessels, pleural squamous epithelial cells, ciliated bronchial epithelial cells, ciliated bronchiolar epithelial cells, non-ciliated bronchiolar epithelial cells, alveolar epithelial cells, macrophages which might be small with a single nucleus or large with many nuclei or which might be of the alveolar histiocyte type, non-nucleated plates, parenchyma, interstitial tissue, and small and large black particles.

(4) LUNG BIOPSY USED FOR DIAGNOSTIC PURPOSES:

(i) Lung biopsy was performed on eight cases of pulmonary tuberculosis; five showed tubercle bacilli either on direct smear or culture or both.

(ii) Lung biopsy was used after death to diagnose two cases of bacterial pneumonia where the antemortem diagnosis had been pulmonary infarction and tuberculosis. A chronic staphylococcal pneumonia was diagnosed mainly from the biopsy findings. A chronic broncho-pneumonia was shown to be pathologically similar to

chronic lobar pneumonia. In a case of asthma associated with bronchopneumonia, lung biopsy excluded an "allergic lung". In one case of bronchopneumonia, even lung biopsy failed to help elucidate the etiology.

(iii) In two cases of pulmonary infarction, two cases of rheumatic pneumonia and one case of an uraemic lung the biopsy findings were compatible with the suspected diagnosis.

(iv) A peripheral carcinoma of the lung, a pulmonary amoebic abscess and a lung abscess associated with bronchiectasis were all diagnosed using lung biopsy.

(v) Biopsy of a case of congenital cystic lung showed that the Friedlander's bacillus, cultured from the sputum, had not come from the lung.

(vi) It must be emphasised that the lung biopsy material obtained for diagnostic purposes must be considered together with a clear picture of the clinical state of the patient. The chief value of biopsy was when the histological or bacteriological findings were compatible with one diagnosis and made other diagnosis unlikely.

(vii) In four cases (three of acute lobar pneumonia and one of tuberculosis) asbestos bodies were present in the biopsy material.

(5) THE PATHOGENESIS OF THE NORMAL RESOLUTION OF ACUTE LOBAR PNEUMONIA.

(i) The literature on the pathogenesis of pneumococcal lobar pneumonia was briefly reviewed. The early animal experiments, the theories of the mechanism of the crisis, and the process of resolution were discussed. The importance of the macrophage reaction in resolution was emphasised. The controversial question of the origin of the macrophages was reviewed. Loosli's conclusion (1942) that the macrophage had their origin from the lymphocytes and monocytes of the blood appeared to be the most acceptable. If this was correct then the inflammatory cell response in the lung fell into line with the cellular response of inflammation in all other parts of the body.

(ii) Curphey (1935) did lung biopsies on living human patients during the resolution of lobar pneumonia and was said to have confirmed the presence of the macrophage reaction during recovery.

(iii) Wood and his co-workers showed that rats with pneumonia treated with sulphapyridine showed an early macrophage reaction during recovery. There was no information as to the changes in the pneumonic lung following penicillin therapy.

(iv) The terms acute and chronic lobar pneumonia were

defined.

(v) Twenty seven lung biopsies were performed on twenty one cases of acute lobar pneumonia both before and after treatment with sulphonamides and penicillin.

(a) Positive cultures of pneumococci were obtained from all cases which had not received treatment. After being on therapy (sulphonamides or penicillin or both) for twenty four hours the lung appeared to be sterile.

(b) It was demonstrated that before therapy the affected lung showed the histological picture of red hepatisation with large masses of fibrin and numerous well preserved polymorphs. During the first day of treatment there was no change in the pathological picture. After two days of adequate chemotherapy the histology was that of early resolution - large masses of fibrin were present with polymorphs (often degenerate) and small macrophages in about equal numbers; the macrophages frequently showed ingested polymorphs. After three of more days of therapy resolution was well established. In fairly well advanced resolution fibrin was present associated with numerous small macrophages and infrequent polymorphs which were occasionally seen within macrophages. In advanced resolution the fibrin was less in amount and was becoming granular, small macrophages were numerous and polymorphs scanty.

Evidence was quoted which suggested that the macrophages removed the fibrin. It might be assumed that the macrophages eventually left the lung which then returned to normal. It would appear that with chemotherapy the stage of grey hepatisation had ceased to exist.

(c) Cells showing the intermediate stages between lymphocyte and monocyte and monocyte and small macrophage were noted and these cells were termed "transitional cells". They were infrequently seen in the slides showing red hepatisation but became numerous during early and fairly well advanced resolution and were still common in advanced resolution. This transitional cell response which seemed to just precede the macrophage response lent support to the theories of Leosli that the macrophages were derived from cells in the blood.

(vi) An attempt was made to relate the general condition of the patient and the physical signs in the chest to the underlying pathological process. During the first five or six days following the beginning of therapy if the patient became non-toxic and apyrexial and actually expressed a feeling of well being then one could usually correctly predict that resolution was progressing satisfactorily. The local physical

signs, alone, gave little indication as to whether the underlying lung was in a state of red hepatisation or resolution.

(6) THE PATHOGENESIS OF THE RESOLUTION OF CHRONIC LOBAR PNEUMONIA.

(i) The definition of "chronic lobar pneumonia" was elaborated.

(ii) The literature on chronic lobar pneumonia and various pulmonary conditions incorrectly termed chronic lobar pneumonia was reviewed. The etiology of delayed resolution was considered and the importance of co-existing syphilis and other concomitant pathological conditions placed in the correct perspective. Therapeutic measures, usually of a general nature, had been recommended by various authors.

(iii) The thirteen patients with chronic lobar pneumonia in the present series were briefly described . Twenty lung biopsies were performed on these thirteen cases. Those cases which had not been treated showed the histological picture of red hepatisation and pneumococci were cultured from the biopsy material. In all cases which had received chemotherapy the biopsy cultures were sterile. The cellular changes in the lungs corresponded closely to those shown by the cases with normal resolution, but in some cases the macrophage

response was somewhat delayed. However, after the macrophage response was fully established resolution proceeded very slowly and all cases examined more than eighteen days after the beginning of therapy showed the histological picture of fibrin and macrophages. In the cases of longer duration large macrophages with a single nucleus, vacuolated cytoplasm and few ingested particles, were frequently seen. These were probably older forms of the small macrophages seen in normal resolution and were termed "chronic pneumonia macrophages".

(v) The clinical features of the cases of chronic lobar pneumonia were discussed. It was shown that the majority were of an older age group than the cases with normal resolution. It was extremely difficult to predict whether a pneumonia would become chronic or would undergo normal resolution. If the patient was admitted with only a slightly raised leucocyte count, if he responded generally to chemotherapy but continued to have a slight intermittent or remittent pyrexia for more than five or six days, and developed a small pleural effusion, then he might go on to the "chronic stage".

(vi) It was probable that the presence of concomitant pathology played little part in delaying resolution. The suggestion was made that there might be an inherent

poor reaction capability in response to certain diseases and that delayed resolution depended on the "soil" not the"seed". By somatyping individuals it might be possible to predict whether a pneumonia would progress to normal or delayed resolution.

(vii) It seemed reasonable to accept that delayed resolution was caused by the fibrin not being removed by the macrophages from the lung.

(a) Jorpes (1947) reported that the fibrin could be dispersed by using heparin and dicoumarol but no work was done along these lines in the present investigation.

(b) Quinine and calcium had been used with some success in the treatment of pneumonia before the era of chemotherapy and antibiotics. Both these substances were said to enhance phagocytosis. "Calgluquine" (Sandoz) was used to try and "stimulate the macrophages". Two cases of chronic lobar pneumonia and one of chronic bronchopneumonia were treated with 10 c.c. of Calgluquine intravenously for seven days. The Calgluquine appeared to accelerate the progress of resolution.

(7) GENERAL CONCLUSIONS:

(1) Aspiration lung biopsy is a relatively safe procedure.

(2) By means of lung biopsy it has been possible :

(a) To establish the sterility of the normal human lung;

(b) To clarify the diagnosis in many various obscure pulmonary conditions;

(c) To demonstrate the stages of the resolution of acute lobar pneumonia following sulphonamide and penicillin therapy; and

(d) To indicate the pathogenesis and cell changes that occur in chronic lobar pneumonia.

APPENDIX.

THE CASE HISTORIES

OF

SEVENTY THREE PATIENTS

ON WHOM

LUNG BIOPSY WAS PERFORMED.

INTRODUCTION.

The appendix contains the case reports of the patients referred to in the main thesis. Many of these cases, especially the controls with normal lungs, were of very great medical interest apart from the biopsy findings. However, for the sake of brevity the cases are discussed and described mainly from the point of view of the findings in the chest and their interpretation. Similarly, when one must deal with seventy three cases, it is necessary to restrict the discussion of the various possibilities to a minimum, especially in the cases done for diagnostic purposes.

The case histories have been made as short as possible. Most negative points have been omitted; the various media used for the culture of the biopsy material have only been mentioned individually where this has been relevant; unless otherwise stated the actual procedure used for performing the lung biopsy was the orthodox method described - comments are made on any variations from the standard technique. The presence of pneumothorax as a complication was always commented on but only in some cases was a negative check X-ray mentioned. Only in cases where it was necessary was the duration of chemotherapy fully described.

Some of the case histories are not as complete as one would have liked but most of these were cases over which one had no personal control, the only contact with the case

being the performance and interpretation of the biopsy. In some cases, for example Case 58, the patient was seen for the first time three weeks after admission.

The cases are arranged in numerical order, and an index will be found on page 515.

Most of the photographs and microphotographs are included in the main text but a few additional ones will be found in the case reports.

All the photographs and microphotographs were taken by the author using an ordinary Zeiss Ikoflex twin lens reflex camera. The photographs of the histology were done by a very simple method. With the microscope horizontal, the upper lens of the camera was placed near to the eyepiece (the camera was set at "infinity"). A picture of the microscopic field appeared on the camera's ground glass screen. The cells were brought into clear focus using the microscope's fine adjustment. The camera was then raised so that the taking lens was opposite the microscope eyepiece, and the shutter was opened for the required time. Ordinary Kodak Super XX 1.20 roll film was used; twelve microphotohraphs were obtained on each spool of film.

The slides of the biopsy material were stained and interpreted by the author. The cultures were examined and reported on by the staff of the Department of Pathology (University of Cape Town).

CASE 1.

G.S. COLOURED MALE. 49 YEARS. PULMONARY INFARCTION.

History:

The patient had been admitted several times in hypertensive congestive cardiac failure and on his previous admission there had been two episodes of cough with very blood stained sputum and profuse sweating but no chest pain. He was again admitted with the symptoms of heart failure.

Examination:

Ill, dyspnoeic, orthopnoeic, distended pulsating neck veins, oedema of legs, six finger hepatomegaly, dullness and crepitations at the bases, cardiomegaly with presystolic gallop rhythm; urine contained two plus albumin.

Course:

He did not respond well to mersalyl, aminophyllin and digitalis. About a month after admission he suddenly complained of pain in the right side of his chest and began to cough up heavily blood stained sputum. Just to the right of the sternum there was a localised area where many resonating crepitations were heard. He went steadily downhill and died two days later in severe congestive cardiac failure.

About 36 hours after death a 19 gauge ordinary aspirating needle was inserted into the third right interspace about 2 cm.

from the right sternal border and the material obtained was smeared onto a slide. This first lung biopsy was by no means a great success. There was much blood present; black particles were scattered through the slide; occasional pleural cells were present; macrophages of the dust cell type were occasionally seen and not infrequent heart failure cells associated with a fibrinous type of material; occasional alveolar cells; numerous bacilli but these were almost certainly postmortem invaders.

Discussion:

Clinically the case was that of pulmonary infarction superimposed upon congestive cardiac failure. The biopsy material was not very helpful. There were some areas of what was possibly fibrin with heart failure cells and much blood; this was possibly compatible with the diagnosis of infarction. One was able to exclude a bacterial pneumonia.

CASE 2.

S.S. COLOURED FEMALE , 6 YEARS. PULMONARY TUBERCULOSIS.

History:

Listless with anorexia and dyspnoea on exertion for three months; slight dry cough for the same period; dyspnoea worse and in addition orthopnoea for a week; pain in the left side of the chest one day. No history of contact with cases of suspected tubercle.

Examination:

Ill, thin, pale, dyspnoeic, cyanosis, clubbing of the fingers, massive general oedema, distended pulsating neck veins, pulsus paradoxus, heart displaced to right and gallop rhythm; left side of chest flattened, resonant, diminished air entry with bronchial breathing and fine crepitations; right side of chest relative dullness with bronchial breathing and crepitations; four finger smooth hepatomegaly; three finger splenomegaly; urine albumin one plus; red cells 3.2 million with 8 gm. haemoglobin; white cells 14,920 with a normal differential count.

Course:

She ran an intermittent pyrexia up to 101 degrees. X-ray showed a large left hydropneumothorax, specks of calcium in the left upper lobe and pneumonic consolidation of the right

middle lobe. She improved slightly after digitalisation. Aspiration of the left side of the chest showed a pneumothorax under slight tension and only air was obtained.

Because of the calcification it was felt that the diagnosis lay between tuberculosis and possibly histoplasmosis. There was no sputum and lung biopsy was performed. The needle was inserted into the third interspace about 2 cm. to the left of the left border of the sternum. The needle entered the pneumothorax but at the depth of about 8 cm. the point came in contact with a solid structure. On aspiration a little thick greenish material was obtained. On staining this was shown to be pus. The pus was sterile and a careful search of the smears showed no organisms.

Penicillin was started with no improvement. About a week later thoracentesis was performed at the left base and two test tubes of pus were obtained. The patient died almost immediately afterwards.

Autopsy:

The left pleural cavity contained about 100 ml. of pus and on the surface of the collapsed left lung was thick purulent material. Numerous small productive tuberculous lesions were present throughout the left lung and there were scattered small areas of calcification. Similar pathology was present at the right apex, and there was a bacterial bronchopneumonia of the right middle and lower lobes. The

normal spleen had apparently been pushed down by the pneumothorax. There were no cardiac lesions.

Discussion:

The finding of pus came as a great surprise. As no organisms were grown from the pus (blood agar and serum broth) and the patient had had no chemotherapy, an ordinary lung abscess seemed to be very unlikely. In retrospect the sterile pus was the clue to the diagnosis of tuberculous empyema. It was disappointing that no bacilli were seen on the direct smear nor was there any growth on the Lowenstein medium (but this was cultured for only two weeks). However, it is known that in empyema the tubercle bacilli may be extremely scanty and only a small drop of pus was available for examination.

CASE 3.

A. VAN G. COLOURED FEMALE. 48 YEARS. LOBAR PNEUMONIA.

History:

Dyspnoea on exertion and oedema of the ankles and lower legs for three years; increasing dyspnoea, orthopnoea and angina pectoris for 2 years; cough with very blood sputum, fever, sweating and headache for five days.

Examination:

Ill, obese, dyspnoeic, sweating, slight oedema of sacrum and legs but neck veins not distended, calves of the legs tender to palpation, apyrexial, pulse 148, blood pressure 160/110 m.m.Hg., cardiomegaly; rhonchi all over but at the left base posteriorly dullness and medium crepitations; urine albumin a trace; white cells 37,000.

Course:

She produced heavily blood stained sputum and remained apyrexial till the day of death when the temperature rose to 101 degrees. She was treated with digitalis, mersalyl and omnopon and deteriorated rapidly. On the third hospital day she was started on penicillin and X-ray showed consolidation of the left lower lobe. E.C.G. demonstrated left axis deviation and tachycardia. She died a few hours after starting penicillin.

Lung biopsy was performed about 12 hours after death. The needle was inserted in the midaxillary line in the left 8th interspace. The histology was that of great masses of fibrin associated with innumerable polymorphs; a few heart failure cells and alveolar cells were also present. No organisms were seen. The picture was that of an acute lobar pneumonia.

Discussion:

The patient was diagnosed as hypertensive cardiac failure with pulmonary infarction. The autopsy picture from the biopsy was that of acute pneumonia which in retrospect fitted well the clinical picture and the leucocytosis. The absence of organisms on the direct smear was possibly due to the penicillin therapy started some hours before death. The very heavy blood staining of the sputum might have been due to the associated congestion of the lungs from her mild cardiac failure.

Lung biopsy may be used after death, as in this case, to try and confirm the clinical diagnosis in cases where autopsy may not be performed.

CASE 4.

W.G. COLOURED MALE, 28 YEARS. ACUTE LOBAR PNEUMONIA.

History:

Seven days previous to admission he had felt ill with pain in the left side of his chest. The next day he refused to eat and was restless and a doctor started sulphadiazine therapy. He became worse and was admitted in a delirious condition.

Examination:

Very ill, toxic, delirious, face flushed, dyspnoea with alae nasi working, temperature 103 degrees, pulse 100/minute, slight icterus; over left lower lobe diminished movement, increased vocal fremitus and resonance, vesicular breathing, medium resonating crepitations; urine one plus of urobilin; red cells 4.08 million; white cells 19,350 with 92 per cent neutrophils.

Course:

He was immediately started on 400,000 units of penicillin and sulphatriad two tablets and he was then given 200,000 units and two tablets respectively four hourly. X-ray showed a left lower lobe consolidation.

Lung biopsy was performed about one and a half hours after the commencement of treatment. The needle was inserted

through the 8th interspace in the left posterior axillary line; there was no cough, pain or haemoptysis. No significant organisms were cultured and the mucopurulent sputum grew salivary organisms only. The stained smears showed many neutrophils associated with masses of fibrin; these cells showed no signs of degeneration; a few macrophages of all types with probably the small macrophage predominating were present; lymphocytes and monocytes seemed to be more frequent than one would have expected from the amount of blood present. The picture was that of red hepatisation. Scanty pneumococci were seen, some free and some ingested by neutrophils; there were none seen within the macrophages.

The day after admission the patient was much better and his temperature had fallen by crisis to normal. The Wassermann reaction was positive and the serum bilirubin 3.1 mg. per cent with other liver function tests normal. He ran an uncomplicated course and by the 12th day his chest was normal both clinically and radiologically but his E.S.R. was 62 m.m. Westergren. He was discharged nine days later with a normal sedimentation rate.

Discussion:

This case was a straight forward acute lobar pneumonia. Of interest was the presence of pneumococci which were apparently prevented from growing on the culture media because of the presence of penicillin given only 90 minutes before. It

was unlikely that the sulphadiazine given outside the hospital had been effective.

CASE 5. AND 5-1.

S.M. COLOURED FEMALE. 74 YEARS. PULMONARY TUBERCULOSIS.

History:

Symptoms referable to diabetes for some years; vague retro-sternal pain for five days; haemoptysis of two cupfuls of blood and blood streaked sputum for four days.

Examination:

Elderly, thin, not ill, not dyspnoeic, pulse 88/minute, apyrexial, blood pressure 220/100 m.m.Hg.; no abnormal physical signs; urine one plus albumin, Benedict test brick, 30 pus cells / hpf; white cells 11,700 with a normal differential.

Course.

The diabetes was controlled by 25 units of soluble insulin twice daily. X-ray showed a diffuse shadow in the right upper lobe and the differential diagnosis lay between tubercle, carcinoma and a low grade pneumonia. The right diaphragm was raised but moved well on screening

Lung biopsy was done through the second interspace about 3 cm. to the right of the right sternal border. Shortly afterwards there was a small haemoptysis which persisted for about three hours. X-ray taken the next day showed no pneumothorax. The biopsy material was sterile. Histologically

large masses of tissue were present in which the individual elements were difficult to identify (at this stage the efficient crushing of the tissue had not been perfected). There was probably some fibrin present, not infrequent elastic fibres and cells of both the alveolar epithelium and the macrophage series; polymorphs were not infrequent but were not numerous. This was the picture of a low grade inflammatory lesion; there were no signs of carcinoma.

Bronchoscopy showed no abnormality; three specimens of gastric juice were negative for tubercle; repeated X-rays showed no change.

Lung biopsy (5-1) was repeated six weeks after the original biopsy. The site was the first interspace about 2 cm. to the right of the right sternal border. There was no growth on the blood agar nor in the serum broth but tubercle bacilli were cultured on the Lowenstein medium. The smear preparations showed no organisms but there were large masses of tissue consisting of fibrinous material with enmeshed polymorphs, alveolar cells and macrophages with occasional elastic fibrils and strands of collagen. Groups of ciliated and non-ciliated bronchiolar epithelial cells were present. The picture was that of a subacute inflammation.

The patient died a month later and autopsy confirmed the diagnosis of fibro-caseous tuberculosis of the right upper lobe.

Discussion:

The lung biopsy findings made a diagnosis of carcinoma unlikely and the combination of the picture of a low grade inflammation with growth of tubercle bacilli on culture made the diagnosis of tuberculosis obvious.

CASE 6. AND 6-1

J.W. COLOURED MALE. 31 YEARS. CHRONIC LOBAR PNEUMONIA.

History:

Malaise and dry cough for four days and then on the day before admission cold shivers, feverishness and delirium. Worked as a labourer in an engineering works, smokes and drinks a fair amount. His wife died of tuberculosis.

Examination:

Ill, toxic, delirious, dyspnoeic with alae nasi working, pale, temperature 101 degrees, pulse 112/minute; over the right upper lobe diminished movement, relative dullness, medium crepitations, bronchial breathing; urine normal.

Course:

X-ray showed a massive right upper lobe pneumonia. He was

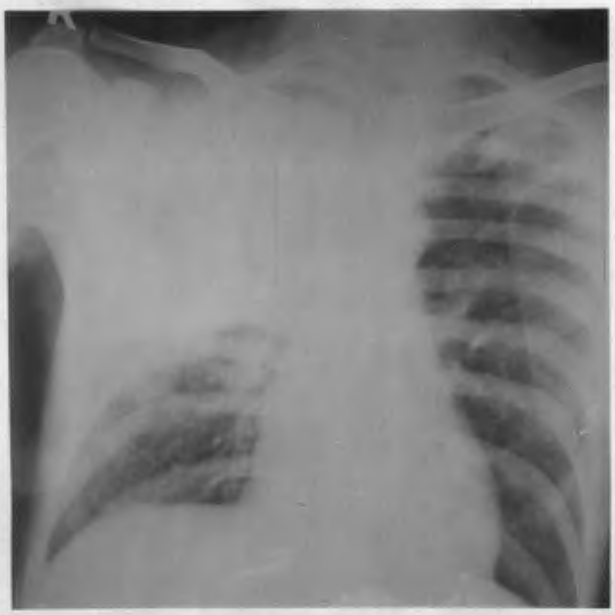


Figure 127. Case 6.
X-ray Chest. PA.
(On Admission)

started on penicillin 200,000 units four hourly and sulphadiad four tablets and then two tablets four hourly. His general condition improved rapidly and on the fourth day lung biopsy was performed through the second interspace about 5 cm. to the right of the right sternal border. There was a small haemoptysis for about 10 minutes afterwards. There was no significant growth from either the biopsy material or from the sputum. Histologically fibrin was present in small masses; polymorphs not infrequent, marked shift to the right and occasional degenerate forms seen; small macrophages frequent but all types also present; transitional cells in fair numbers; an occasional macrophage contained ingested polymorphs. The picture was that of fairly advanced resolution.

Although his temperature had come down by crisis to a low level he continued to be intermittently or remittently pyrexial (up to 100 degrees) for about six weeks. His general condition was excellent and although the physical signs were less marked there was still a large area posteriorly where there was still dullness, increased vocal resonance and crepitations and the X-ray showed that some resolution had occurred but was by no means complete. At this stage a second Lung biopsy (6-1) was performed, this time through the 5th interspace; the needle was inserted just anterior to the lateral border of the right scapula and pushed inwards, upwards and backwards. There were no

untoward events except that for 48 hours he complained of a slight stabbing pain in the region of the right nipple but the pain was not pleuritic in nature. X-ray showed a shallow pneumothorax. The biopsy material was sterile and the smears showed large masses of fibrin, polymorphs in proportion to the blood present, many macrophages (mostly of the small type and not infrequently ones twice this size with a single nucleus and very vacuolated cytoplasm with few ingested particles; dust cells were also not uncommon), transitional cells common but not numerous. The pathology was that of advanced resolution.

Two fresh sputa grew salivary organisms only and four 24 hour sputa and a gastric juice had been negative for tubercle. The Wassermann reaction was negative. Although his temperature had been gradually subsiding he was started on Streptomycin (0.5 Gm twice daily) and a few days later he became apyrexial. After 60 days in hospital his chest was normal on examination but X-ray showed resolution to be incomplete. He was discharged and returned to the out patient department for a check X-ray thirteen days later; this showed a further degree of resolution but the lung had not yet returned to normal. He did not attend again. On admission his red cell count was 2.17 million and the cells were hypochromic with some anisocytosis and poikilocytosis. Iron therapy improved this anaemia, the etiology of which was uncertain.

Discussion:

There seemed little doubt that this patient fell into the group of chronic lobar pneumonia. In spite of his general condition being excellent, his temperature persisted as did the physical signs and X-ray appearance. Patholgically resolution was proceeding but apparently at a slow rate.

CASE 7. AND 7-1.

G.K. NATIVE MALE. 52 YEARS. NORMAL LUNG. CREPITATIONS AT RIGHT BASE.

History:

Difficulty in starting micturition and burning in the hypogastrium during micturition for one year; pain between the shoulders and pain in the neck for three weeks.

Examination:

Cervical fibrositis and pyuria. Chest normal.

Course:

Catheterisation showed a stricture near the external sphincter. The pain in the neck and back responded to methyl salicylate liniment. X-ray chest showed an enlarged heart, a normal left lung and slight elevation of the right diaphragm.

Lung biopsy was performed on the left lung through the 8th space just behind the posterior axillary line. There was no cough, pain or haemoptysis. The biopsy material was sterile. There were numerous red cells with a corresponding number of white cells, occasional groups of alveolar cells and severallarge masses of parenchyma.

He was treated with sulphatriad and discharged.

About two months later he was admitted to another hospital with a history suggestive of either "catheter fever" or coronary thrombosis. He was ill and dyspnoeic and medium crepitations were heard at the right base posteriorly and there were a few crepitations at the left base. There was a neutrophil leucocytosis and X-ray showed a patchy consolidation of both basal regions. Six days after admission he was much improved and lung biopsy (7-1) was performed, this time on the right side through the 8th interspace in the midaxillary line. There were no sequelae. Pale transparent brownish threads of material were obtained which looked unlike material from the lung. The histology was that of groups of liver cells. These were needless to say sterile on culture. He gradually improved and was discharged finally quite fit.

Discussion:

The normal lung biopsy need little comment. In retrospect when one considered that the right diaphragm was raised and that it came still higher in the recumbent position, the position of the second biopsy was rather low; yet the needle was inserted into the area where the crepitations were maximal.

CASE 8.

G.J. COLOURED MALE. 45 YEARS. NORMAL LUNG.

History:

Gradual onset of a left sided paralysis over about 12 hours, five days before admission; past history of veneral disease.

Examination:

Left sided hemiplegia; left pupil Argyll Robertson in type; chest normal.

Course:

X-ray chest was normal and lung biopsy was performed through the 8th interspace about 2 cm. behind the right posterior axillary line. The biopsy was done with undue caution and the needle was inserted only very superficially. A little slightly milky fluid was obtained which on culture grew scanty colonies of diphtheroids and staphylococcus albus. The slides showed only a few red cells, a few non-nucleated plates and very scanty groups of cells which were probably alveolar in type. So little material was obtained that this was considered as a biopsy failure. No pneumothorax was shown on subsequent X-ray.

The cerebrospinal fluid showed changes compatible with syphilis and the C.S.F. Wassermann was positive. He was treated with bismoxyl and penicillin, and discharged much

improved.

Discussion:

This patient's hemiplegia was probably due to thrombosis of a vessel with syphilitic endarteritis. The failure to obtain material from the lung illustrated that one must be reasonably bold when doing a lung biopsy.

CASE 9.

C.M. NATIVE MALE. 30 YEARS. ACUTE LOBAR PNEUMONIA.

History:

Cough with a little yellow sputum, pleuritic pain in the right lower chest, shortness of breath and loss of appetite for two days; headache, feverishness and sweating for one day.

Examination:

Ill, dyspnoeic, sweating, no sputum, temperature 102.5 degrees, pulse 108/minute; over right lower lobe diminished movement, increased vocal fremitus and resonance, relative dullness and bronchial breathing; urine normal; red cells 4.72 million; white cells 28,700 with 98 per cent neutrophils.

Course:

X-ray showed consolidation of the right lower lobe and lung biopsy was performed within an hour of admission. The site of biopsy was the 8th interspace in line with the angle of the right scapula. There were no after effects and the infiltration of the local anaesthetic abolished the pleuritic pain. X-ray next day showed no pneumothorax. Pneumococci were grown on the blood agar and in the serum broth. The slides showed many neutrophils associated with masses of fibrin. The polymorphs were well preserved and only very infrequently was one seen within a macrophage. Macrophages

of all types were present but scanty and the small macrophages were in the majority. Transitional cells were not uncommon. Pneumococci were numerous and mostly extracellular although some had been ingested by polymorphs; a pneumococcus was seen within a macrophage only once. The pathological picture was red hepatisation.

He was started on 400,000 units of penicillin and four tablets of sulphatriad and was then given 200,000 units and two tablets respectively four hourly. His temperature fell by crisis although there was an occasional slight pyrexia till the sixth day. On the 14th day the chest was normal clinically and he was discharged a few days later but the last X-ray had not shown complete resolution. His Wassermann reaction was negative.

Discussion:

This was a classical straight forward case of acute lobar pneumonia where the organism was obtained from the lung biopsy material. No sputum was available. Histiologically the case was one of red hepatisation.

CASE 10.

B.B. NATIVE MALE. 58 YEARS. CARCINOMA OF THE LUNG.

History:

Dry irritating cough for one year; loss of weight some months; hoarseness of the voice two months.

Examination:

Thin but not ill, apyrexial, no Virchow-Trossier gland; slight dullness at right apex with occasional crepitations; urine and blood normal.

Course:

X-ray showed a rounded opacity which was not completely homogeneous in character nor completely segmental; no breaking down was seen; manycalcified foci were present. Two sputa contained salivary organisms and no tubercle bacilli were seen. Bronchoscopy normal and vocal cords moved equally. There was a very occasional pyrexia up to 100 degrees.

For the lung biopsy, the needle was inserted in the third interspace just behind the right anterior axillary line. At about the depth of 3 cm. a firm resistance was encountered, insertion with aspiration was performed in two directions and a small amount of very milky slightly bloody fluid was obtained. For several hours afterwards his mucoid

sputum was slightly streaked with blood. X-ray showed no pneumothorax. The biopsy cultures were sterile. Histology showed many dust cells, and groups of ciliated and non-ciliated bronchiolar epithelial cells; in addition there were many groups of probably malignant cells - these were very much larger than the bronchiolar cells and packed often in tight masses, there was some variation in nuclear size and often little cytoplasm; there were some small areas of fibrin with polymorphs suggesting that there was some associated inflammatory reaction.

Several attempts at bronchography failed to fill the upper lobe. In spite of the biopsy findings he was given a course of antibiotic therapy but went steadily downhill and died about 3 months after admission.

Autopsy:

This had to be limited to the right lung which showed old pleural adhesions especially at the apex; in the upper lobe there was a firm pale mass about 6 cm. in diameter in the centre of which was a small area of softening and cavitation. Many small areas of calcification were scattered through the lung. The glands were large and firm. Histologically the lesion was a spheroidal cell carcinoma of the lung with secondary suppuration.

Discussion:

The clinical picture suggested a carcinoma and the lung biopsy was considered to confirm this although as will be seen in Case 59 metaplasia of alveolar epithelium may give a picture very suggestive of carcinoma. The diagnosis of lung abscess was very unlikely as the biopsy material was sterile. Had operation been performed early this patient's life might have been saved.

CASE 11.

H.L. COLOURED MALE. 51 YEARS NORMAL LUNG.

History:

Five weeks history of classical gastric ulcer pain. Smoked about 10 cigarettes a day.

Examination:

Slight epigastric tenderness; chest normal.

Course:

Barium meal showed a small gastric ulcer on the lesser curvature. He responded well to conservative treatment with diet, alkalis and bed rest. X-ray chest was normal.

Lung biopsy was performed through the 7th interspace just below the angle of the right scapula. The needle was inserted into the lung four times in different directions. There was no cough or haemoptysis but immediately after the needle had been withdrawn he complained of a slight stabbing pain just above the nipple and this pain was slightly worse on coughing. X-ray showed a small pneumothorax in the upper zone of the right lung. There was no growth on the blood agar and only coliform organisms were isolated from the serum broth. The slides showed numerous red cells with a corresponding number of white cells; there were many macrophages of all types and one of the dust cells had ten nuclei; occasional

groups of alveolar cells; many groups of ciliated bronchial epithelial cells; large masses of parenchyma; small portions of interstitial tissue; diffusely scattered black particles probably carbon.

Discussion:

The interest of this case lay in the many macrophages which were of all types. There were in some areas as many as 20 per high power field. Many of the cells were large with multiple nuclei and packed with particles. The patient was not a heavy smoker and thus smoking would not account for the many macrophages. This case was in contra-distinction to Godlowski's normal of 3-5 macrophages per high power field over 100 fields.

CASE 12.

W.T. NATIVE MALE. 46 YEARS. PULMONARY TUBERCULOSIS.

History:

Flitting type of arthralgia involving first his shoulders, then his wrists and finally his ankles for two months; this was associated with pains in the left side of his body and loss of weight for the same duration.

Examination:

Ill, temperature 99 degrees, slight tenderness in left loin; no other abnormal physical signs; urine S.G. 1020 with three plus albumin and numerous red cells and pus cells; white cell count 21,000.

Course:

Agglutination tests for typhoid were negative. X-ray showed extensive infiltration of the left midzone with lesions to a lesser extent at the right base. He was given Duracillin (2 c.c twice daily) but continued to run an intermittent and remittent pyrexia up to 100 degrees. About two weeks after admission a gastric juice examinatin showed a fair number of tubercle bacilli. He was started on Streptomycin (0.5 gm. twice daily) and his temperature became normal.

Lung biopsy was performed after he had been on streptomycin for 19 days. The needle was inserted in the 6th inter-

space in the left posterior axillary line. There were no sequelae. Culture grew no significant organisms. The smear preparations showed many macrophages mostly of the small type but dust cells were also frequent. Several masses of material contained elastic and collagen fibres and many cells difficult to identify but which were not polymorphs. The picture was that of a chronic inflammatory lesion.

A gastric juice examination three days later showed no tubercle bacilli. Other investigations suggested that the kidney lesion was probably tuberculous. He was finally transferred to a tuberculosis hospital.

Discussion:

This was a known case of tuberculosis and the lung biopsy was done to try and demonstrate that tubercle bacilli could be obtained by biopsy. This particular case was a failure. Possible factors were that the patient was on streptomycin and that the lung biopsy was done at the edge of the lesion where one would expect the streptomycin to have its earliest and best effect.

CASE 13.

J.F. COLOURED MALE. 54 YEARS. NORMAL LUNG.

History:

Complete loss of appetite, marked loss of weight and weakness for six weeks.

Examination:

Thin, icteric, clubbing, Virchow-Trossier gland present, large nodular hepatomegaly; chest normal; urine one plus urobilin; blood normal.

Course:

Barium meal showed a large fungating carcinoma of the stomach extending down the greater curvature from the fundus. Using a lung biopsy technique and a lung biopsy needle a liver biopsy was done (this time intentionally) and the smears showdd many tumour cells. X-ray chest was normal.

Lung biopsy was done through the 8th interspace just below the angle of the left scapula. Only a little tissue in the form of small droplets of blood were obtained. There were no sequelae. The only growth was in the form of diphtheroids in the serum broth. The slides showed a fair number of red cells and a fair number of small macrophages.

The patient went steadily downhill and died about a

month and a half after admission. Autopsy confirmed the diagnosis of carcinoma of the stomach with secondaries in the liver.

Discussion:

This case suggested that material was more difficult to obtain from normal lungs than from pathological cases.

CASE 14.

K.M. NATIVE MALE. 28 YEARS. NORMAL LUNG.

History:

Even the interpreters could not speak the patient's language.

Examination:

Not ill, right sided hemiplegia, blood pressure in the arms 180/120 m.m.Hg. and in the legs 230/130 m.m.Hg.; urine and blood normal.

Course:

Wassermann reaction was negative and the cerebrospinal fluid normal. Intravenous pyelogram was normal; X-ray chest normal.

Lung biopsy was done through the 7th interspace about 10 cm. from the midline of the back on the right. There were no sequelae. Culture was sterile. The slides showed many red cells; a few groups of pleural cells; macrophages of all types but most frequently with one or two nuclei and containing black particles; small groups of alveolar cells; occasional groups of ciliated bronchial epithelial cells; occasional masses of parenchyma; and scattered black particles.

He gradually improved and was discharged with only the facial paralysis persisting. His blood urea had been normal and his blood pressure persistently raised.

Discussion:

This was probably a case of essential hypertension. The biopsy was one of the few to be "contaminated" with pleural cells.

CASE 15.

E.N. NATIVE FEMALE. 25 YEARS. **NORMAL LUNG.**

History:

This was very complicated but in essence she had had diarrhoea for seven months starting when she was four months pregnant. There had also been loss of appetite and weight.

Examination:

Thin, drowsy, apathetic, weak, very pale, temperature 101.2 degrees, tongue pale and smooth; chest normal; urine normal; red cells 0.9 million; white cells 2,400; smear slightly hypochromic with considerable anisocytosis and poikilocytosis.

Course:

Reticulocyte count 2.9 per cent, serum bilirubin normal, gastric juice normal, bone marrow showed many giant metamyelocytes and myelocytes. No pathogens were grown from the stool. Wassermann negative. Penicillin "brought" the temperature to normal and kaolin and belladonna controlled the diarrhoea. Blood transfusion caused improvement but neither iron nor liver elicited a reticulocyte response. Reticulocytes were increased by giving folic acid. X-ray chest was normal.

Lung biopsy was performed through the 8th interspace below the angle of the right scapula. After biopsy there was a slight sticking pain in that area but no pneumothorax was seen on subsequent X-ray. Cultures were sterile. On the slides were many red cells; macrophages of all types, alveolar cells, and many areas of parenchyma.

She was discharged feeling fit after a stay in hospital of two and a half months.

Discussion:

The differential diagnosis seemed to lie between steatorrhoea and the anaemia of pregnancy. The response to only folic acid seemed a little in favour of the later. Unfortunately there were no facilities to perform fat balance studies. Quite large areas of parenchyma were obtained by lung biopsy showing that quite large amounts of tissue might be obtained even from a normal lung.

CASE 16.

R.B. COLOURED MALE, 40 YEARS. NORMAL LUNG.

History:

Lightning pains in the calves for three months; failing vision, giddiness and general weakness for two months.

Examination:

A classical case of tabes dorsalis with bilateral optic atrophy; urine and blood normal.

Course:

Blood and cerebrospinal fluid examination confirmed the presence of syphilis. X-ray chest showed a slightly enlarged heart (his blood pressure was 150/100 mm.Hg.) and ?catarrhal changes at the right base.

Lung biopsy was performed through the 8th interspace in line with the angle of the right scapula. Immediately afterwards there was a small haemoptysis of about two tablespoonfuls of bloody mucoid sputum. There was no pneumothorax. Culture on the blood agar grew two colonies of staphylococcus albus and two colonies of B.subtilis and the serum broth and Lowenstein medium were sterile. The slides showed many red cells; numerous macrophages of all types; alveolar cells singly and in small groups; non-nucleated plates; parenchyma; occasional masses of inter-

stitial tissue and much scattered pigmented particles. Many of the macrophages were of the small type and might have been related to the "?catarrhal inflammation".

He was given a course of treatment with penicillin and bisoxyl and discharged improved but his dimness of vision remained unaltered.

Discussion:

This was a straight forward case of tabes dorsalis. In the lung biopsy material although many of the macrophages were small they resembled dust cells rather than the macrophages of a resolving pneumonia. The cytoplasm was less vacuolated and the majority contained at least a few black particles.

CASE 17.

J.M. INDIAN MALE. 46 YEARS. NORMAL LUNG.

History:

Vague pains all over and a coarse tremor of the hands for five months; he had consumed large quantities of alcohol for years and had had one attack of delirium tremens.

Examination:

Ill, temperature 102 degrees; cirrhotic liver; chest normal; white cells 5,500 with a normal differential count.

Course:

He was treated with aspirin and vitamins and gradually his temperature subsided over about three weeks. His Wassermann reaction was doubtful and the Kahn positive; liver function tests were grossly abnormal; Paul's test, Brucella agglutination test, blood and stool cultures all negative. X-ray chest normal.

Lung biopsy was done when he had improved. The needle was inserted through the 6th interspace in the right posterior axillary line. There were no immediate sequelae but about five minutes later he complained of a stabbing pain in the region of the right lung apex and this pain was worse on deep breathing and on movement. The pain was mild and lasted about 90 minutes. X-ray showed a shallow

pneumothorax. There was no growth on any of the culture media used. The slides showed many red cells; macrophages of all types; alveolar cells singly and in small groups; non-nucleated plates; parenchyma; occasional masses of interstitial tissue, and scattered black particles.

He was discharged feeling fit.

Discussion:

This patient had an alcoholic cirrhosis of the liver and a temperature which remained a pyrexia of uncertain origin.

CASE 18.

P.J. NATIVE FEMALE. 49 YEARS NORMAL LUNG.

History:

Amenorrhoea for three months; vague generalised aches and pains and hot flushes for five weeks.

Examination:

No abnormalities on physical examination and urine and blood normal.

Course:

Wassermann reaction and X-ray chest both negative. Stilboestrol helped her little and symptoms waxed and waned.

Lung biopsy was done through the 7th interspace in left posterior axillary line. There were no sequelae. Cultures were sterile. There was a fair amount of blood present; scattered macrophages mostly dust cells; small portions of parenchyma and interstitial tissue.

She left hospital at her own request but stated that the lung biopsy had improved her greatly.

Discussion:

This case was probably passing through the difficult phase of the menopause.

CASE 19.

J.D. COLOURED MALE. 36 YEARS. CHRONIC PNEUMONIA.

History:

Pleuritic pain below the angle of the left scapula, shortness of breath, cough with a slight amount of blood stained sputum, fever, headache, sweating, loss of appetite, nausea and weakness all for four days and of sudden onset.

In 1942 he had been in a sanatorium for seven months. In 1948 an X-ray showed no pathology except a thickened upper main fissure on the right. In 1949 he entered hospital with a five day history of pain in the right chest, dyspnoea and haemoptysis for five days and X-ray showed consolidation of the right upper and middle lobes and of the dorsal segment of the lower lobe; there was a mitralised heart. On admission his temperature had been 103 degrees and he was given penicillin 200,000 units and then 100,000 units four hourly. The temperature came down by crisis and from the fifth day he was apyrexial. Penicillin was stopped after two weeks. Forty days after the original X-ray there were still crepitations and bronchial breathing over the affected area and X-ray showed some resolution. Gradually the physical signs and X-ray pathology returned to normal and he was discharged after having been in hospital about three months. This was obviously the history of a chronic pneumonia.

He was a vegetable hawker, was a fairly heavy drinker and smoked 20 cigarettes a day. He ate only one meal a day.

Examination:

Very ill, dyspnoeic, temperature 96.5 degrees, pulse 118/minute; heart not enlarged and the murmurs of aortic incompetence and mitral stenosis were just audible; over left lower lobe diminished movement, relative dullness, harsh vesicular breathing with medium crepitations; urine albumin a trace; red cells 4.2 million; white cells 12,000 with 88 per cent neutrophils.

Course:

X-ray confirmed the left lower lobar pneumonia. He was started on penicillin 400,000 units and sulphatriad four tablets and then given 200,000 units and two tablets respectively four hourly. For two days after admission his temperature was 99 degrees and from then onwards, except for peaks of 98.8 degrees on the 6th and 9th days he remained apyrexial. His physical signs remained unaltered although his general condition rapidly improved and X-ray showed some resolution.

Lung biopsy was done three weeks after admission. The needle was inserted into the 8th interspace about 5 cm. behind the left posterior axillary line with the patient in the horizontal position. As the needle was inserted bloody

material spurted up into the syringe and some blood welled up into the barrel. The needle was immediately withdrawn. About a minute later the patient had a haemoptysis of about three to four tablespoonfuls and at the same time became very dyspnoeic and the pulse rate was increased. Then about a minute later he complained of a stabbing pain in the epigastrium on breathing and this lasted about seven minutes. He then settled down and became quite comfortable. There was slight blood streaking of the sputum for 24 hours. X-ray showed no pneumothorax. The cultures were sterile except for a few colonies of organisms which were obviously contaminants. Histologically there were small areas of fibrin with not very numerous small macrophages and some larger macrophages of the "chronic pneumonia type". The picture was that of very advanced resolution.

Penicillin was discontinued about a week later. Resolution continued gradually and by the 45th day there were no abnormal physical signs and the X-ray showed complete resolution. A subsequent bronchogram of the left lower lobe and lingula of the upper lobe was normal. Four 24 hour sputa had been negative for tubercle, and the Kahn and Berger tests were positive.

Discussion:

This case was obviously one of chronic pneumonia. He was extremely ill on admission which may have accounted for the

absence of temperature and the only slight leucocytosis. Of great interest was that he had had chronic pneumonia on the right side about a year before. It was possible that his rheumatic heart may have played a part in determining this chronicity. The lung biopsy showed that the lung was sterile and that resolution was proceeding.

CASE 20.

H. DU P. COLOURED MALE. 33 YEARS. PULMONARY INFARCTION.

History:

On his first admission he was in a state of cardiac failure. He was hypertensive (blood pressure 140/120 mm.Hg.) but after some weeks of bed rest this fell to normal. An alcoholic history and a three finger firm hepatomegaly suggested a possible beri-beri heart but he did not respond to thiamin and Vitamin B complex therapy. He responded well to digitalis but the oedema and albuminuria persisted. Acute nephritis was probably the best diagnosis. He was discharged much improved with only a trace of albumin in the urine.

He was re-admitted six weeks later with a history of anorexia, nausea and vomiting after meals, and headaches for five weeks; swelling of the feet and a non-productive cough for 2 weeks and swelling of the face for one week. He was a heavy smoker.

Examination:

Well nourished, not toxic, oedema of face, ankles and sacrum, slightly distended neck veins, apyrexial, pulse 120/minute, blood pressure 120/105 mm.Hg., cardiomegaly with triple rhythm; three finger tender hepatomegaly; chest normal; urine two plus albumin, S.G. 1012, two or three granular casts and occasional red cells in each high power field;

red cells 5.5 million; white cells 11,160 with a normal differential count.

Course:

The Wassermann reaction was negative; blood urea 34mg. per cent; serum albumin 2.6gm. and globulin 1.9gm.; serum cholesterol 120mg. per cent. X-ray chest showed an enlarged left ventricle and the E.C.G. was one of left axis deviation. Liver function tests were normal. The patient did not have a diuretic response to digitalisation but with the use of mersalyl the oedema gradually subsided.

A week after admission he suddenly developed a pain in the right axilla and medium resonating crepitations were heard over this area; X-ray showed a small area of pneumonic consolidation in the right middle lobe associated with thickening of the short interlobar fissure. His temperature was 99 degrees. Lung biopsy was performed into the area of the most numerous crepitations, that is through the 6th interspace in the right anterior axillary line. During the insertion blood welled up into the syringe and the needle was withdrawn. About five minutes later there was a small haemoptysis and he then vomited about a quarter of a cupful of gastric contents. No pneumothorax was produced. The cultures were sterile. Histologically there was much blood present and large masses of fibrinous material with rather scanty cells mainly small macrophages and

polymorphs. He had received no chemotherapy. There was no subsequent pyrexia and the physical signs in the chest subsided rapidly. Casts, red cells and albumin persisted in the urine. Muscle biopsy was normal. He was discharged much improved but died at home about 10 days later.

Discussion:

The actual type of nephritic lesion was a little uncertain, but an acute nephritis going on to a subacute stage seemed a likely diagnosis. The pulmonary episode was unaccompanied by a pyrexia and cleared rapidly without chemotherapy. The biopsy cultures were sterile which almost excluded a pneumonia and the picture of a fibrinous exudate with scanty cells did not appear to be that of a bacterial pneumonia. The clinical picture was that of a pulmonary infarct and the biopsy findings were probably compatible with such a diagnosis.

Although the description of a pneumonia in early resolution quite closely resembled the description in this case, it is difficult to quite describe in words why these slides did not appear to be that of a pneumonia. After looking at many biopsy slides one acquires an impression of the pathology difficult to describe and possibly akin to "clinical sense".

CASE 21.

D.A. COLOURED FEMALE. 14 YEARS. ?RHEUMATIC PNEUMONIA.

History:

Slight dyspnoea on exertion for two years; cough with white or yellow sputum for two weeks; flitting polyarthritis involving the right knee, metatarsophalangeal joint of the left big toe, left shoulder, left knee, left ankle for five days; stabbing pain in region of angle of right scapula occurring only on coughing for two days; no sore throat; no vaginal discharge.

Examination:

Not acutely ill, joints normal, temperature 100 degrees, pulse 108/minute, no signs of cardiac failure, mitral stenosis with cardiomegaly; rhonchi both lungs and occasional crepitations at the bases; urine normal; red cells 3.8 million; white cells 18,320 with a normal differential count; E.S.R. 55 mm. in one hour (Wintrobe).

Course:

Her temperature and tachycardia subsided "in response to" salicylate therapy and about a week after admission she felt quite fit and the E.S.R. was normal. On the 11th day a tender mass of glands appeared under the right sterno-mastoid muscle. This subsided in two days but then her

face, chest wall and sacrum were noticed to be oedematous; there was dyspnoea but no distended neck veins; at the right base there was dullness with medium resonating crepitations and in the right axilla increased vocal resonance and ?bronchial breathing; urine normal; white cells 11,360 with a normal differential count; X-ray showed a mitralised heart, increased vascular markings, and a small effusion in the right anterior costo-phrenic angle with an area of pneumonitis or infarction in the posterior basic segment. She was apyrexial.

Lung biopsy was done through the 7th interspace just below the angle of the right scapula into the area of most numerous crepitations. There were no sequelae. Culture showed no pathogens. Histologically there were small areas of fibrinous or albuminous exudate with not infrequent macrophages mostly of the small type. Polymorphs were in numbers compatible with the amount of blood present. The picture was not that of a bacterial pneumonia but was compatible with that of an early rheumatic pneumonia or possibly a pulmonary infarct.

Digitalis produced a good diuretic response and over a week the physical signs subsided without any chemotherapy. She ran a very occasional pyrexia up to 99.5 degrees. The Wassermann reaction was negative and two sputa were negative for tubercle. She was discharged fit but an aortic diastolic murmur became audible in addition to the mitral stenotic

murmur.

Discussion:

There was little doubt that the patient had rheumatic fever. The differential diagnosis of the pulmonary lesion lay between a mild rheumatic pneumonia and pulmonary infarction. The clinical picture and the biopsy finding were against a bacterial pneumonia. Pulmonary infarction is unusual at this age but the picture was also not classical of rheumatic pneumonia. The biopsy really only helped to exclude a bacterial pneumonia.

CASE 22.

J.L. COLOURED MALE. 82 YEARS. ?PNEUMONIA.

History:

Pain in the chest and progressive dyspnoea for two days; he was brought in having been picked up in a collapsed state in the street.

Examination:

Emaciated, very dyspnoeic, pale, temperature 101 degrees; in the right midzone diminished movement increased vocal fremitus and resonance, bronchial breathing and numerous resonating crepitations; rhonchi all over both sides of the chest; urine normal; red cells 2.17 million; white cells 11,000.

Course:

He was immediately started on penicillin 400,000 units and sulphatriad four tablets and then received 200,000 units and two tablets respectively every four hours. His temperature fell to subnormal the next day but that night he deteriorated and he died on the morning of his third day in hospital. A single sputum grew no pathogenic organisms and was negative for tubercle. A portable X-ray showed extensive infiltration of both lung fields with a cavity in the right midzone and probably also one in the left subclavicular

region.

No autopsy was available and lung biopsy was performed through the fourth interspace in the right midclavicular line (about six hours after death). The striking feature of the histology was the small areas of fibrin associated with innumerable polymorphs showing a shift to the left; macrophages of the dust cell type were present but scanty; no organisms were seen on the slides stained with Gram or Ziehl Neelsen.

Discussion:

The biopsy appearance was classical of a very acute bacterial pneumonia. It was felt that had this been tuberculosis of the very acute spreading type then surely tubercle bacilli would have been found, if not in the sputum, at least from the biopsy material. On the other hand the presence of cavities was against an ordinary pneumonia. The absence of organisms could be accounted for by the previous penicillin therapy. The absence of tubercle bacilli and the presence of the innumerable polymorphs seemed to sway the balance in favour of a bacterial pneumonia. Multiple lung abscesses with bronchopneumonia seemed unlikely but could not be excluded.

CASE 23.

J.L. COLOURED MALE, 49 YEARS. ACUTE LOBAR PNEUMONIA.

History:

Cold shivers, fever, sweating, pleuritic pain in the left upper chest anteromedially for five day; mucopurulent blood stained sputum, dyspnoea, anorexia, diarrhoea with six or seven watery brown stools a day for two days and herpes febrilis for one day. He did not drink alcohol and smoked 20 cigarettes a day; diet was poor consisting mainly of bread and potatoes with occasionally fish and vegetables.

Examination:

Thin, ill, dyspnoeic, alae nasi working, herpes febrilis on the upper lip, temperature 101 degrees, pulse 104; over the left upper lobe diminished movement, increased vocal resonance, relative dullness, bronchial breathing and medium resonating crepitations; urine normal; red cells 4.34 million; white cells 13,300.

Course:

Lung biopsy was done shortly after admission, the needle being inserted through the second interspace about 5 cm. to the left of the left sternal border. Immediately afterwards there was a small haemoptysis. X-ray showed consolidation of the left upper lobe and no pneumothorax.

Pneumococci were cultured from both the blood agar and the serum broth. On the slides there were large masses of fibrin associated with many well preserved polymorphs. These showed little definite shift in either direction. Scanty macrophages of all types were present and very occasionally contained an ingested polymorph. Transitional cells were present in small numbers. There were many scattered black particles and in one large mass of tissue was seen a single structure closely resembling an asbestos body. Pneumococci were very scanty in the direct smear. The picture was that of red hepatisation.

Immediately after biopsy he was started on penicillin 400,000 units and sulphatriad four tablets and then received 200,000 units and two tablets respectively four hourly. The next day his temperature had fallen by crisis to normal and a fresh sputum grew salivary organisms only. His Wassermann reaction was negative and two sputa (24 hour) were negative for tubercle. After the first two days he remained apyrexial. His physical signs rapidly diminished and his chest was normal clinically by the 8th day and there was complete X-ray resolution by the 18th day.

Discussion:

This was a classical case of acute lobar pneumonia admitted in the stage of red hepatisation. Biopsy culture grew pneumococci but a sputum culture after only a few injections of penicillin was negative.

CASE 24.

N.A. COLOURED MALE. 40 YEARS. CHRONIC LOBAR PNEUMONIA.

History:

Generalised body pains, feverishness, shivering, headache, pleuritic pain over left lower chest, dyspnoea, cough with a small amount of greenish sputum for six days. About five months previously he had been treated for a large gastric ulcer by partial gastrectomy; since the operation he had had frequent colds and had lost weight. He was a painter and did not drink but smoked a good deal.

Examination:

Thin, toxic, dyspnoeic with alae nasi moving, temperature 101.5 degrees, pulse 100; over left lower lobe diminished movement, increased vocal fremitus and resonance, relative dullness and bronchial breathing but no crepitations; urine one plus urobilin and occasional hyalo-granular casts; red cells 4.15 million; white cells 30,500 with 97 per cent neutrophils.

Course:

X-ray showed consolidation of the left lower lobe but in addition there was bilateral upper zone scarring, and fibrosis with areas of calcification in the right infra-clavicular region; the trachea was a little retracted to

the right.

Lung biopsy was performed shortly after admission, the needle being inserted through the 8th interspace about 5 cm. to the left of midline posteriorly. About 15 minutes afterwards there was a very slight haemoptysis and the sputum was blood streaked for about the next 12 hours. X-ray showed no pneumothorax. Pneumococci were grown both on the blood agar and in the serum broth. The sputum showed a good growth of pneumococci. On the slides there were large masses of fibrin with innumerable well preserved polymorphs. Macrophages and transitional cells were present but not frequent and only very occasionally was a polymorph seen within a macrophage. Pneumococci were numerous and a fair number had been ingested by the polymorphs.

He was immediately started on penicillin 200,000 units and sulphatriad four tablets and then received 100,000 units and two tablets respectively four hourly. His temperature fell by crisis to normal the next day. He remained apyrexial and penicillin was stopped on the 7th day. His physical signs gradually altered, bronchial breathing becoming less marked and crepitations appearing. On the 10th day he felt perfectly fit but his temperature was 99.5 degrees, on the 11th day 102 degrees, on the 12th day 99.5 degrees, on the 13th day 99.5 degrees and on the 14th day 101 degrees. Penicillin was started again. X-ray showed that a fair degree of resolution had occurred and the physical signs

were dullness, vesicular breathing and medium crepitations. His temperature was normal the next day but on the following day (that is the 16th day) it was again 102 degrees. At this stage he insisted on going home and he left hospital having been given sulphatriad to take with him. He returned to the out patient department about two weeks later and stated that he felt fit except that he was slightly short of breath on exertion. There was no cough or sputum. Unfortunately no physical examination was done but X-ray showed little change in the area of consolidation. The Wassermann reaction was negative.

Discussion:

This patient still showed considerable consolidation with no signs of further resolution 29 days after the onset of chemotherapy. He was included under the chronic group because it was obvious that resolution was unlikely to be complete for some days if not weeks and this would bring him well into the group of over 30 days duration. The reason for the pyrexial "relapse" was obscure. Factors possibly contributing to the slow resolution were the partial gastrectomy, the smoking and the old healed tuberculous lesions at the apices.

CASE 25.

S.A. COLOURED MALE. 20 YEARS. NORMAL LUNG.

History:

Headache, feverishness, anorexia, nausea, cramplike abdominal pains for six days and vomiting watery material three times a day for five days.

Examination:

Drowsy but not toxic, apyrexial, nil abnormal on physical examination; urine normal; white cell count 19,500 with 11 per cent eosinophils, 69 per cent neutrophils, and 20 per cent lymphocytes.

Course:

He remained apyrexial. Paul's test, brucella agglutination test and Widal all negative. The stool contained a moderate number of ova of ascaris lumbricoides. The E.S.R. was normal and Wassermann reaction negative. Hexyl resorcinol resulted in the passage of one round worm. Penicillin was given but the gradual improvement in his general subjective state seemed quite unrelated to antibiotic therapy. X-ray chest was normal.

Lung biopsy was performed through the 8th interspace about 4 cm. behind the right posterior axillary. Very soon afterwards he complained of a slight pleuritic pain in the

CASE 25.

S.A. COLOURED MALE. 20 YEARS. NORMAL LUNG.

History:

Headache, feverishness, anorexia, nausea, cramplike abdominal pains for six days and vomiting watery material three times a day for five days.

Examination:

Drowsy but not toxic, apyrexial, nil abnormal on physical examination; urine normal; white cell count 19,500 with 11 per cent eosinophils, 69 per cent neutrophils, and 20 per cent lymphocytes.

Course:

He remained apyrexial. Paul's test, brucella agglutination test and Widal all negative. The stool contained a moderate number of ova of ascaris lumbricoides. The E.S.R. was normal and Wassermann reaction negative. Hexyl resorcinol resulted in the passage of one round worm. Penicillin was given but the gradual improvement in his general subjective state seemed quite unrelated to antibiotic therapy. X-ray chest was normal.

Lung biopsy was performed through the 8th interspace about 4 cm. behind the right posterior axillary. Very soon afterwards he complained of a slight pleuritic pain in the

right subclavicular region and this pain was worse on movement. It lasted about two hours. About 20 minutes after biopsy he coughed up a trace of blood. X-ray showed a very small shallow pneumothorax laterally at the level of the second rib to the right. The cultures were sterile and the slides showed numerous red cells, scanty small and large macrophages, occasional masses of perenchyma, and small groups of non-ciliated bronchiolar epithelial cells.

He was discharged feeling fit.

Discussion:

The cause of his symptoms remained obscure but might have been related to the ascaris infestation.

CASE 26.

M.B. COLOURED MALE. 29 YEARS. ACUTE LOBAR PNEUMONIA.

History:

Cough with a little white sputum for seven days; cold shivers for five days; pleuritic pain in the right lower chest, feverishness, sweating and dyspnoea for four days; blood stained sputum for 3 days. He had been given tablets which were probably sulphadiazine on the day before admission. Did not smoke and drank moderately.

Examination:

Ill, dyspnoeic, alae nasi working, temperature 100.4 degrees, pulse 96/minute; vocal fremitus and resonance increased in the right midzone anteriorly and decreased at the left base, relative dullness and harsh vesicular breathing with medium crepitations over right midzone and breath sounds absent at left base where there was stony dullness; urine normal; red cells 4.4 million; white cells 15,000 with 88 per cent neutrophils.

Course:

X-ray showed consolidation of the right middle and lower lobes with a small pleural effusion at the left base. Shortly after admission lung biopsy was performed through the 4th interspace about 4 cm. to the right of the right sternal

border. Biopsy was immediately followed by an alarming reaction with dyspnoea, coughing and a haemoptysis of about three tablespoonfuls of blood. He complained afterwards of headache. There was slight blood staining of the sputum for 24 hours. X-ray showed no pneumothorax. The cultures were sterile. The slides showed large masses of fibrin associated with many but not innumerable well preserved polymorphs which showed no definite shift in either direction. A few macrophages of all types were present and very occasionally contained an ingested polymorph. Transitional cells were seen in small numbers. Pneumococci were very scanty. The picture was that of red hepatisation.

He was started on penicillin 400,000 units and sulpha-triad four tablets and then given 200,000 units and two tablets four hourly. After two days he became apyrexial. The day after admission the sputum grew salivary organisms only. On the 5th day herpes febrilis appeared on his upper lip. The Wassermann reaction was positive. Penicillin was continued for 17 days. Rather gradually the physical signs diminished but he continued to cough up mucopurulent sputum. Six sputa were negative for tubercle (three of these were 24 hour specimens). By the 20th day there were no abnormal physical signs and by the 26th day X-ray resolution was complete. Bronchogram of the right lung showed no abnormality.

Discussion:

Most of the clinical features were in favour of this being a pneumococcal lobar pneumonia, the negative biopsy cultures being due to sulphonamide having been given the day before; pneumococci were seen but were very scanty. The histology was that of red hepatisation. The bronchogram was done to exclude bronchiectasis which was suspected because of the quite copious mucopurulent sputum.

CASE 27.

N.M. COLOURED FEMALE. 14 YEARS. CONGENITAL CYSTIC LUNG.

History:

The patient came to the out patient department complaining of cough productive of half a cup of yellow sputum daily for several weeks. Nil of note was found on physical examination but X-ray chest showed a honey-comb appearance of the right upper lobe. About three days later she coughed up about a cupful of bright red blood. Admission was arranged.

Examination:

Not ill, no dyspnoea, no clubbing, temperature 99 degrees, slight dullness at right apex with medium resonating crepitations; urine normal; red cells 4.68 million; white cells 12,000 with neutrophils 48 per cent, eosinophils 4 per cent and lymphocytes 48 per cent.

Course:

A single sputum was obtained and showed a heavy growth of Friedlander's bacillus on the blood agar. The patient would not produce another sputum and the question arose as to whether the Friedlander's bacillus could be the cause of the X-ray picture or whether it might be present in the form of a secondary invader of the cystic bronchiectasis. Her good general condition made it unlikely that she was a case of

even a very chronic Friedlander bacillus pneumonia but to make absolutely certain a lung biopsy was performed. The needle was inserted through the second interspace just lateral to the right midclavicular line and one gained the impression that there was thickened pleura present. After the biopsy the patient coughed up a minute particle of blood which was plated out immediately. About five minutes after the biopsy the patient complained of a pleuritic pain in the region of the puncture area and this was worse on movement. The pain was slight and remained for 24 hours. No pneumothorax was present. No pathogens were cultured from the biopsy material and there was no growth of Friedlander's bacillus from this specimen of sputum. The biopsy histology was that of rather dense portions of tissue with scattered pigmented particles (probably interstitial of fibrous tissue); occasional small amounts of fibrin unassociated with polymorphs; occasional groups of alveolar cells; and a fair number of dust cells. The material was probably from the cyst walls and showed in addition possibly a very mild inflammatory reaction.

It was considered that the biopsy excluded Friedlander's bacillus pneumonia, and the subsequent bronchogram showed the suspected cystic dilatation of the branches of the bronchial tree to the right upper lobe and also dilatation of the bronchi to the dorsal segment of the lower lobe.

Her Wassermann reaction was persistently positive.

Discussion:

This patient's lesion was probably that of a congenital cystic lung or possibly an acquired bronchiectasis. The lung biopsy was valuable in excluding a Friedlander's bacillus infection. Friedlander's bacillus is known to be a common inhabitant of the respiratory tract normally but it is a secondary invader in various disease processes. The patient's blood Wassermann was persistently positive and she was most probably a congenital syphilitic subject showing as yet no stigmata.

CASE 28.

B.M. NATIVE MALE. 29 YEARS. ACUTE LOBAR PNEUMONIA.

History:

Coldness, headache and malaise for four days; feverishness, sweating, cold shivers and pleuritic pain in the left lower chest for three days; dyspnoea and herpes febrilis for two day; cough with a little blood stained sputum and pleuritic pain in the right lower chest for one day. About six hours before admission he had been given 400,000 units of penicillin by his doctor. The patient did not drink nor smoke; diet poor consisting mainly of mealie meal porridge.

Examination:

Toxic, dyspnoeic, jaundiced, herpes febrilis on upper lip, temperature 99 degrees, pulse 104/minute; over right lower lobe diminished movement, increased vocal fremitus and resonance, relative dullness, bronchial breathing, medium crepitations and a friction rub; urine albumin a trace and bile and urobilin present; red cells 4.2 million; white cells 27,900.

Course:

Soon after admission lung biopsy was done through the 8th interspace in the right posterior axillary line. There were no sequelae and the pleuritic pain was abolished. There

was no sputum available. Cultures were sterile. Histologically there were large masses of fibrin associated with many but not innumerable well preserved polymorphs which showed no definite shift in either direction. A few macrophages of all types were present and very occasionally contained an ingested polymorph. Transitional cells were observed in small numbers. No pneumococci were seen. The picture was that of red hepatisation.

The patient was started on penicillin 200,000 units and sulphatriad four tablets and then continued on 200,000 units of penicillin and two tablets of sulphatriad four hourly. That evening his temperature rose to 102.5 degrees but then came down rapidly and he was apyrexial from the sixth day onwards. Two sputa were negative for tubercle and his Wassermann reaction was positive. X-ray was only done on the 6th day and confirmed the area of consolidation at the right base and showed no pneumothorax. Penicillin was stopped on the 20th day. Resolution proceeded normally and the chest was clear clinically on the 23rd day and radiologically on the 26th day. The right costophrenic angle remained obscured due to an adhesion and possibly a little pleural thickening.

DISCUSSION:

The interest of this case was the negative culture six hours after an injection of penicillin. Otherwise the case seemed a straight forward lobar pneumonia except that there was the unusal feature of pleuritic pain starting of the left side when

his pneumonia was on the right.

CASE 29.

I.S. COLOURED MALE. 46 YEARS. CHRONIC LOBAR PNEUMONIA.

History:

Pleuritic pain in the left chest, cough with blood stained sputum, feverishness with cold shivers and loss of appetite for ten days. Both he and his wife had been treated for venereal disease. He drank moderately and used to smoke.

Examination:

Not very ill, dyspnoea slight, temperature 99 degrees, pulse 84/minute, over the left midzone posteriorly there was increased vocal fremitus and resonance and relative dullness with bronchial breathing and medium crepitations whilst at the base there was stony dullness with distant bronchial breathing; urine normal; red cells 5.3 million; white cells 25,100 with 87 per cent neutrophils.

Course:

X-ray showed a left lower lobe consolidation with a small effusion and slight pneumonic changes were present in the right middle lobe. He was started on penicillin 400,000 units and then 200,000 units four hourly but in spite of this he continued to be pyrexial in the region of 100 degrees for eight days. A week after admission about 10 c.c. of sterile exudate was aspirated from the chest. Two fresh sputa grew

salivary organisms only and two sputa were negative for tubercle. The patient felt perfectly fit. Gradually the fluid was absorbed and the consolidation began to resolve. About three weeks after admission the X-ray showed some resolution with probably thickened pleura present. Lung biopsy was performed through the 7th interspace just below the angle of the left scapula. The needle was felt to penetrate thickened pleura. There were no sequelae. The material was sterile. Histologically several large masses of material with many cells were seen but it was uncertain whether this was fibrin or not. Frequent small lymphocytes were seen and small macrophages were present in fair numbers. Transitional cells were not uncommon. Polymorphs were present in proportion to the amount of blood. The picture was that of very advanced resolution.

Resolution continued at a slow pace and by the 43rd day the only abnormal physical signs could be attributed to thickened pleura and X-ray showed clearing of the opacity at the left base but with pleural thickening or encysted fluid obscuring the posterior costo-phrenic angle. The patient was sensitive to iodine and no bronchogram could be done.

Discussion:

The feature of this pneumonia was the associated effusion although only a little fluid was obtained. The pyrexia was prolonged. There was residual thickened pleura. There was no obvious reason for the prolonged duration of his illness.

CASE 30.

S.C. COLOURED MALE. 13 YEARS. ACUTE NEPHRITIS. ACUTE LOBAR PNEUMONIA.

History:

Headache, pain between the shoulders and cough with a little sputum, which was not blood stained, for eight days; swelling of the face, dark urine and oliguria for five days. No history of a sore throat.

Examination:

Very ill, nephritic facies, very dyspnoeic, alae nasi working, temperature 100.8 degrees; over left lower lobe increased vocal fremitus and resonance, relative dullness, bronchial breathing and medium resonating crepitiations; blood pressure 190/140 mm.Hg; heart and optic fundi normal; tenderness in the loins; urine two plus albumin, numerous red cells and granular, hyaline and epithelial casts; red cells 4.4 million; white cells 18,000 with 80 per cent neutrophils.

Course:

He was at once started on penicillin 200,000 units and then 100,000 units four hourly and his diet was the usual one for acute nephritis namely glucose water and fruit juices. By the following day his temperature was 99.5 degrees and he felt much improved and physical signs were unchanged. Lung biopsy was performed through the 8th interspace just medial

to the line of the angle of the left scapula. Immediately afterwards he coughed up about a tablespoonful of blood and blood streaking of the sputum continued for about an hour. X-ray showed a right basal consolidation with some thickening of the lesser fissure and on the left side consolidation at the base with a small pleural effusion. The biopsy material was sterile and histologically showed fibrin and fairly numerous macrophages of the small type seen in a resolving pneumonia. Polymorphs were not infrequent some showing signs of early degeneration but only occasionally were polymorphs seen within macrophages. Transitional cells were fairly frequent. No pneumococci were seen. The picture was that of rather early resolution.

The blood urea was 48 mg. per cent. From the fourth day onwards he was apyrexial. Over about four weeks his blood pressure, blood urea and urine returned to normal. Resolution of the chest pathology proceeded rapidly and by the 14th day he was normal on clinical examination and X-ray showed complete resolution.

Discussion:

The association of lobar pneumonia and acute nephritis was very unusual. However in 1942 a case was described of a man of 63 years who had acute nephritis and lobar pneumonia concurrently. He was given sulphonamides and died on the 8th day. Autopsy confirmed the diagnosis. The case was

presented at the Massachusetts General Hospital but unfortunately there was no discussion on the relationship between these two conditions. Of great interest in the present case was the rapid resolution. If concomitant conditions played an important role in causing delayed resolution then surely one would have expected this case to have become chronic pneumonia.

CASE 31.

F.B. COLOURED FEMALE, 23 YEARS. ?CHRONIC LOBAR PNEUMONIA.

History:

Her illness commenced two weeks prior to admission with severe frontal headache, a dry cough and pleuritic pain in the right lateral part of the chest. After a week the headache and chest pain disappeared but the cough persisted and in addition she was feverish and sweated a lot especially at night. She had been a student midwife in Cape Town till 1948 since which time she had been doing clerical work in Villiersdorp. A routine X-ray in 1947 had shown the chest to be normal.

Examination:

Not ill, no dyspnoea, temperature 100.2 degrees, pulse 120; at right base diminished movement, increased vocal fremitus and resonance, relative dullness and bronchial breathing with fine and medium crepitations; urine normal; red cells 4.05 million, white cells 8,100 with 76 per cent neutrophils and 24 per cent lymphocytes.

Course:

X-ray showed consolidation and a moderate effusion at the right base and consolidative congestive change at the left peri-hilar area extending to the upper zone and base rather like the picture of the "uraemic lung"; over the whole

lateral aspect of the left lung there was a pleural reaction. Lung biopsy was attempted - the chest was infiltrated in the 8th interspace in line with the angle of the right scapula; the biopsy needle was then inserted to a depth of about 4 cm. but when the stylette was withdrawn air sucked in. The needle was removed. X-ray showed a small hydro-pneumothorax. In spite of 200,000 units of penicillin four hourly she continued to be pyrexial (in the region of 100 degrees) for about two weeks. X-ray taken just after her last day of pyrexia showed a fair degree of resolution of the right lower zone consolidation, and absorption of the air and most of the fluid; but there was now a small left basal effusion possibly with underlying consolidation and the fluid had seeped over the left apical region. Penicillin was stopped a week after she had become apyrexial. Almost throughout her course she had felt perfectly well. After two weeks of normal temperature there was still diminished movement, dullness and decreased air entry at the right base but no alteration in vocal fremitus or resonance and no crepitations. The E.S.R. was 45 m.m. in one hour (Westergren).

At this stage <u>lung biopsy</u> was performed through the 8th interspace just behind the right posterior axillary line. There were no sequelae. The cultures were sterile. The slides showed no fibrin and small macrophages and transitional cells were scanty. Small lymphocytes were not infrequent. There were several sheets of non-ciliated

bronchiolar epithelial cells. The picture was compatible with very advanced resolution or even with a normal lung. Gradually the fluid was absorbed until by the 45th day there only remained bilateral pleural thickening and the E.S.R. was normal. There remained slight dullness and diminished air entry at the right base compatible with pleural thickening. Throughout her course there remained unchanged a fan shaped infiltration of the left upper and middle zones and this closely resembled a tuberculous lesion. Six gastric juice examinations were negative for tubercle and the Mantoux (1/10000) test was positive. She was discharged and attended as an outpatient every two months and there has been no alteration in the X-ray picture. The radiological changes might be due to thickened pleura. Her Wassermann reaction was negative.

Discussion:

The first problem was whether to include this case in the chronic pneumonia group. This might be one of the pneumonias with insidious onset described by Scadding (1939) but the appearance of new exudation at the left base whilst the patient was on chemotherapy seemed very unusual for a pneumococcal pneumonia. This case was included under the chronic pneumonia group with the reservation that possibly it might be some other type of pathology, possibly virus in nature. The lung biopsy showed most probably the picture of a normal lung. The physical signs at the time of biopsy

could have been accounted for by thickened pleura. The raised sedimentation rate might have been due to pathology persisting on the left side (the biopsy was done on the right side).

CASE 32.

M.M. NATIVE FEMALE. 23 YEARS. PULMONARY TUBERCULOSIS.

History:

Pleuritic pain just to the right of the sternum, feverishness with cold shivers, sweating especially at night, cough with about half a cupful of yellow sputum daily, dyspnoea, loss of appetite and loss of weight for five weeks; the sputum increased, and became dark brown and very foul smelling for one week.

Examination:

Thin, very ill, foul breath, copious offensive purulent sputum containing brown altered blood, temperature 101 degrees, pulse 104/minute; over the right upper chest anteriorly diminished movement increased vocal fremitus and resonance, relative dullness, bronchial breathing and a few crepitations; urine one plus albumin; red cells 3.3 million and smear hypochromic; white cells 26,600 with 92 per cent neutrophils.

Course:

X-ray showed cavitation plus consolidation of the right upper lobe, multiple small cavities being present; very early "fluffy" consolidation at both bases. A sputum grew mixed organisms and histologically there were no elastic fibres.

She was started on penicillin 500,000 units six hourly and postural drainage and in addition she received a course of sulphatriad for ten days. Within two days the sputum was no longer offensive but there was no improvement in her general condition and her temperature remained between 100 and 103 degrees. Five sputa (three of which were 24 hour specimens) were negative for tubercle. Her Wassermann reaction was positive. After two weeks she was started on streptomycin (0.5 Gm. twice daily) and P.A.S. (12 Gm. daily by mouth in divided doses). Both her temperature and general condition rapidly showed a marked improvement but X-ray showed the areas of consolidation at the bases to have progressed, and there was now in addition a soft opacity in the left infraclavicular region. Another 24 hour sputum was negative for tubercle.

Lung biopsy was performed through the third interspace about 4 cm. to the right of the right sternal border. There were no sequelae. All the cultures were sterile. Histologically there were large masses of structureless material containing nuclear remnants and probably most closely resembling caseous material; occasional areas of rather dense tissue with fibroblasts and scanty polymorphs and a fair number of small dust cells; Sheets of ciliated bronchiolar epithelial cells were not infrequent; some areas with elastic fibres and some associatdd fibrin. The picture was a very mixed one suggesting a chronic inflammation. On the

slide stained with Ziehl Neelsen there were not infrequent acid and alcohol fast bacilli morphologically identical to M. tuberculosis. The day after biopsy a sputum report came back stating that "one tubercle bacillus had been seen" but guinea pig inoculation of this same sputum was negative. Two more 24 hour sputa were again negative for tubercle.

The patient continued on streptomycin and P.A.S. and rapidly improved generally and on discharge to a tuberculosis hospital she felt quite fit although there was little definite change in the X-ray appearance.

Discussion:

This patient's history and clinical picture very closely resembled that of a lung abscess but the X-ray strongly suggested tuberculosis. Numerous sputa were negative for tubercle but lung biopsy showed a chronic type of inflammation probably with caseation and the diagnosis was clinched by the direct demonstration of tubercle bacilli. It was unusual that a positive culture on the Lowenstein medium was not obtained. It was possible that this patient did have a lung abscess which may have reactivated a quiescent tuberculous focus. In this case one could truly state that the diagnosis was made by lung biopsy.

CASE 33.

A.I. MOSLEM MALE. 49 YEARS. ACUTE LOBAR PNEUMONIA.

History:

Cough with yellow sputum containing occasional brown and red areas, pleuritic pain in the left lower chest posteriorly and dyspnoea for seven days; herpes febrilis and anorexia for three days.

Examination:

Ill, dyspnoeic, alae nasi working, herpes febrilis on lower lip, temperature 99.5 degrees, pulse 114/minute; over left lower lobe increased vocal fremitus and resonance, relative dullness, bronchial breathing and medium resonating crepitations; urine one plus albumin; red cells 3.74 million; white cells 20,800 with 78 per cent neutrophils.

Course:

Shortly after admission lung biopsy was performed through the 9th interspace just behind the left posterior axillary line. There were no sequelae, and infiltration of the local anaesthetic removed the pleuritic pain. The biopsy culture showed a good growth of pneumococci; from the sputum there grew mixed organisms with very scanty colonies of pneumococci. Histologically there were large masses of fibrin with numerous well preserved polymorphs but occasional degenerated forms were seen; there was no particular shift

in either direction; macrophages were not very infrequent and very occasionally contained a degenerate polymorph; some transitional cells were present; pneumococci were scanty but small Gram positive particles in many polymorphs were possibly degenerate digested organisms. The picture was that of late red hepatisation. X-ray taken the next day showed no pneumothorax and confirmed the consolidation of the left middle and lower zones.

He was started on penicillin 200,000 units and sulphatriad four tablets and then given penicillin 100,000 units and sulphatriad two tablets four hourly. His Wassermann reaction was negative. The temperature came down by crisis and from the third day onwards he was apyrexial. He showed rapid clinical and radiological resolution so that his chest was clear by the 18th day and his X-ray normal, except for slight residual tenting of the diaphragm on the left side, by the 27th day.

Discussion:

This was a straight forward case of acute pneumococcal lobar pneumonia admitted in the stage of late red hepatisation and progressing normally to resolution.

CASE 34.

J.M. COLOURED MALE. 45 YEARS. ASBESTOSIS AND PULMONARY TUBERCULOSIS.

History:

Dyspnoea on exertion for six weeks; pleuritic pain in the left lower chest with copious yellow mucopurulent sputum for four weeks; for about the same duration loss of weight and night sweats.

A year previously he had been in Somerset Hospital with a right upper lobar pneumonia which responded clinically to chemotherapy but there were no records of sputum examinations and no check X-ray was done before discharge. For about three years he had complained of "chronic bronchitis".

He had lost an arm in Egypt in 1945 whilst in the army; there was no history of contact with tuberculosis or asbestos.

Examination:

Ill, very dyspnoeic, temperature 102 degrees, pulse 120/minute; over the right apex vocal fremitus was increased and there were numerous medium crepitations; posteriorly over the left midzone bronchial breathing was heard; no neck rigidity; urine trace of albumin; red cells 3.7 million; white cells 12,400 with 75 per cent neutrophils.

Course:

He was started on penicillin and sulphatriad. On the second day X-ray showed a right sided pneumonic consolidation affecting the right upper lobe with bronchogenic spread to the right middle and lower lobes; there was a large cavity in the right upper zone showing a fluid level; on the left side extensive infiltration with cavitation throughout the left lung field. Chemotherapy was stopped. On the fifth day a sputum was sent for examination and lung biopsy was done through the second interspace about 3 cm. to the right of the right border of the sternum. The subsequent events are described fully in the section on Complications of Lung Biopsy. The patient collapsed immediately after biopsy but with adrenaline and oxygen he appeared to improve. It seemed that he would almost certainly recover but during that night he deteriorated and died about seventeen hours after the biopsy. Biopsy cultures showed no growth on the blood agar and in the serum broth but tubercle bacilli were grown on the Lowenstein medium. The sputum grew mixed organisms and contained tubercle bacilli. Histologically the biopsy material showed fibrin with a fair number of polymorphs and many dust cells; there were many scattered black pigmented particles; asbestos bodies were numerous and these varied from long thin fibres to short fibres with the classical segmented appearance and clubbed ends; some of the macro-

phages had ingested the asbestos fibres; tubercle bacilli were present.

Autopsy:

Both pleural cavities were obliterated by dense adhesions. In the right lung was a large cavity in the apical region. In this cavity large blood vessels were present lying most superficially on the inner surface (see Figures 128 and 129). There was widespread tuberculosis throughout both lungs and a small cavity at the left apex. The lung between the areas of tuberculosis was excessively firm and rather brownish in appearance. The right ventricle showed some hypertrophy indicating that probably the lung lesions were

Figure 128. Case 34. Pleural surface of right upper lobe to show thickened pleura. Note the small tubercles in the membranes over the base of the brain.

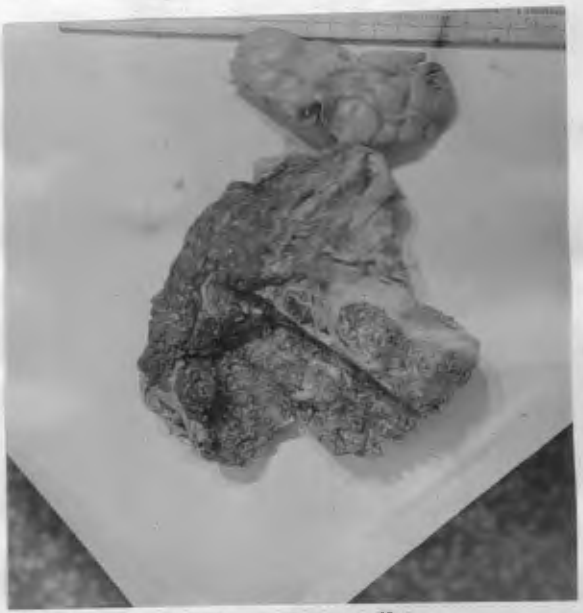


Figure 129. Case 34. Cut surface of lung with the large cavity exposed to demonstrate the large blood vessels on its inner surface. (lower part of specimen).

of such standing as to give a mild chronic cor pulmonale. Over the vertex of the brain there was a gelatinous greenish exudate and this was also seen at the base where there were also small groups of white tubercles in the membranes. Histologically the meninges showed a moderate inflammatory cell infiltration consisting of polymorphs and macrophages. The vessels of the Circle of Willis were carefully dissected and traced into the brain as far as possible but no signs of air embolism could be found. The histology of the lung was that of tuberculosis and asbestosis.

Discussion:

This case was obviously one of tuberculosis and lung biopsy was done simply to see if tubercle bacilli could be easily obtained by this direct method. The finding of "asbestosis" came as a surprise. The death of this patient was a great shock and changed ones whole attitude towards lung biopsy. From this time onwards cases were only done if they could lie absolutely flat and no cases with suspected cavities were biopsied. The stage seemed set for air embolism in this case where there were blood vessels in close contact with air needing only the needle to make the communication. It was felt that possibly had the patient not had tuberculous meningitis in addition he might have survived the probable air embolus.

CASE 35.

D.M. NATIVE MALE. 51 YEARS. CHRONIC LOBAR PNEUMONIA.

History:

Pleuritic pain in the left chest for two days and cough with mucoid sputum for one day. He was a labourer and drank a fair amount.

Examination:

Not toxic, no dyspnoea, apyrexial, pulse 72/minute; medium resonating crepitations over the left lower lobe posteriorly were the only abnormal physical signs; urine normal; red cells 3.8 million; white cells 17,500 with neutrophils 60 per cent, lymphocytes 39 per cent and mononuclears one per cent; smear slightly hypochromic.

Course:

He was started on Duracillin 1 c.c. but the next day he was given penicillin 400,000 units four hourly and sulphatriad four tablets and then two tablets four hourly. He ran an intermittent pyrexia up to 100 degrees for four days and during this time he occasionally coughed up blood stained sputum. On examination on the fifth day there was now dullness and bronchial breathing in addition to the crepitations. X-ray (for the first time) on the 14th day showed consolidation of the posterior part of the upper lobe and upper part of the lower lobe. About three weeks after ad-

mission his physical signs were unaltered and lung biopsy was performed through the 8th interspace just behind the left posterior axillary line into the region where the signs were most marked. There were no sequelae and X-ray the next day showed some resolution and slight elevation of the left diaphragm but no pneumothorax. The cultures were sterile and the sputum grew salivary organisms only. The slides showed very little fibrin but there were numerous small macrophages; in addition there were a fair number of macrophages of the larger type with a single nucleus, vacuolated cytoplasm and few or no ingested particles; many transitional cells present; the polymorphs were in numbers proportional to the blood present. The picture was that of very advanced resolution.

Penicillin was discontinued a month after admission. The patient during all this time felt perfectly fit. Gradually the signs altered and by the end of seven weeks there was more clearing to be seen on the X-ray but there seemed a residual area of fibrosis in the left upper zone. By the 67th day there were no longer any physical signs except possibly a little diminished air entry at the left base and X-ray showed a little pleural thickening in this region. Bronchogram of the left lung showed no abnormality. The Wassermann reaction was negative.

Discussion:

This patient was seen at a very early stage of his illness and this might have accounted for the fact that he was not very ill on admission in spite of the leucocytosis; it might also explain why his physical signs only developed fully a few days after admission. This apparent worsening of the physical signs in spite of chemotherapy could only be explained on an inflammatory response to toxic products from the pneumococci lysed by the penicillin. The biopsy picture showed the expected macrophage response.

Factors determining chronicity were possibly the slight anaemia and the fibrosis at the left apex which was probably an old healed tuberculous lesion.

CASE 36 AND 36-1.

P.F. COLOURED MALE, 35 YEARS. SPLEEN AND NORMAL LUNG.

History:

The patient gave a history of progressive cardiac failure over about four and a half months.

Examination:

Gross cardiac failure, clubbing of the fingers, apyrexial, collapsing pulse, cardiomegaly with the murmurs of mitral stenosis and aortic regurgitation, no splenomegaly; urine two plus albumin; red cells 3.82 million; white cells 6,300 with 72 per cent neutrophils and 28 per cent lymphocytes.

Course:

He responded fairly well to digitalisation, mersalyl and aminophyllin but he ran an intermittent pyrexia up to 100 degrees. Blood culture was negative. He was started on a course of penicillin (100,000 units four hourly for 28 days). After two weeks he became apyrexial. X-ray chest showed mainly a left ventricular enlargement and no pulmonary pathology. His general condition was fair when on the 23rd day he suddenly became very dyspnoeic and restless, crepitations were heard at both bases but mostly on the left side and he died in cardiac failure the next morning.

Lung biopsies were performed five hours after death. A

needle was first inserted into the 6th interspace about 7cm. to the left of the midsternal line into the area where there had been the most crepitations. The slides showed innumerable small round cells which were obviously lymphocytes and the conclusion was that the material had been obtained from the spleen. The second biopsy (36-1) was done through the second interspace about 5 cm. to the right of the midsternal line. The material obtained consisted of a little blood, frequent macrophages of all types, numerous alveolar cells singly and in groups, groups of ciliated and non-ciliated bronchiolar epithelial cells and areas of interstitial tissue. Numerous small Gram negative bacilli were seen but these were almost certainly postmortem invaders.

Discussion:

This patient probably had subacute bacterial endocarditis super-imposed upon a rheumatic heart. He died probably from congestive heart failure following a pulmonary embolus. The lung biopsy material at the left base was almost certainly obtained from the spleen and that from the right apex was normal tissue.

CASE 37 AND 37-1.

C.S. COLOURED FEMALE. 50 YEARS. CHRONIC LOBAR PNEUMONIA.

History:

Pleuritic pain in the left chest, dyspnoea at rest, and cough with muco-purulent sputum for two weeks; dysuria, frequency and a sore area on the perineum for two days. Did not smoke nor drink. A domestic servant and supported a husband and children.

Examination:

Thin, dirty and neglected, necrotic ulcer on the perineum and several sore areas on the buttocks; toxic,dyspnoeic with movement of alae nasi, temperature 100 degrees; crepitations and bronchial breathing at the left base; urine normal; red cells 4.0 million; white cells 21,000 with 75 per cent neutrophils and 25 per cent lymphocytes.

Course:

She was started on penicillin 100,000 units four hourly and sulphatriad four tablets and then two tablets four hourly. For four days her temperature remained raised even to 101.5 degrees. The temperature then fell to normal but for the next three weeks there were occasional peaks to 99 degrees. A week after admission there was bronchial breathing over the left midzone posteriorly and at the base medium crepitations were heard. Lung biopsy was done firstly through

the 5th interspace about 5 cm. to the left of the midline posteriorly into the area of bronchial breathing. There were no sequelae but the patient cried afterwards because she said she was nervous. She was then given one and a half grains of seconal and fifteen minutes later a second biopsy was done through the 8th interspace about 2 cm. behind the left posterior axillary line. Again there were no sequelae (37-1). The material from both biopsies was sterile. There was no sputum available. Histologically in the biopsy from the upper lobe there were large masses of fibrin with innumerable small macrophages; transitional cells frequent; polymorphs few in number some well preserved and others degenerate and occasionally seen within macrophages. The picture was that of fairly advanced resolution. The second biopsy from the lower lobe showed no fibrin and material was scanty; small macrophages the predominant cell with a fair number of transitional cells and alveolar cells; polymorphs scanty. The picture was compatible with very advanced resolution. This was exactly what one would have anticipated.

X-ray taken four days later (for the first time) showed consolidation of the left lung involving the upper lobe and the upper part of the lower lobe. There was no pneumothorax. The sore areas in her genital region rapidly healed and her general condition became greatly improved. Penicillin was stopped after three weeks. After a month and a half in

hospital only occasional crepitations remained where there had been bronchial breathing and the X-ray showed some resolution. By the 48th day the chest was clear clinically. She was finally discharged on the 89th day with resolution not quite completed. Her Wassermann reaction was negative.

Discussion:

The clinical condition of this patient on admission made it hard to credit her story that she had been ill outside for as long as two weeks. This type of patient was notoriously unreliable in the estimation of time. On admission she appeared to be a straight forward case of lobar pneumonia but she ran a very chronic course. The lung biopsy showed that resolution was already well under way by the end of the first week. She was thin and in a very neglected condition and this might have contributed to the slow resolution.

CASE 38.

S.A. COLOURED MALE. 29 YEARS. ACUTE LOBAR PNEUMONIA.

History:

Pleuritic pain in the right lower chest with cough productive of white sputum occasionally blood streaked, feverishness and sweating for five days. His only occupationshad been a vegetable hawker, assistant to a plumber and cutting open fish on a trawler. There was no history of contact with asbestos. He smoked 10-20 cigarettes a day and drank alcohol occasionally.

Examination:

Toxic, dyspnoea with alae nasi working, temperature 102.5 degrees; over right lower lobe diminished movement, increased vocal fremitus and resonance, relative dullness, bronchial breathing and coarse crepitations; urine normal; white cell count 11,600.

Course:

He was started on penicillin 300,000 units and sulphatriad four tablets and then received penicillin 100,000 units and sulphatriad two tablets four hourly. His temperature on the day of admission rose to 104 degrees and then fell by crisis and from the sixth day he remained apyrexial. Although the temperature responded well he remained very ill and on

the fourth day the penicillin was increased to 250,000 units four hourly and in addition he was given streptomycin 0.5 gm. twice daily. On the fifth day he was much improved and the physical signs were unchanged. His sputum was muco-purulent with rusty areas. Lung biopsy was performed through the 7th interspace just below the angle of the right scapula. There were no sequelae and X-ray showed an area of consolidation involving the dorsal and posterior basal segments of the right lower lobe and the lesser fissure was thickened but there was no pneumothorax. The biopsy material was sterile and the sputum grew mixed organisms. The slides showed great masses of fibrin with a fair number of cells; the majority of the cells were small macrophages but polymorphs were not infrequent and it was common to find small macrophages containing recognisable partly digested polymorphs; transitional cells were frequent. The picture was that of fairly advanced resolution. In the Ziehl Neelsen slide one macrophage was seen containing many dust particles and an asbestos body. No asbestos bodies were seen on the direct smears of the sputum.

The patient gradually improved and streptomycin was stopped after six days and penicillin after twelve days. His chest was normal clinically after 18 days and three days later an X-ray showed almost complete resolution. His Wassermann reaction was negative.

Discussion:

This patient ran a normal course for a pneumococcal lobar pneumonia. In spite of the severity of the illness, the poor leucocyte response and the probable presence of slight "asbestosis" resolution proceeded perfectly normally. Of great interest was the presence of numerous macrophages when the physical signs were bronchial breathing and crepitations.

CASE 39.

C.M. NATIVE FEMALE. 18 YEARS. TUBERCULOSIS OF ABDOMEN, LUNGS AND BRAIN.

History:

Anorexia, loss of energy, loss of weight, abdominal pains, headaches, and neck stiffness for two months; dry cough and pain in the interscapular region for two weeks. She was about sixteen weeks pregnant.

Examination:

Toxic, dyspnoeic with alae nasi working, temperature 103 degrees, pulse 150/minute; postero-laterally over the right lower chest there was diminished movement, dullness, bronchial breathing and medium resonating crepitations; mentally dull but no neck rigidity; generalised abdominal tenderness but no rigidity; pregnant uterus felt; urine albumin one plus and numerous pus cells; red cells 2.37 million; white cells 4,600 with neutrophile 76%, lymphocytes 22% and monocytes 2%; smear slightly hypochromic; E.S.R. 67m.m. in one hour(wintrobe).

Course:

X-ray showed the right lower lobe to be partially atelectatic or consolidated and the left base also showed some opacity resembling patchy consolidation. She showed no response to penicillin and aureomycin, her temperature remaining between

99 and 104 degrees. On the fourth day after admission lung biopsy was performed through the fifth interspace about 5cm. to the right of the midsternal line (into an area where numerous crepitations were heard). Aspiration was performed and only a little clear fluid was obtained; the needle was reinserted and biopsy was done in two directions and a little milky brownish fluid was obtained. There were no sequelae. A little thick white sputum grew a mixed growth of organisms predominantly B. Friedlanderi and alkaligenes. The biopsy cultures were sterile. Histologically there were small masses of tissue consisting of a fibrinous material with occasional elastic fibres, a few neutrophils, macrophages and alveolar cells; there were many scattered black particles. No organisms were seen. The picture was that of a rather chronic inflammatory lesion.

About 10 days later slight neck rigidity developed and the cerebro-spinal fluid showed a raised pressure, raised protein, low chloride, normal sugar and raised cells mainly lymphocytes. Streptomycin was given intrathecally and started intramuscularly. A few days later chloromycetin was also commenced. Sputa and gastric washings were negative for tubercle, blood cultures were sterile and liver aspiration showed no abnormality. The patient continued to deteriorate and died about three weeks after admission.

Autopsy:

The lower lobes of both lungs showed collapse and there were many scattered small tubercles especially on the right side. The peritoneal cavity was 'peppered' with confluent tubercles and the omentum was heavily infiltrated. No ascites was present but the mesenteric glands formed a solid caseous mass, and the paraortic glands were also involved. Tubercles were present in both liver and spleen. There were over a hundred tuberculomata scattered through the brain, the average size being 2cm. in diameter. There were no signs of tuberculous meningitis.

Discussion:

This patient obviously had a widespread tuberculosis. The value of the biopsy was to indicate that there was a chronic inflammatory process in the lung from which organisms were not isolated. This made it very unlikely that her main pathology lay in the chest. Tubercle was the most likely diagnosis from the lung biopsy but it was disappointing that no bacilli were seen on the direct smear nor grown from the biopsy material on the Lowenstein medium. Once again it was important that the Friedlander's bacillus grown from the sputum was not isolated from the lung biopsy material.

CASE 40.

M.D. COLOURED FEMALE. 23 YEARS. LOBAR PNEUMONIA. LIVER BIOPSY.

History:

Cough with white sputum, dyspnoea, feverishness, headache, loss of appetite and nausea for five days.

Examination:

Ill, dyspnoeic, temperature 104 degrees; over left lower lobe increased vocal fremitus and resonance, relative dullness and bronchial breathing; urine normal; white cells 28,500.

Course:

Penicillin and sulphadiazine caused her temperature to fall by crisis. On the third day there were signs of consolidation at both bases and the sputum was rusty. Lung biopsy was attempted through the 8th interspace below the angle of the right scapula. There were no sequelae. The biopsy cultures were sterile and the sputum grew alkaligenes faecalis. Histologically the biopsy material showed many sheets of liver cells. X-ray four days later showed bilateral basal consolidation but no pneumothorax. Resolution proceeded normally and the chest was clear clinically by the 19th day and X-ray showed complete resolution by the 27th day. Her Wassermann reaction was negative.

Discussion:

This case was probably a bilateral basal pneumococcal pneumonia. The biopsy needle obviously must have penetrated the diaphragm and entered the liver. The biopsy was done at a reasonable level and into an area where physical signs were marked. The presence of the liver cells came as a great surprise. One could assume only that there was some degree of associated collapse with a raised diaphragm.

CASE 41.

M.C. COLOURED MALE. 27 YEARS. ACUTE LOBAR PNEUMONIA. ASBESTOSIS.

History:

Pleuritic pain in the left chest at the base postero-laterally, dry cough, dyspnoea, sweating, feverishness for 36 hours. There was no history of past illness and careful questioning revealed no occupational contact with asbestos.

Examination:

Nutrition fair, very toxic, sweating, dyspnoeic with movement of alae nasi, temperature 100 degrees, pulse 120/minute; over left lower lobe increased vocal fremitus and resonance, relative dullness, medium crepitations and bronchial breathing; urine normal; red cells 4.0 million; white cells 6,950 with 76% neutrophils and 24% lymphocytes.

Course:

He was started on penicillin 200,000 units and sulphatriad four tablets and then received penicillin 100,000 units and sulphatriad two tablets four hourly. His temperature fell by crisis and from the fourth day he was apyrexial. A sputum examined on the day after admission grew salivary organisms only and no tubercle bacilli were seen.

On the third day he was still toxic and pyrexial (100 degrees)

his physical signs were unaltered except that the breath sounds were now vesicular in type. X-ray showed consolidation of the left middle and lower zones with a small associated pleural exudate; the right lung showed a well marked shadowing in the midzone bordered inferiorly by the lesser fissure. Lung biopsy was performed through the 8th interspace just below the angle of the left scapula. A small amount of brownish fluid was obtained. There were no sequelae. The cultures were sterile and the sputum grew mixed organisms. Histologically large masses of fibrin were present; polymorphs and small macrophages in approximately equal numbers; most of the polymorphs well preserved but many were smaller than normal and showed signs of degeneration; the macrophages were of all types and not infrequently contained two partially digested polymorphs; transitional cells frequent; asbestos bodies fairly frequent and found together with the other cells associated with the fibrin and completely or partly, in some cases, ingested by macrophages. The picture was that of early resolution associated with 'asbestosis'. No asbestos bodies were seen on the direct smears of the sputum.

Resolution was rapid and uneventful, there being no abnormal physical signs in the chest by the 14th day and complete X-ray resolution by the 23rd day. The X-ray showed no signs of asbestosis.

Discussion:

This patient had probably pneumococcal lobar pneumonia. A peculiarity was the low total white cell count but he was very ill on admission. A striking feature was the normal rapid resolution in spite of asbestosis, a poor leucocyte response and a small associated pleural effusion. The stage was set for a chronic pneumonia but resolution proceeded normally.

CASE 42.

E.N. COLOURED FEMALE. 21 YEARS. ACUTE LOBAR PNEUMONIA.

History:

The patient had been delivered of a normal child without complications 18 days before admission. She remained in bed for eight days. She had been up for five days when she suddenly felt a pleuritic pain in the left chest anteriorly in the region of the second and third ribs; this was associated with slight dyspnoea and a cough with at first no sputum and the next day a little brownish sputum was produced. Her symptoms persisted till her admission five days later.

Examination:

Not toxic, slight malar flush, slight dyspnoea with movement of the alae nasi; temperature 103.5 degrees; slightly diminished movement over the left upper chest, and over a small area anteriorly over the second and third interspaces on the left there was slight dullness and medium resonating crepitations; urine normal; red cells 4.16 million; white cells 19,500 with 83 per cent neutrophils.

Course:

X-ray showed an area of consolidation in the left midzone (see Figure 130). Lung Biopsy was performed soon after admission through the second interspace about 5 cm. to the left of the midsternal line. About five minutes later there

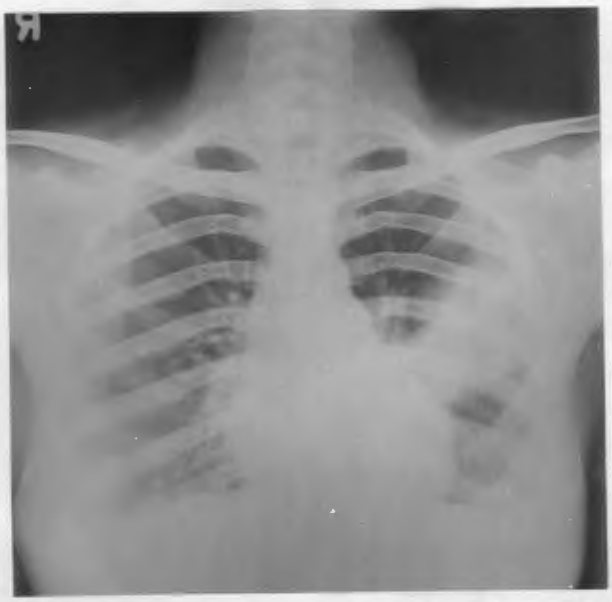


Figure 130. Case 42.
X-ray Chest. PA.
(On Admission).

was very slight blood streaking of the mucopurulent sputum and this persisted for 24 hours. Biopsy culture grew pneumococci but the sputum grew only "very scanty colonies of ?pneumococci". The slides showed masses of fibrin with numerous well preserved polymorphs; macrophages were scanty and transitional cells infrequent; very occasionally a polymorph was seen within a macrophage. Pneumococci were very scanty. The picture was that of red hepatisation.

She was given penicillin 100,000 units four hourly and sulphatriad four tablets and then two tablets four hourly. Her temperature fell to normal by crisis. X-ray showed no pneumothorax. Resolution proceeded rapidly and the chest was clear clinically by the 11th day and radiologically

by the 12th day.

Discussion:

The interest in this case was the high temperature but the patient did not look ill and had few abnormal physical signs. The X-ray picture could have been that of a virus pneumonia. The clue to the pneumococcal etiology was the high leucocyte count and the diagnosis was established by the classical histological picture of red hepatisation and the culture of pneumococci from the biopsy material. Although the pneumonia occurred during the puerperium resolution was perfectly normal.

CASE 43.

L.C. COLOURED MALE.12 YEARS. ?URAEMIC LUNG.

History:

Malaise for four weeks; dyspnoea, pain in the right hypochondrium, headaches and vomiting for three weeks. No past illnesses.

Examination:

Generalised oedema including the face, dyspnoea, distended neck veins, apyrexial, pulse 106, blood pressure 205/155 m.m.Hg., gross cardiomegaly with gallop rhythm and systolic murmurs at all areas and soft diastolic at aortic area; dullness with medium resonating crepitations at the right base; fundi showed early papilloedema, arteriovenous nipping and exudates particularly in the macular region; tender hepatomegaly; urine S.G. 1016, albumin two plus, hyaline, granular and epithelial casts with occasional red and white cells; red cells 3.3 million; white cells 15,000 with neutrophils 31 per cent and lymphocytes 69 per cent; smear showed anisocytosis, poikilocytosis and some macrocytosis; E.S.R. 4 m.m. in one hour (Wintrobe).

Course:

Blood urea 128 mg. per cent, low albumin;globulin ratio, normal serum cholesterol; E.C.G. showed slurred QRS

complexes but no left ventricular strain. X-ray chest showed congestive changes in both lung fields especially at the right base where there was probably a small hydrothorax. Digitalisation caused only moderate improvement. A week after admission over the right lower lobe there was increased vocal fremitus and resonance, relative dullness, bronchial breathing and medium resonating crepitations. Lung biopsy was performed through the seventh interspace about 4 cm. to the right of the midline of the back. Immediately afterwards he coughed up a little bloody mucoid sputum which was plated out. He complained of mild pleuritic pain in the right lower chest laterally and X-ray the next day showed a small pneumothorax laterally at the level of the 5th and 6th ribs. The biopsy cultures were sterile and only staphylococcus albus was grown from the sputum. The slides showed a fibrinous material with quite frequent small macrophages and not infrequent easily recognisable monocytes; polymorphs were scanty. The picture was compatible with that of an uraemic lung.

The specific gravity of the urine varied from 1008 to 1025 but he went steadily downhill to die in congestive cardiac failure and uraemia. No autopsy was available.

Discussion:

There was little doubt that the patient died of nephritis but the exact type seemed uncertain; probably an acute nephritis going on to a stormy subacute stage was most acceptable. He showed signs of consolidation at the right base and the lung biopsy showed that this was not an acute bacterial pneumonia. This left the possibilities of an uraemic lung or just severe congestion with a small hydrothorax and some underlying atelectasis. The histology was compatible with the former but, without further experience with the biopsy histology of passive congestion, the latter cannot be excludéd.

CASE 44 AND 44-1.

K.R. COLOURED FEMALE. 18 YEARS. LUNG ABSCESS AND BRONCHIETASIS.

History:

Pleuritic pain in the left lower chest in the anterior axillary line, dyspnoea, cough with mucopurulent sputum and feverishness for one day. A year previously she had had a left sided pneumonia and ten years before that another attack of pneumonia but she was uncertain which side had been involved.

Examination:

Toxic, dyspnoeic with alae nasi working, sweating, temperature 103.8 degrees, pulse 160/minute, respirations 64/minute; over the left lower lobe diminished vocal fremitus and resonance, dullness and diminished vesicular breathing with medium resonating crepitations; urine normal; red cells 4.38 million; white cells 24,100 with 90 per cent neutrophils.

Course:

She was started on penicillin 200,000 units and sulphatriad four tablets and then given 100,000 units and two tablets respectively four hourly. Her temperature gradually settled by lysis over 12 days. X-ray showed a left sided pleural effusion with underlying consolidation. On the

third day she was much less toxic and the physical signs were unaltered except that there was now bronchial instead of vesicular breathing. An unsuccessful attempt was made to aspirate the fluid through the 9th interspace posteriorly. The sputum contained many pus cells but only salivary organisms were obtained on culture; three 24 hour specimens were negative for tubercle. The Wassermann reaction was negative.

On the 5th day another attempt at aspiration was made through the 7th interspace in the left posterior axillary line. Only a little bloody material was obtained in the local anaesthetic syringe. This material was treated as a lung biopsy. There were no sequelae. The material was sterile on culture. Histologically there were masses of tissue consisting almost entirely of densely packed polymorphs with possibly a fibrinous matrix; macrophages were scanty. The E.S.R. was 122 m.m. in one hour (Westergren).

Five days later an intentional lung biopsy (44-1) was attempted. The tissues in the 8th interspace below the angle of the left scapula were infiltrated with local anaesthetic but when the needle was inserted deeply to infiltrate the lung pus was obtained. The lung biopsy needle was then inserted and at the depth of about 3 cm. creamy thick pus was readily obtained; 3ml. were removed and 500,000 units of penicillin injected through the needle.

There were no sequelae. The pus was sterile and guinea pig inoculation was negative. The dosage of penicillin was doubled.

She maintained a steady rate of improvement and the physical signs gradually disappeared and the chest was normal by the 36th day. Bronchogram showed well marked cylindrical bronchiectasis with bulbous terminations of the bronchial tree to the posterior basic segment of the left lower lobe with probably some cylindrical dilatation of the bronchial tree to the anterior basal segment of the same lobe.

Discussion:

This patient appeared to be a straight forward lobar pneumonia with a little pleural exudate. Attempted aspiration was negative but the material obtained resembled the wall of a lung abscess and at the subsequent lung biopsy pus was obtained. The underlying pathology was shown to be a bronchiectasis. If the lung biopsy had not been done the diagnosis would have been lobar pneumonia associated with bronchiectasis.

CASE 45 AND 45-1

H.K. COLOURED MALE.18 YEARS. ACUTE LOBAR PNEUMONIA.

History:

Pleuritic pain in right lower chest and left lower chest, cough with white sputum, dyspnoea, feverishness and headache for four days; blood in the sputum one day. On the day before admission he had started taking sulphonamides - four tablets and then two tablets four hourly - and had taken 12 tablets (6.0 gm.) before admission.

Examination:

Toxic, dyspnoeic, alae nasi working, temperature 102.5 degrees, sputum rusty;over the left lower lobe increased vocal fremitus and resonance, relative dullness and bronchial breathing; urine normal; red cells 5.12 million; white cells 20,650 with 84 per cent neutrophils.

Course:

Lung biopsy was performed shortly after admission. The needle was inserted through the 7th interspace just below the angle of the left scapula. There were no sequelae. The biopsy material was sterile; unfortunately the sputum culture was mislaid. The slides showed large masses of fibrin with innumerable well preserved polymorphs; macrophages were scanty and only very occasionally contained a

polymorph; transitional cells were infrequent; no pneumococci were seen. The picture was that of red hepatisation.

He was started on penicillin 200,000 units and sulphatriad four tablets and then penicillin 100,000 units and sulphatriad two tablets four hourly. His temperature fell to normal by crisis and from the second day he remained apyrexial. X-ray showed an area of consolidation involving the left lower lobe with an associated exudate along the greater fissure; also an area of consolidation affecting the posterolateral segment of the right upper lobe with an associated exudate along the horizontal fissure; no pneumothorax.

By the sixth day the patient's general condition was excellent and over the left lower lobe there was diminished movement, increased vocal resonance and bronchial breathing but no crepitations; just below the middle of the right clavicle there was increased vocal resonance. The leucocyte count was 9,100. Lung biopsy 45-1 was repeated on the left side through exactly the same area as before. There were no sequelae and the biopsy material was sterile (the mucoid sputum grew salivary organisms only). The histology showed considerable less fibrin than before and very numerous small macrophages and frequent transitional cells; polymorphs were scanty and mostly well preserved but some showed signs of degeneration; only very infrequently were polymorphs within macrophages. The slides showed advanced

resolution.

The patients signs rapidly disappeared and the chest was clinically normal by the 13th day and radiologically clear after 15 days.

Discussion:

There seemed little doubt clinically that the patient had had a pneumococcal lobar pneumonia. The picture on admission was that of red hepatisation and five days later although the local physical signs were unchanged the pathological picture was that of resolution with numerous small macrophages. Of interest was the sterile biopsy after only 6 gm. of sulphonamide.

CASE 46.

F.S. EUROPEAN MALE. 69 YEARS. BRONCHOPNEUMONIA. LIVER BIOPSY.

History:

Malaise for three months; dyspnoea at rest with boutes of coughing for six weeks.

Examination:

Dyspnoea on the slightest exertion, temperature 100.6 degrees; generalised diminution of chest movement more on the right than left; over the lower part of right chest, both anteriorly and posteriorly, dullness, increased vocal fremitus and resonance and diminished air entry; medium crepitations all over right chest; at left base crepitations only; urine normal; blood normal.

Course:

X-ray done two weeks before admission showed a diffuse opacity of both lung fields especially the right base. A course of aureomycin had caused no improvement and X-ray on admission showed consolidation of the right middle lobe and right base with a small pleural effusion and in addition the left middle and lower zones were more infiltrated. He deteriorated during a course of terramycin but gradually improved when streptomycin was started. The temperature settled and the X-ray showed some resolution. Salivary

organisms were cultured from the sputum.

After being about a month in hospital lung biopsy was attempted. The needle was inserted through the 5th interspace in the right anterior axillary line to a depth of about 3 cm.; when the syringe was attached and suction maintained blood slowly welled into the syringe; the needle was immediately withdrawn. There were no sequelae. The material was sterile. The slides showed many groups of liver cells.

X-ray done the next day showed that the right diaphragm was slightly raised. Gradually resolution occurred and he was finally discharged feeling fit.

Discussion:

The diagnosis of the pulmonary condition was one of some difficulty. A virus pneumonia was most favoured but the lesion showed no responses to the appropriate antibiotics. The response to streptomycin suggested that it might have been an unusual tuberculous manifestation.

Information might have been obtained from the lung biopsy and it was very surprising to find that the material was of hepatic origin. The biopsy had been done quite high up in the chest, the crepitations were maximal in that area, and the needle had not been inserted very deeply. The cause of the "liver biopsy" was probably the slightly

raised right diaphragm together with the horizontal position which was adopted for lung biopsy.

CASE 47.

F.A. COLOURED FEMALE. 31 YEARS. PULMONARY TUBERCULOSIS.

History:

The patient had been in hospital in 1942 with a lung abscess and had left after six weeks symptomless but with the abscess still present radiologically. She was well until 1946 when she coughed up about a pint of blood and from that time onwards she had attended tuberculosis clinics. She had been coughing especially when lying on her right side and her sputum had been yellow or "pink" for four months; feverishness and loss of weight for two months; dyspnoea on exertion for one month; coughing worse when she lay on the left side for three days. She was pregnant.

Examination:

Not toxic, early clubbing of the fingers, apyrexial, no dyspnoea; at the right base diminished vocal fremitus and resonance; dullness at both bases with scattered crepitations and rhonchi; pregnancy of 18-20 weeks; urine normal; red cells 3.1 million; white cells 6,850 with 58 per cent neutrophils, 38 per cent lymphocytes and 4 per cent monocytes; smear normal; E.S.R. 58 m.m. in one hour (Wintrobe).

Course:

X-ray showed the lung fields to be unevenly stippled throughout by a hard fine miliary type of lesion; areas of greater translucency were present in the infraclavicular regions, at the extreme apices and in the anterolateral segment of the right lower lobe; cavities were present in the right apex, right midzone and also in the left midzone (very early). She remained apyrexial. No significant organisms were cultured from the sputum; gastric washings and sputum were negative for tubercle. The Mantoux test (1/1000) was positive. No KP was seen with a slit lamp.

Lung biopsy was performed through the 7th interspace just below the angle of the left scapula. Thickened pleura could be felt. The needle was inserted but only a very little bloody material was obtained and thus the needle was reinserted and this time sufficient material was aspirated. About five minutes after biopsy she coughed up a very small particle of bright blood. X-ray showed no pneumothorax. There was no growth on the blood agar nor in the serum broth but there was a good growth of tubercle bacilli on the Lowenstein medium. Histologically small masses of material were present consisting of fibrinous strands, elastic fibres, fibroblasts, occasional macrophages and alveolar cells and scattered black particles;

polymorphs were scanty. The picture was that of a chronic inflammatory lesion. A careful search of the direct smear showed no tubercle bacilli. The patient left hospital on her own accord before the results of the biopsy cultures could be reported.

Discussion:

The history and the X-ray picture suggested the diagnosis of tuberculosis but the tubercle bacillus was never isolated from the sputum nor from the gastric washings. Finally a very reluctant diagnosis of possibly Boeck's sarcoid was made. The lung biopsy cultures established the diagnosis of tuberculosis.

CASE 48.

J.G. COLOURED MALE. 23 YEARS. ACUTE LOBAR PNEUMONIA.

History:

Pleuritic pain in the region of the left nipple, cough with mucopurulent sputum, sweating and anorexia for four days. He had received both penicillin and sulphonamides before admission. He worked as a bar boy and drank a fair amount.

Examination:

Not toxic, slight dyspnoea, apyrexial; over left upper lobe diminished movement, increased vocal fremitus and resonance, dullness, bronchial breathing and medium crepitations; urine normal; red cells 4.31 million; white cells 24,100 with 90 per cent neutrophils.

Course:

X-ray showed a left upper lobe consolidation. Soon after admission lung biopsy was performed through the second interspace about 5 cm. to the left of the midsternal line. The needle was inserted and material spurted into the syringe. About a minute later he coughed up about three tablespoonfuls of bright red blood; there was neither distress nor pain; the sputum was blood streaked for twelve hours. X-ray showed no pneumothorax. The biopsy material

was sterile and the rusty sputum grew salivary organisms only. The slides showed great masses of fibrin with many well preserved polymorphs; macrophages and transitional cells were not very infrequent but only very occasionally was an ingested polymorph seen; no pneumococci were seen. The picture was that of the very early transition from red hepatisation to resolution - macrophages were present in greater numbers than was usual in red hepatisation.

He was started on penicillin 200,000 units and sulphatriad four tablets and was then given penicillin 100,000 units and sulphatriad two tablets four hourly. On the day of admission his temperature reached 99 degrees but from then onwards he was apyrexial. He made a rapid recovery, the chest being clear clinically after 11 days.

The X-ray showed complete resolution after 14 days but the diaphragm was left adherent laterally obliterating the left costophrenic angle.

Discussion:

It seemed probable that the crisis was induced by chemotherapy before the patient entered hospital and the pathological picture was that of the earliest stage of resolution.

CASE 49 AND 49-1.

P.F. COLOURED MALE, 41 YEARS. BRONCHOPNEUMONIA.

History:

Attacks of allergic asthma for 10 years; two months before admission an X-ray chest had shown only the changes of emphysema. A week prior to admission he had had a severe attack of asthma. This lasted two days and five days later he was admitted for investigation.

Examination:

Not ill or toxic but temperature 102 degrees, pulse 120; chest moved poorly, was emphysematous and occasional rhonchi heard all over; urine normal; red cells 3.11 million; white cells 13,000 with 79 per cent neutrophils, 18 per cent lymphocytes and 3 per cent monocytes; smear normal.

Course:

He was treated with Mist. asthmatica and aminophyllin tablets and X-ray on the third day showed areas of patchy consolidation at the right base. Meanwhile his temperature came to normal and from the sixth day he was apyrexial. From the fourth day crepitations were heard at the right base posteriorly and X-ray on the 7th day showed some clearing.

On the 12th day there were still crepitations as before and lung biopsy was performed through the 7th interspace

just behind the right posterior axillary line. The needle was inserted cautiously and there was a little delay before suction was applied. At first the negative pressure was maintained and then there was a sudden release and air filled the syringe. The needle was withdrawn and contained only a very little material. About five minutes later he complained of a stabbing pain just below the right clavicle but this was not pleuritic nor made worse by movement. The biopsy cultures were sterile and from the mucoid sputum there grew only salivary organisms. X-ray the same day showed a well marked pneumothorax. Histologically material was scanty and consisted of macrophages with one or two nuclei and varying numbers of black particles scattered diffusely through the slide; occasional non-nucleated plates were present; there were very infrequent rounded areas (as if a drop of fluid had dried) containing polymorphs, smear cells, a few squamous cells and innumerable organisms of all types even spirochaetes (see Figures 131 and 132).

By the 28th day the chest was clear clinically and the pneumonic process almost resolved. Seventeen days after the first biopsy a second biopsy was performed (49-1), that is on the 29th day. A little air was still present and the needle was thus inserted up to the hilt (8 cm.) and suction was performed during the withdrawal. A little pinkish material was obtained. There were no sequelae and X-ray taken four

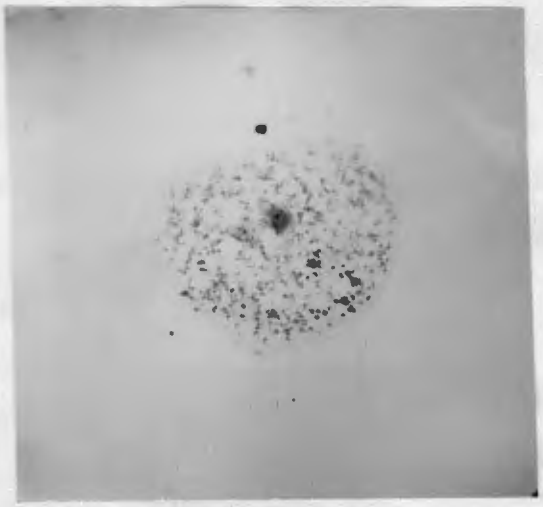


Figure 131. Case 49.

"Drop" of material. Low power to show general appearance.

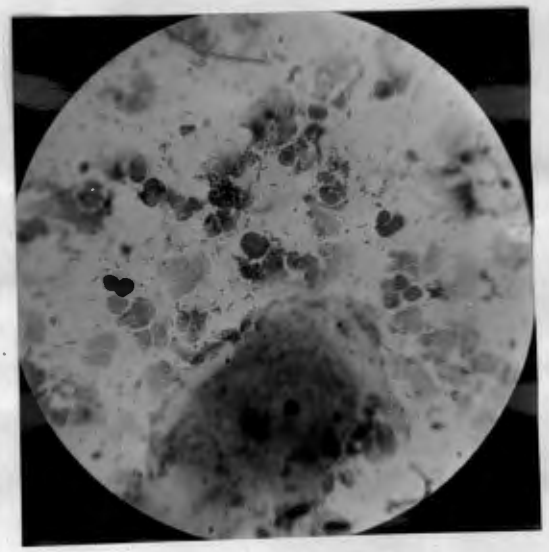


Figure 132. Case 49.

Oil immersion appearance of the same area. Note the polymorphs, pus cells and numerous mixed organisms.

days later showed that the original pneumothorax had been completely reabsorbed. The cultures of this biopsy were mislaid. The slides again showed scattered macrophages with occasional areas of normal appearing parenchyma and interstitial tissue. On the one slide was one "drop" area as before. A bronchogram of the right lower and middle lobes showed no abnormality.

Discussion:

The asthma was probably allergic in nature and the broncho-pneumonia coincidental. The absence of eosinophils on the biopsy slides made an allergic pneumonia (Loeffler type) unlikely. The peculiar collections of organisms and cells had the appearance of being unrelated to the biopsy material

and these areas were probably artefacts possibly present on the slide before the biopsy. The pneumothorax occurred whilst the needle was still in the lung.

CASE 50.

A.K. COLOURED MALE. 42 YEARS. ACUTE LOBAR PNEUMONIA.

History:

Malaise with generalised body pains and a feeling of coldness for three days; rusty sputum and cough for two days.

Examination:

Toxic, slight dyspnoea, temperature 100.5 degrees; over the left lower lobe diminished movement, relative dullness, diminished vocal fremitus and resonance, bronchial breathing and a few fine and medium crepitations; urine normal; red cells 4.34 million; white cells 22,760 with 89 per cent neutrophils.

Course:

X-ray showed an area of consolidation involving the left lower lobe and also consolidation of one of the lateral segments of the right upper lobe. Lung biopsy was performed soon after admission. The needle was inserted through the 8th interspace about 2 cm. behind the left posterior axillary line; the stylette was removed, suction applied and a little opalescent fluid and air entered the syringe. It was obvious that the needle point was in the pleural cavity and the needle was withdrawn. The needle was then reinserted very deeply and this time a little brownish

fluid was obtained. X-ray showed a considerable pneumothorax although there was no pain (see Figure 133).

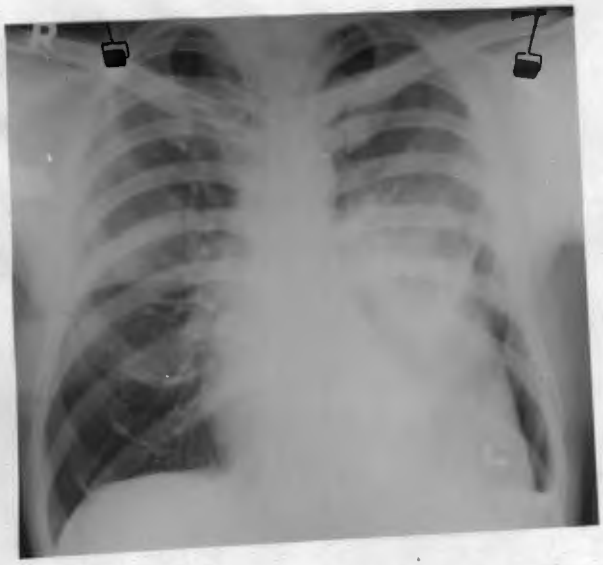


Figure 133. Case 50.

X-ray Chest. PA.
(The day after lung biopsy).

Pneumococci were cultured from both the biopsy material and the sputum but the fluid obtained from the pleural cavity was sterile. The slides showed large quantities of fibrin with many well preserved polymorphs; macrophages and transitional cells were scanty and only occasionally was an ingested polymorph seen. Pneumococci were fairly frequent and only occasionally within polymorphs. The pathological picture was that of red hepatisation.

He was given penicillin 100,000 units four hourly and sulphatriad four tablets and then two tablets four hourly. His temperature rose that evening to 104.8 degrees but the next day fell to normal by crisis and from the 5th day he

remained apyrexial. The general condition of the patient rapidly improved but the X-ray showed that there was a small pleural effusion. The physical signs and the X-ray signs gradually began to return to normal and on the 15th day the only abnormal feature was diminished air entry at the left base and the X-ray showed that much of the fluid had been absorbed.

On the 30th day he developed a phlebothrombosis of the veins of the right calf and this gradually subsided over the next three weeks. By the 43rd day the X-ray showed only slight pleural thickening over the middle and lower parts of the left lung and some obliteration of the left costo-phrenic angle. His Wassermann was negative.

Discussion:

The patient presented as a classical lobar pneumonia with a small effusion - of great interest was that the effusion was sterile although pneumococci were isolated from the underlying lung. The duration of the X-ray signs was probably related to the pneumothorax and the accumulation of more fluid and it was felt that this patient did not really fall into the chronic group. Phlebothrombosis was said to occur in about 1 per cent of convalescent pneumococcal pneumonia patients (Reimann, 1938).

CASE 51.

F.K. NATIVE FEMALE. 23 YEARS. ACUTE LOBAR PNEUMONIA.

History:

Cough with yellow-white sputum and pleuritic pain in the right upper chest anteriorly for eight days.

Examination:

Toxic, dyspnoeic, alae nasi moving, temperature 103.5 degrees, sputum muco-purulent; over the right upper lobe diminished movement, increased vocal fremitus and resonance, relative dullness and bronchial breathing; urine normal; red cells 3.7 million; white cells 29,000 with 93% neutrophils.

Course:

She was started on penicillin 200,000 units and sulphatriad four tablets and was then treated with penicillin 100,000 units and sulphatriad two tablets four hourly. Her temperature fell by crisis and from [redacted] the third day she was apyrexial. Sputum culture after one day of chemotherapy grew salivary organisms only. After two days the sputum was mucoid and her general condition was much improved; the physical signs were as before except that there were now in addition numerous medium crepitations. Lung biopsy was performed through the second interspace about 5cm. to the right of the midsternal line. Two minutes afterwards there was a very slight trace of blood in the sputum.

The biopsy cultures were sterile and the sputum grew salivary organisms only. Histologically fibrin was present in small amounts; Numerous small macrophages and fairly frequent transitional cells were present; polymorphs were scanty, some well and others poorly preserved and very occasionally a polymorph was seen within a macrophage. The pathology was that of advanced resolution. X-ray showed a right upper lobe consolidation and no pneumothorax. Resolution proceeded rapidly and after 14 days there were no abnormal physical signs and the chest was clear radiologically. Her Wassermann reaction was negative.

Discussion:

This patient was admitted with the signs of a pneumococcal lobar pneumonia. The histological picture after two days of chemotherapy showed numerous macrophages.

CASE 52.

S.I. MOSLEM MALE. 12 YEARS. RHEUMATIC PNEUMONIA.

History:

Two months before admission he had been kept in bed for three weeks with a febrile illness characterised by joint pains. He then went back to school but for a week before admission he had felt malaise, praecordial pain, palpitations and dyspnoea on exertion.

Examination:

Ill, early clubbing of the fingers, pulse 120/minute, temperature 99 degrees, cardiomegaly with the murmurs of mitral stenosis; no signs of cardiac failure, but his face was slightly oedematous; urine normal; red cells 2.75 million and smear slightly hypochromic; white cells 13,400 with normal differential count; E.S.R. 47.8 m.m. in one hour (Wintrobe).

Course:

The urine soon after admission showed a slight albuminuria. He seemed to do quite well on salicylates until the middle of the second week when the swelling of the face became more marked, a profusion of epithelial casts and a few red cells appeared in the urine, signs of congestive failure appeared and X-ray showed

a patch of consolidation in the right upper lobe. Within 24 hours consolidation had involved the whole of the right upper lobe and a small haemoptysis occurred. Culture of the sputum showed no pneumococci and the temperature never rose above 99.5 degrees. The child was extremely ill and was started on penicillin, digitalis and mersalyl. Four days later he experienced an attack of acute pulmonary oedema and almost died. Eight days after the onset of the consolidation the physical signs were diminished movement, increased vocal fremitus and resonance, relative dullness, and bronchial breathing over the right upper lobe. There was no sputum. Lung biopsy was done through the second interspace about 4cm. to the right of the midsternal line. When the plunger of the syringe was withdrawn air bubbled into the syringe and thus the needle was withdrawn about 2cm. with the suction maintained (instead of being inserted). There was a very slight haemoptysis which was plated out. The biopsy material was sterile and the sputum grew salivary organisms only. Histologically there were large masses of fibrin with numerous enmeshed red cells and a few small macrophages and alveolar cells with occasional polymorphs. The picture was that of much fibrin with a very poor cell response.

X-ray showed no pneumothorax. Three days after biopsy crepitations were heard over the right upper lobe but clinical

resolution was not complete for a further two weeks. By this time the urine had returned to normal (the blood urea was never raised) and the murmurs of aortic regurgitation became audible. X-ray showed complete resolution forty days after the onset of the consolidation. His Wassermann reaction and a blood culture were both negative.

Discussion:

It would seem reasonable to assume that the patient had had acute rheumatic fever. The pulmonary lesion did not behave like a pneumococcal lobar pneumonia and the histology did not appear like that of normal resolution. The biopsy findings were compatible with the diagnosis of rheumatic pneumonia.

CASE 53 AND 53 - 1.

D.J. COLOURED MALE. 32 YEARS. CHRONIC LOBAR PNEUMONIA.

History:

The patient was a thoroughly unreliable witness. For one day he had had a pleuritic pain in the right lower chest antero-laterally and a cough with a little mucoid sputum. He worked as a labourer loading oil drums and mealie sacks, and had never been ill before; his diet was adequate.

Examination:

Toxic, sweating, dyspnoeic with alae nasi working, pulse 130/minute, temperature 103.6 degrees; over the right middle and lower lobes diminished movement, relative dullness, increased vocal fremitus and resonance, bronchial breathing and coarse crepitations; urine trace of albumin, one plus urobilin, occasional granular and hyaline casts; white cells 17,000 with 89% polymorphs.

Course:

He was started on penicillin 500,000 units and sulphatriad four tablets and was then given penicillin 100,000 units and sulphatriad two tablets four hourly. His temperature fell by crisis but for 12 days it remained at a lower level varying from

normal to 100 or 101 degrees. X-ray showed consolidation of the right middle and lower lobes.

On the third hospital day his sputum showed rusty areas and he was still toxic with physical signs little changed except that bronchial breathing was no longer heard (his total leucocyte count at this time was 22,500). Lung biopsy was done through the 8th interspace just lateral to the angle of the right scapula. The pleuritic pain was relieved but his sputum was blood streaked for about 10 hours afterwards. X-ray showed no pneumothorax. The biopsy cultures were sterile and the sputum grew mixed organisms and beta-haemolytic streptococci. The slides showed large masses of fibrin with fairly numerous well preserved polymorphs (but not quite as many as was usually seen) and scanty macrophages and transitional cells. The picture was that of red hepatisation with a rather poor polymorph response.

The day after biopsy he began to improve and four days later he was much better but the physical signs were unaltered. Lung biopsy (63-1) was performed through the same area as before; the needle was inserted, the syringe attached and suction applied; blood welled up into the syringe and the needle was withdrawn. No pneumothorax was present on the subsequent X-ray. The mucoid sputum grew the same organisms as before and the biopsy material was sterile. The histology

showed large masses of fibrin with few or no polymorphs and no macrophages were seen. It was felt that this picture might be due to blood without any pulmonary tissue. If this was a true biopsy then there was fibrin with a very poor cell response. A drop of blood was taken from the patient's finger, allowed to stand for somewhat longer than the biopsy material remained on the slide before smearing, and then crushed and smeared as a biopsy; no fibrin was seen. Thus possibly the fibrin seen on the biopsy smears did really come from the lung.

After two weeks in hospital the physical signs were unchanged but by the end of the third week there was no dullness and crepitations were few in number. By the 24th day the chest was clear clinically but X-ray resolution was not complete until the 65th day (there was a little residual pleural thickening in the costo-phrenic angle). The patient was sensitive to iodine and no bronchogram could be done. His Wassermann reaction was negative. Somatype rating: 3.5 1/2 .2. that is an endomesomorph.

Discussion:

It was probable that the patient was a pneumococcal lobar pneumonia with slow resolution. The biopsy histology suggested that there was a considerable delay in the macrophage response but it was uncertain if the material from the second biopsy was truly pulmonary in origin. Beta-haemolytic streptococci were twice isolated from the sputum but were not obtained from the biopsy cultures making it very unlikely that they were the causative organisms. There seemed no obvious cause for the prolonged course.

CASE 54.

A.P. COLOURED MALE. 20 YEARS. ACUTE LOBAR PNEUMONIA.

History:

Pleuritic pain in the right lower chest, cough with blood stained sputum, dyspnoea, feverishness, sweating, and nausea with anorexia for four days. He had been taking sulphadiazine for three days before admission (36 tablets in all). About four years previously he had had "bronchitis" lasting 4-5 days and had experienced a similar pain in the right chest. He smoked about 20 cigarettes a day and his work was to clean the gold dust machine in a printing works.

Examination:

Toxic, sweating, dyspnoeic, alae nasi working, sputum stained with fresh blood, pulse 132/minute, temperature 102.8 degrees; over the right lower lobe diminished movement, increased vocal fremitus and resonance and bronchial breathing; urine albumin a trace and urobilin one plus, few granular casts; red cells 4.44 million; white cells 26,500 with 91% neutrophils.

Course:

He was given penicillin 400,000 units and then penicillin 200,000 units and sulphatriad two tablets four hourly. His temperature fell by crisis and from the sixth day he was

apyrexial. The sputum grew salivary organisms and beta-haemolytic streptococci. X-ray showed consolidation of the right middle and lower zones. On his third day in hospital the sputum was mucopurulent with small rusty areas; his general condition was much improved; the physical signs were unaltered except that there were now in addition a few fine crepitations. Lung biopsy was performed through the 8th interspace about 3cm. behind the right posterior axillary line. There were no sequelae and X-ray showed some resolution but no pneumothorax. The biopsy cultures were sterile and the sputum grew mixed organisms including beta-haemolytic streptococci. The slides showed much fibrin with many well preserved polymorphs but there were also many small macrophages and transitional cells; not infrequently phagocytosed polymorphs in macrophages were seen. The picture was that of early resolution.

Resolution was rapid and the chest was clear clinically by the 12th day and X-ray resolution was complete after 22 days. The somatype rating was 1.7.2. that is a mesomorph.

Discussion:

This was a straight forward case of acute lobar pneumonia with normal resolution.

CASE 55.

R.LE R. COLOURED FEMALE. 26 YEARS. ACUTE LOBAR PNEUMONIA.

History:

Pleuritic pain in the left hypochondrium, for four days; shortness of breath, feverishness, cough with white mucoid sputum for two days. She had had chest trouble since childhood and every year for about two weeks she experienced an attack of coughing and about half a cup of yellowish sputum would be produced daily. The attacks occurred during the winter. She had had two attacks of pleuritic pain in the left side twelve and five years previously; she had to go to bed during these attacks.

Examination:

Toxic, dyspnoeic, alae nasi working, pulse 128/minute, temperature 103.2 degrees; just to the right of the sternum anteriorly fine resonating crepitations; over left lower lobe diminished movement, increased vocal fremitus and resonance, bronchial breathing and medium crepitations, and at the extreme base stony dullness; urine normal; red cells 3.53 million; white cells 20,000 with 89% neutrophils.

Course:

She was given penicillin 400,000 units and sulphatriad four tablets and then penicillin 200,000 units and sulphatriad two

tablets four hourly. Her temperature fell by crisis to normal the next day but she ran occasional peaks of 99 degrees for 17 days. X-ray showed consolidation of the left posterior basal segment with some associated pleural fluid and the right lung was clear. After four days the signs were unaltered except that the breath sounds were no longer bronchial in type. Lung biopsy was done through the 8th interspace just below the angle of the left scapula. A few minutes after biopsy she coughed up a little blood streaked sputum. The X-ray showed no pneumothorax. The biopsy cultures were sterile and the sputum grew mixed organisms. Histologically there were small areas of fibrin but on the whole cells were scanty; small macrophages were the predominant cells although some dust cells were present; black particles were scattered in many areas. The picture was that of advanced resolution.

Gradually resolution progressed and after 16 days the chest was clear clinically and there was X-ray resolution after 31 days except for a little left basal pleural thickening. Bronchogram of the left lower lobe and lingula showed no abnormality. Her Wassermann was positive. The somatype rating was 1 . 4 . 5. that is a mesoectomorph.

Discussion:

This patient ran a slightly longer course than usual but was

still included in the group of acute pneumonia with normal resolution. She certainly had a long standing history of chest trouble which suggested an underlying bronchiectasis but this was not confirmed by the bronchogram.

CASE 56 AND 56-1.

S.P. COLOURED MALE. 14 YEARS. ACUTE LOBAR PNEUMONIA.

History:

The patient was mentally deficient and gave a completely unreliable history. He complained of pleuritic pain in the region of the right nipple, cough with a little sputum and a watery diarrhoea for two weeks.

Examination:

Toxic, dyspnoeic with alae nasi working, temperature 103 degrees; over the right upper lobe diminished movement, increased vocal fremitus and resonance, relative dullness and loud bronchial breathing; urine trace of albumin; red cells 4.36 million; white cells 18,950 with 95% polymorphs.

Course:

He was started on penicillin 400,000 units and sulphatriad four tablets and then received penicillin 200,000 units and sulphatriad two tablets four hourly. Lung biopsy was performed the day after admission (he had received 800,000 units of penicillin and four tablets of sulphatriad - there had been some delay in two doses of the latter). The needle was inserted through the second interspace about 3cm. to the right of the right sternal border. On removing the stylette blood

welled out of the needle; the syringe was attached and suction applied and the needle withdrawn instead of being advanced. There was a slight haemoptysis and the sputum was slightly bloody for about two hours. The physical signs were exactly the same as on admission but his temperature had come down by crisis to 99 degrees. The biopsy material was sterile and the sputum grew mixed organisms. Histologically there were large masses of fibrin with numerous well preserved polymorphs; small macrophages and transitional cells were not infrequent and occasional polymorphs were seen within macrophages; no pneumococci were seen. The picture was that of late red hepatisation.

X-ray showed consolidation in the right upper and middle lobes and no pneumothorax was present. From the sixth day he was apyrexial. After five days the physical signs were unchanged except that there were in addition fine crepitations in the region of the right nipple. The sputum was mucoid. Lung biopsy (56-1) was performed through the same area as before and was followed by a haemoptysis of about a tablespoonful of blood and the sputum was blood stained for an hour. The cultures were sterile and the sputum grew coliform organisms. The slides showed large masses of fibrin which in some areas appeared to be slightly granular; small macrophages were very numerous and transitional cells frequent; polymorphs were scanty and in varying stages of degeneration and were occasionally seen within

macrophages. The slides showed fairly advanced resolution. X-ray showed a fair amount of resolution and no pneumothorax.

Resolution proceeded normally and the chest was clear clinically after eight days. X-ray resolution was complete after 14 days. Somatype rating was 2 . 6 . 2 . , that is a mesomorph.

Discussion:

The patient had a lobar pneumonia which ran a normal course. The biopsies showed the progress from polymorphs to macrophages over four days.

CASE 57 AND 57-1.

S.M. NATIVE MALE. 29 YEARS. ACUTE LOBAR PNEUMONIA.

History:

Malaise, cold shivvers and feverishness for four days; pleuritic pain in the left lower chest laterally and cough with a little sputum for two days. He had taken four tablets of sulphonamide on the morning of admission.

Examination:

Toxic, dyspnoeic, alae nasi working, temperature 102 degrees, sputum mucopurulent; over the left lower lobe diminished movement, relative dullness, increased vocal fremitus and resonance, bronchial breathing and a few medium crepitations; urine contained two plus urobilin; red cells 4.3 million; white cells 24,450 with 95% neutrophils.

Course:

Lung biopsy was performed soon after admission (about six hours after the four tablets of sulphonamide) and the needle was inserted through the 8th interspace below the angle of the left scapula. A small amount of thick 'mucoid' material was obtained and the biopsy was followed by a small haemoptysis. The pleuritic pain was abolished by the infiltration of the local anaesthetic. Pneumococci were cultured from

both the biopsy material and the sputum. X-ray showed consolidation in the left mid and lower zones and also an area in the right basal region; no pneumothorax. The slides showed large masses of fibrin with very numerous well preserved polymorphs; transitional cells were not infrequent but small macrophages were scanty and only very occasionally contained a polymorph; a fair number of dust cells were present; pneumococci were fairly frequent. The slides showed red hepatisation.

He was started on penicillin 200,000 units and sulpha-triad four tablets and then 100,000 units and two tablets respectively were given four hourly. The temperature fell by crisis to normal the next day and from the fourth day he remained apyrexial. On the day after admission the sputum became rusty.

After three days the physical signs were slight dullness, increased vocal fremitus and resonance, vesicular breathing and occasional medium crepitations; the sputum was muco-purulent. Lung biopsy (57-1) was performed through the same site as before and was followed by two tablespoonfuls of bloody mucoid sputum and blood staining continued for an hour. X-ray showed some resolution and no pneumothorax. The cultures were sterile and the sputum grew salivary organisms only. The histology showed a fair amount of

fibrin with numerous small macrophages and a fair number of transitional cells; scanty well preserved polymorphs were seen. The slides showed advanced resolution.

Clinical resolution was complete after 13 days and complete radiological resolution after 30 days (but there was a period of three weeks between the X-ray after the last biopsy and the check X-ray so that probably radiological resolution was completed earlier than is stated here). His Wassermann test was positive. Somatype 1 . 7 . 2 . , that is a mesomorph.

Discussion:

This patient had a pneumococcal lobar pneumonia and it was of interest to see the change from the polymorphs to macrophages over three days.

CASE 58, 58-1 AND 58-2.

S.P. COLOURED MALE. 47 YEARS. CHRONIC LOBAR PNEUMONIA.

History:

Pleuritic pain in right lower chest, dyspnoea, feverishness and sweating for six days; dry cough for four days; delirious for two days. In 1940 he had had "bronchitis" and "coughed a lot". He had worked as a painter and a farm labourer. For years he had been in the habit of drinking eight tots of brandy and three bottles of beer daily.

Examination:

Thin but not malnourished; temperature 99.5 degrees; over right lower lobe dullness and bronchial breathing; urine normal; no blood counts were done.

Course:

X-ray showed consolidation of the right middle and lower lobes. He was given penicillin 500,000 units twice daily and sulphatriad four tablets and then two tablets four hourly. His general condition improved but he ran an intermittent pyrexia up to 99-100 degrees for over a month. Two weeks after admission the physical signs were unchanged and the patient felt perfectly fit but X-ray showed no change in the consolidation and in addition there was now a small pleural effusion.

Lung biopsy was attempted three weeks after admission. The needle was inserted through the 8th interspace below the angle of the right scapula. There were no sequelae. The biopsy cultures were sterile and the mucoid sputum grew salivary organisms only. The slides showed mainly groups of liver cells. Two days later crepitations were heard in addition to the bronchial breathing and another lung biopsy (58-1) was attempted. The needle was inserted in the 7th interspace just above the site of the previous biopsy. During the local infiltration pleural fluid had been aspirated, and thus the biopsy needle was inserted deeply, suction applied and the neddle withdrawn rather than advanced; but some pleural fluid entered the syringe and the slides prepared showed so few cells as to be absolutely useless. The fluid was a sterile exudate containing polymorphs and lymphocytes and the biopsy material was also sterile. There was no pneumothorax. The patient remained in status quo but on two separate occasions 240 c.c. and 45 c.c. of sterile exudate were aspirated.

Forty-two days after admission the physical signs were dullness with increased vocal fremitus and resonance (except at the extreme base where they were diminished), diminished air entry and bronchial breathing loudest just below and lateral to the angle of the right scapula. Lung biopsy (58-2) was performed through the 7th interspace just below and

lateral to the angle of the right scapula. There were no sequelae. No sputum was being produced. The biopsy material was sterile. Slides showed small areas of fibrin with fairly numerous small macrophages and transitional cells; some of the macrophages were of the large "chronic" type; polymorphs were present in proportion to the blood present. The slides showed very advanced resolution.

A week later crepitations were again heard. Two weeks after this the physical signs were unaltered. The patient was given 10 c.c. of Calgluquine intravenously daily for seven days. During this course the physical signs rapidly diminished so that by the end of the week the chest was normal clinically. X-ray showed complete resolution. The previous X-ray taken three weeks before had shown little alteration. The whole process had taken 70 days from the time of admission. His Wassermann reaction was negative. Somatype rating 2 . 4 . 4 ., that is a mesoectomorph.

Discussion:

Unfortunately the notes of the condition of this case on admission were very incomplete. However the history and physical signs suggested that he had been a case of pneumococcal lobar pneumonia. The biopsy of liver was a great surprise as it was felt that the needle was inserted at quite a reasonable level and into the area of maximal physical signs. The final biopsy showed the expected macrophage response. The

importance of this case was the apparent dramatic response to Galgluquine.

There seemed little reason for the chronic course except the old attack of bronchitis and the excessive consumption of alcohol.

CASE 59 AND 59-1.

D.A. COLOURED MALE. 58 YEARS. CHRONIC STAPHYLOCOCCAL PNEUMONIA.

History:

Sticking pain starting in the region of the right nipple and radiating round to the epigastrium (worse on deep breathing but not on coughing) and cough with white sputum for two months; dyspnoea on exertion for six weeks. He had always lived in Cape Town except for a short visit to Durban in 1914.

Examination:

Thin and showed signs of loss of weight; early clubbing of the fingers; temperature 99.8 degrees, pulse 90/minute, blood pressure 185/112 m.m. Hg.; no dyspnoea but signs of fluid in the right side of the chest from the sixth rib downwards and a friction rub heard in the third space anteriorly; urine one plus urobilin; red cells 3.68 million; white cells 7,850 with neutrophils 62%, lymphocytes 33%, monocytes 3% and eosinophils 2%; E.S.R. 36 m.m. in one hour (Wintrobe).

Course:

X-ray of the chest showed a fairly large right sided pleural effusion which had partially collapsed the middle and lower lobes. The fluid was aspirated and proved to be a bloody

sterile exudate and guinea pig inoculation was negative. In all, three aspirations were done. He continued to run a temperature from 99-102 degrees. About two weeks after admission he was given penicillin (100,000 units four hourly) but the pyrexia showed no response. About this time X-ray showed diminution of the effusion but there was increased atelectasis of the upper zone and the heart was drawn a little to the right. Bronchoscopy showed no abnormality and on thoracoscopy the pleural space was seen to be traversed by a forest of fibrinous strands typically non-malignant and resembling a tuberculous pleurisy. After a month he was given streptomycin (0.5 gm. twice daily) and this was continued for 41 days without any alteration in the pyrexia. A fresh sputum had grown salivary organisms only and three 24 hour specimens and two gastric washings had shown no tubercle bacilli. A warm stool grew no pathogens and no amoebae were seen. Biopsy of a small axillary lymph gland revealed reactive changes only. After two months X-ray of the chest showed partial atelectasis of the right lung with collapse of the middle lobe, thickened costo-phrenic pleura and only a small amount of fluid.

Two and a half months after admission the patient was in status quo - still pyrexial, the trachea and heart over to the right, and dullness, diminished vocal fremitus and resonance and very poor air entry over the right lower lobe.

Lung biopsy was performed through the 7th interspace in line with the angle of the right scapula. During the infiltration thickened pleura was felt and a small amount of heavily blood stained effusion was aspirated into the local anaesthetic syringe. There were no sequelae to the biopsy. The mucopurulent sputum grew mixed organisms only but from both the blood agar and serum broth biopsy cultures there was a good growth of coagulase positive staphylococcus aureus (Micrococcus pyogenes aureus) sensitive to penicillin and streptomycin. Histologically there were large masses of fibrin with rather scanty cells which were mainly 3-4 lobed polymorphs, dust cells and occasional small macrophages; the striking feature was small sheets of cells with a very large nucleus (with up to three nucleoli) and showing a fair amount of pleomorphism - these cell groups were sometimes enmeshed in the fibrin; no organisms were seen.

During the whole of the fourth month and half of the fifth month in hospital he received courses of penicillin, streptomycin and aureomycin with no response, his temperature remaining as before. A blood count during the fourth month showed a leucocytosis of 15,300 with a normal differential count except that there were 14% eosinophils; the E.S.R. was 58 m.m. in one hour (Wintrobe). Lung biopsy (59-1) was repeated after he had been in hospital three and a half months (that is in the middle of the fourth month and one month after the first biopsy).

The site was the same and again bloody fluid was aspirated into the local anaesthetic syringe. Thickened pleura was felt and there were no sequelae. The sputum grew mixed salivary organisms with scanty colonies of staphylococcus aureus. The biopsy cultures again grew staphylococcus aureus which was still sensitive to streptomycin but insensitive to penicillin. Histologically there was less material present and although there was fibrin, in addition there were denser areas where cells resembling fibroblasts were not infrequently associated with the fibrin; otherwise the picture was unaltered although the groups of pleomorphic cells were not as numerous as in the previous biopsy; extremely scanty single Gram positive cocci were seen.

A bronchogram confirmed the partial collapse of the right middle and lower lobes and no broncho-stenotic cause was revealed. X-rays showed no change after five months. After no response to penicillin inhalations he was discharged to a home for the chronic sick.

Discussion:

This was an extremely difficult case to interpret clinically. The lung biopsy showed fibrin associated with a pure culture of staphylococcus aureus and it would be fair to assume that the patient had a chronic staphylococcal pneumonia. The next biopsy showed the same picture again but the fibroblasts suggested that fibrosis was progressing and again a staphylo-

coccus aureus was cultured. One must assume that there were many areas of fibrosis surrounding the organisms so that antibiotics could not penetrate in sufficient concentrations to be effective. The peculiar groups of cells from the biopsies were difficult to interpret. They might have been tumour cells but the patient was not clinically a widespread pulmonary carcinoma and there were the persistent positive cultures of staphylococci. It seemed most likely that these were alveolar cells which had undergone metaplasia in response to the chronic inflammatory process.

Gibson and Belcher (1951) in a very useful paper on staphylococcal pneumonia stated that the bacteriological criterion for the diagnosis was a pure or almost pure culture from the sputum of lung puncture.

CASE 60 AND 60-1.

P.H. COLOURED MALE. 21 YEARS. ACUTE LOBAR PNEUMONIA.

History:

Pleuritic pain in the left lower chest laterally with cough and a little blood stained sputum for four days. He had taken six tablets of sulphonamide (two tablets four hourly) before admission. He was in the habit of being drunk nightly and smoked 20 cigarettes a day.

Examination:

Not toxic, dyspnoeic, movement of alae nasi slight, temperature 103 degrees, sputum rusty, over left lower lobe diminished movement, diminished vocal fremitus and resonance, relative dullness, bronchial breathing with a few fine crepitations; urine urobilin three plus; red cells 4.3 million; white cells 15,500 with 95 per cent neutrophils.

Course:

Soon after admission lung biopsy was performed through the 7th interspace just below the angle of the left scapula. There were no sequelae. The biopsy cultures were sterile and the sputum grew salivary organisms only. Histologically a fair amount of fibrin was present with frequent well preserved polymorphs; macrophages were not infrequent and only occasional ingested polymorphs seen; transitional

cells present in fair numbers; no pneumococci seen. The picture was that of late red hepatisation.

He was started on penicillin 200,000 units and sulphatriad four tablets and was then given penicillin 100,000 units and sulphatriad two tablets four hourly. X-ray showed consolidation of the left mid and lower zones with probably a small associated effusion. His temperature fell to normal by crisis on the second day and he then remained apyrexial. After three days the sputum was mucoid; physical signs were increased vocal fremitus and resonance, no dullness, and diminished vesicular breathing. Lung biopsy (60-1) was repeated through the same site as before and there were no sequelae. There was no growth in the biopsy cultures and the sputum grew salivary organisms only. The slides showed fibrin to be present but tending to become granular; macrophages numerous and transitional cells frequent; polymorphs were not infrequent some well preserved and others degenerate; occasionally polymorphs were seen within macrophages. The pathology was that of fairly advanced resolution.

Clinical resolution was complete after nine days and X-ray after four days had shown marked resolution. He left hospital on his own accord before a final X-ray could be taken. Resolution was proceeding so rapidly that it was felt justifiable to include the case in the acute

group with normal resolution.

Discussion:

This patient showed the clinical picture of a lobar pneumonia. The negative cultures after twelve hours of sulphonamide were of interest.

CASE 61.

D.M. COLOURED FEMALE, 28 YEARS. NORMAL LUNG.

History:

Sudden onset of aphasia and a right sided hemiplegia four hours before admission.

Examination:

Drowsy, no neck rigidity, motor aphasia, right sided hemiplegia; loud systolic murmur at apex with accentuated second pulmonic sound; urine and blood normal.

Course:

The cerebro-spinal fluid was blood stained and xanthochromic. She gradually improved, power and speech slowly returning. Three blood cultures were negative but an Osler's node appeared on the left thumb. She was given penicillin because of an intermittent temperature and then, when there was no response, streptomycin. She complained of intermittent headaches. After about two months in hospital she suddenly became comatose with neck rigidity and the C.S.F. was heavily blood stained. She died a few hours later. The chest had been normal both clinically and on X-ray.

Lung biopsy was done through the second interspace about 5 cm. to the right of the midsternal line (about one

hour after death). The slides showed much blood, macrophages of all types, alveolar cells, ciliated bronchial epithelial cells and pleural cells. Many mixed organisms were present on the Gram stained slide but these were probably postmortem invaders.

Autopsy:

Incompetent mitral valve with healed vegetations of subacute bacterial endocarditis; old infarcted areas in kidneys and spleen; an aneurysm with surrounding old haemorrhage in the left cerebral cortex; large recent haemorrhage almost replacing the right frontal and parietal areas. A section from the lung where the biopsy was performed showed some emphysema and marked oedema.

Discussion:

The patient probably had a rheumatic heart with subacute bacterial endocarditis. She died from haemorrhage in the brain from either mycotic or coincidental congenital aneurysms. The lung biopsy showed a fair number of small macrophages but not nearly as numerous as was usual in a resolving pneumonia.

CASE 62 AND 62-1.

J.M. NATIVE MALE. 29 YEARS. AMOEBIC ABSCESS OF THE LUNG.

History:

The patient sustained a blow on the right side of the chest with a chain two months before admission and had had slight pain in this region ever since. For a month he had had a mild diarrhoea with yellow watery stools three or four times a day and once or twice at night. For a week there had been an acute episode with severe pain in the right chest, dyspnoea and sputum which was first purulent and then bloody. He lived at the native township of Langa (just outside Cape Town).

Examination:

Not toxic, slight dyspnoea with slight movement of alae nasi, temperature 100.4 degrees; over the right chest posteriorly from about the 5th rib downwards there was dullness with increased vocal resonance and grossly diminished air entry but no bronchial breathing nor crepitations; liver just palpable, normal in consistency but tender; urine one plus urobilin; red cells 4.5 million; white cells 14,450 with 80 per cent neutrophils.

Course:

X-ray showed a postero-lateral shadow with a rounded upper

border in the right costo-phrenic angle. No chemotherapy was given. The day after admission the patient's condition was unchanged and lung biopsy was attempted through the 7th interspace just lateral to the angle of the right scapula. The needle was inserted to the depth of about 6 cm., the syringe attached and suction applied; dark red thick material oozed into the syringe and the needle was withdrawn. There were no sequelae. Examination of the fresh material showed numerous pus cells, red cells and necrotic material; there were a fair number of long thin greenish crystals which were identified as most likely haemochromogen (as the result of the breakdown of blood); no amoebae were seen. The histology of the slides was similar but no organisms were seen. All the biopsy cultures were sterile. The sputum which was copious, brownish-red and thick grew mixed salivary organisms.

In spite of full doses of penicillin and sulphatriad (100,000 units and two tablets four hourly) the physical signs remained the same (except for the addition of a few medium crepitations) and his temperature continued between 99 and 103 degrees; his sputum persistently contained much dark red altered blood. The neutrophil leucocytosis persisted. After five days the penicillin dosage was doubled without any improvement except that the sputum became rather darker brown in colour. A sigmoidoscopy showed 30 cm. of normal bowel. After 12 days chemotherapy was stopped but his temperature continued

up to 101 degrees. Three days after stopping penicillin, emetine (1gr. nightly for ten nights) was started and after the third injection he became apyrexial and from then onwards his temperature remained normal. After the seventh injection the physical signs were only dullness and diminished air entry and aspiration of the pulmonary mass was attempted. A 15 cm. lung biopsy needle was used; this was attached to the syringe and then inserted into the same area as before; aspiration was attempted at different depths during the insertion; after going in for 8-9 cm. only a small amount of bloody material was obtained. After the biopsy he complained of a slight pain in the right upper chest anteriorly. X-ray showed a fair sized pneumothorax but the opacity showed little change. The biopsy cultures were sterile and the sputum grew salivary organisms only. Histologically material was scanty and showed dust cells, alveolar cells and occasional alveolar histiocytes. The cells were not abnormal and the pulmogram could well have been that of a normal lung. It was obvious that the mass had not been entered.

After the course of emetine he was given a course of stovarsol and then a course of E.B.I. About two weeks after the cessation of the emetine hydrochloride the chest was clear clinically and the lesion at the right base had considerably diminished in size. He was discharged fit about a week later.

Discussion:

There was little doubt that the rounded mass in the right lung was aspirated during the first biopsy. The material was sterile pus. Tuberculosis was excluded by the direct smear and cultures and also the sputum did not contain tubercle bacilli and in addition there was the apparent response to emetine therapy. An infected haematoma (from the original trauma) should not have been sterile. A resolving haematoma should not have suddenly given the clinical picture of an acute pulmonary condition eight weeks after the original trauma. He had slight diarrhoea, a tender liver, a persistent neutrophil leucocytosis and pyrexia and showed no response to penicillin or sulphatriad but appeared to respond rapidly to emetine. In addition the mass contained sterile pus with products of blood breakdown. The most likely diagnosis seemed to be that of amoebic abscess of the lung.

CASE 63.

B.M'K. NATIVE MALE. 52 YEARS. **CHRONIC LOBAR PNEUMONIA.**

History:

Generalised weakness for a year; pleuritic pain in the right lower chest postero-laterally, cough with mucoid sputum, dyspnoea and feverishness for ten days; sputum blood stained for six days. Sulphonamide (two tablets four hourly) for the first five days of his illness had caused no improvement. Two years previously he had been in Groote Schuur Hospital with a macrocytic anaemia (red cells 2.74 million), grossly disturbed liver function tests and generalised osteosclerosis; his anaemia did not respond to liver, iron, vitamin C, thyroid or folic acid. He occasionally drank alcohol but not excessively. For many years he had been a carpenter's assistant.

Examination:

Toxic, dyspnoeic, pale, temperature 101.5 degrees, sputum rusty; no hepatomegaly; over right lower lobe diminished vocal fremitus and resonance, relative dullness, bronchial breathing and a few crepitations; urine one plus urobilin; red cells 2.33 million and the smear showed slight hypochromia, aniscocytosis, macrocytosis, occasional polychromatophylic cells, target cells and normoblasts; white cells 9,000 with neutrophils 71 per cent, lymphocytes 26 per cent and

eosinophils 3 per cent.

Course:

He was given penicillin 400,000 units and then 200,000 units four hourly. His temperature fell by crisis but for a further ten days he ran a low intermittent pyrexia to 99.5 degrees. X-ray showed consolidation of both lower and upper lobes on the right and a small effusion. A fresh sputum grew salivary organisms only.

Two weeks after admission the breathing was vesicular but otherwise the signs were unchanged and the patient felt perfectly well. Penicillin was stopped three days later. Five weeks after admission there was dullness and fairly numerous crepitations over the right lower lobe and the X-ray showed some resolution. Lung biopsy was performed through the 7th interspace just below the angle of the right scapula. About five minutes later he coughed up about two tablespoonfuls of bloody mucoid sputum. X-ray showed no pneumothorax. The biopsy cultures were sterile and salivary organisms were grown from the sputum. The slides showed a fair number of small macrophages and transitional cells and not infrequently large "chronic pneumonia macrophages"; no fibrin was seen. The interpretation was that there was very advanced resolution. About eight days later there was only very slight dullness at the base and X-ray showed almost complete resolution - this was after the patient had been in hospital 52 days.

Meanwhile his blood condition was investigated - iliac puncture was unsuccessful because of the hardness of the bones and the osteosclerosis was confirmed on X-ray. A course of Vitamin B 12 caused no improvement in the anaemia. His Wassermann reaction was negative. Liver function tests were grossly abnormal. He was finally given a blood transfusion and discharged.

Discussion:

This is not the place to enter into a discussion on this patient's interesting blood condition and its possible relationship to the osteosclerosis (which was of uncertain etiology) and the hepatic dysfunction. Certainly this patient was a chronic pneumonia. The anaemia and the liver condition may have caused the poor leucocyte response and the slow resolution of the lesion.

CASE 64.

B.B. NATIVE MALE. 40 YEARS. CHRONIC BRONCHOPNEUMONIA.

History:

Dysphagia for solid foods for five months; cough with dyspnoea and a little sputum for two weeks. He was a labourer in the brickfields but had worked in the mines on the Rand as a young man.

Examination:

Toxic, dyspnoeic, alae nasi working, inspiratory and expiratory stridor, temperature 100 degrees, blood pressure 154/110 m.m.Hg.; rhonchi all over the chest the only abnormality; urine albumin a trace and one plus urobilin; red cells 5.46 million; white cells 24,250 with 95 per cent neutrophils.

Course:

The bronchospasm responded to intravenous aminophyllin and subcutaneous adrenaline. The next day he was given penicillin 200,000 units and sulphatriad four tablets and then penicillin 100,000 units and sulphatriad two tablets four hourly. He showed little response, and remained ill with a temperature between 99 and 103 degrees. X-ray showed a patchy left basal consolidation and an area of consolidation in the right upper zone. After nine days he

was started on streptomycin (0.5 gm. twice daily). A fresh sputum had grown salivary organisms and four 24 hour sputa had been negative for tubercle. X-ray showed that the consolidation on the right was resolving but his sputum about this time became first bloody and then rusty and examination showed diminished vocal fremitus and resonance, dullness, and diminished air entry at the left base.

About four weeks after admission the patient had greatly improved but the physical signs were unchanged except that there were now in addition fine and medium crepitations. The X-ray showed resolution on the right and some resolution at the left base. His temperature had settled to the region of 99 degrees. Lung biopsy was done through the 8th interespace just lateral to the line of the angle of the left scapula. Shortly after biopsy the patient collapsed but recovered very soon afterwards - this was probably a form of syncope rather than air embolism (the features were described fully under "Complications of Lung Biopsy" page 79). He coughed up about three tablespoonfuls of bloody mucoid sputum and blood staining of the sputum continued for about an hour. X-ray showed no pneumothorax. Salivary organisms were cultured from the sputum; the blood agar culture of the biopsy material was sterile but a coagulase positive staphylococcus albus was grown in the serum broth. This latter was probably a contaminant. Histologically there were small amounts of fibrin with fairly

numerous small and large single nuclear macrophages. The picture was exactly similar to advanced resolution of the ordinary lobar pneumonia except that the macrophages appeared somewhat fewer in number.

X-ray showed the trachea to be indented and displaced forward and barium swallow showed a marked stricture of the oesophagus at the level of the tracheal bifurcation. He was given a course of Calgluquine (10 c.c. daily for seven days) and the X-ray appeared to show some resolution during this period although this was not generally accepted. Oesophagoscopy showed a query benign stricture. He became more dyspnoeic and coughed up more and more sputum which became blood stained. He finally died from acute respiratory obstruction.

Discussion:

The patient had tracheal obstruction, an oesophageal stricture and a chronic bronchopneumonia. The clinical picture was most likely due to a carcinoma of the oesophagus, the obstruction to the trachea possibly playing a part in the etiology and the chronicity of the bronchopneumonia. Lung biopsy was interesting in that it showed similar changes in the resolution of a bronchopneumonia as those seen in lobar pneumonia. The Calgluquine may have temporarily increased the rate of resolution.

CASE 65.

J.M. COLOURED MALE. 38 YEARS. CHRONIC LOBAR PNEUMONIA.

History:

Cough with mucopurulent sputum, pleuritic pain in the right upper chest both anteriorly and posteriorly and feverishness for seven days. For five years, every six months, he had had an attack of cough and dyspnoea but no feverishness, lasting three weeks. For many years he had drunk one or two bottles of wine daily. His fingers and toes had been abnormal in shape for as long as he could remember.

Examination:

Toxic, dyspnoeic, alae nasi working, gross clubbing of the fingers and toes, (see Figures 135 to 137) mucopurulent sputum, pulse 140/minute, temperature 103 degrees; over the right upper lobe diminished movement, increased vocal fremitus and resonance, relative dullness, bronchial breathing and numerous medium crepitations; over the right lower lobe the findings were similar but bronchial breathing was not present; urine urobilin two plus; red cells 4.51 million; white cells 9,850 with 90 per cent neutrophils.

Course:

He was given penicillin 200,000 units and sulphatriad four tablets and then 100,000 units and two tablets respectively four hourly. His temperature fell by crisis but continued to fluctuate at a low level between 99 and 101 degrees for six days and then between normal and 100 degrees for a further five days. X-ray showed massive consolidation of almost the whole of the right lung. (See Figure 134). Salivary organisms were cultured from a fresh sputum taken twelve hours after the beginning of chemotherapy. His general condition rapidly improved but the physical signs remained unaltered. About ten days after admission the physical signs and X-ray appearance were just as on admission but he felt perfectly fit. The sputum was mucoid with purulent areas. Lung biopsy was done through the third interspace in the right midclavicular line. The patient had a haemoptysis of a tablespoonful of blood and showed a mild collapsed condition (see Complications of Lung Biopsy page 80 for full details) and the sputum remained blood stained for two hours. X-ray showed no pneumothorax. The sputum grew salivary organisms and a coagulase positive staphylococcus aureus but the biopsy material was sterile. Histologically there were great masses of fibrin some with few or no cells and other areas with a fair number of cells; small macrophages were numerous and very vacuolated and transitional cells were frequent;

polymorphs in a good state of preservation were not uncommon. The picture was that of fairly advanced resolution but the cell response appeared to be less than one would have expected. Also, at this stage after 10 days of chemotherapy, one would have expected very numerous macrophages, diminished fibrin and extremely scanty polymorphs, that is the stage of advanced resolution. One felt that one could predict from the clinical course and the biopsy findings that this patient would go on to a chronic stage.

Two days later he was given a course of Calgluquine (10 c.c. daily for seven days). By the end of the course the only physical signs were harsh vesicular breathing with increased vocal resonance and fremitus. X-ray showed a fair degree of resolution as compared with the X-ray taken immediately before Calgluquine was started. For the next two weeks, after Calgluquine had been stopped, he remained in status quo both clinically and radiologically. Then over ten days he progressed to complete clinical and radiological resolution - he had been in hospital for 45 days. Bronchogram could not be done because of iodine sensitivity. His Wassermann was positive. The somatype rating was 1 . 4 . 4½., that is a mesoectomorph.

Discussion:

This case was of interest in that one could predict that he would run a chronic course. Resolution appeared to be retarded but during the course of Calgluquine it seemed to progress more rapidly. When the injections were stopped resolution again became slow and this lasted for two weeks. Complete resolution then took place over 10 days. The clubbing of the fingers and toes was probably of the congenital variety. Factors which may have been related to the slow resolution were the attacks of "bronchitis" and his consumption of alcohol.

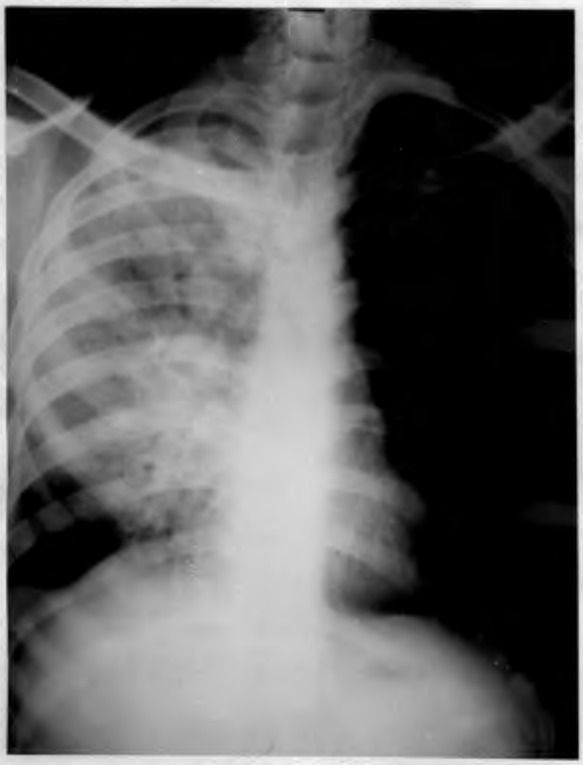


Figure 134. Case 65.

X-ray Chest. PA.
(At the time of the lung biopsy).

CONGENITAL CLUBBING OF THE FINGERS AND TOES.

Figure 135. Case 65.

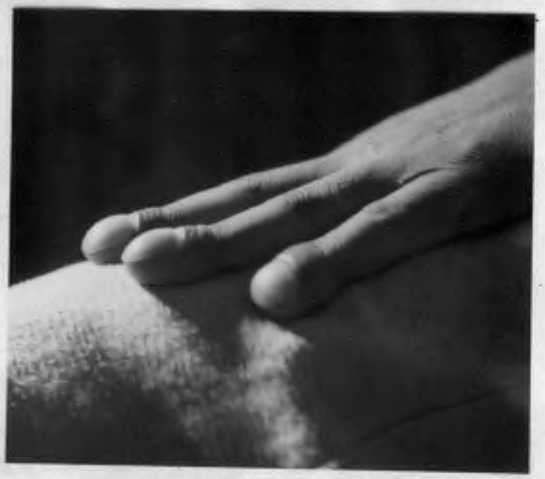


Figure 136. Case 65.

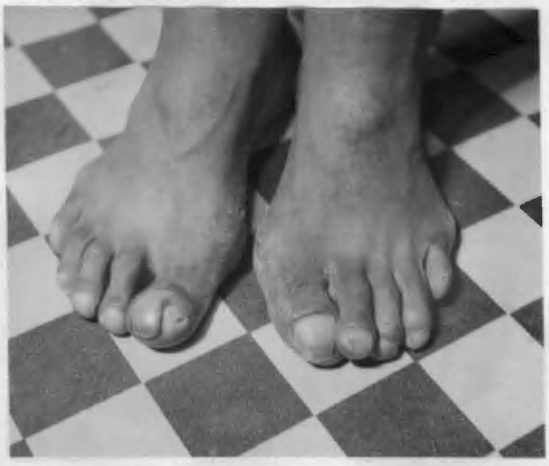


Figure 137. Case 65.

CASE 66.

J.M. COLOURED MALE, 29 YEARS. NORMAL LUNG.

History:

Pain in the right hypochondrium and dark urine for four days.

Examination:

Toxic, jaundiced, chest normal, slight tenderness in the right hypochondrium but no hepatomegaly; urine contained bile and urobilin; white cells 14,200 with 73 per cent neutrophils.

Course:

He was treated as an infectious hepatitis but went rapidly downhill, began to vomit bloody material and became maniacal. Liver dullness diminished rapidly, liver function tests were grossly abnormal and the blood urea was 9 mg. per cent. He died after four days in hospital.

Lung biopsy was performed almost immediately after death. The needle was inserted through the 3rd interspace in the left midclavicular line. The slides showed many red cells, macrophages mainly of the small type, scanty alveolar cells, a few groups of ciliated bronchiolar epithelial cells, small portions of interstitial tissue and

a fair number of scattered black particles.

Autopsy:

This was limited to the abdomen. The macroscopic and microscopic picture of the liver was that of acute yellow atrophy.

Discussion:

This patient was probably a case of infectious hepatitis which ran an unusual course to acute yellow atrophy. The lung biopsy material showed the expected features of normal lung tissue.

CASE 67.

J.S. NATIVE MALE, 29 YEARS. ACUTE LOBAR PNEUMONIA.

History:

Shivering, cough with yellow sputum, pleuritic pain in right lower chest laterally for five days; dark red blood in the sputum for two days.

Examination:

Toxic, dyspnoea slight, temperature 102 degrees, pulse 110/minute; over right upper lobe increased vocal fremitus and resonance, slight dullness and diminished air entry; urine a trace of urobilin; red cells 4.25 million; white cells 11,900 with 87 per cent neutrophils.

Course:

Because of the very slight signs and low leucocyte count he received no treatment on the night of admission. The next morning X-ray showed a gross consolidation of the right upper lobe but the physical signs were unaltered. The sputum was mucopurulent with occasional areas of red blood. The temperature was subnormal. Lung biopsy was performed through the second interspace about 6 cm. to the right of the mid-sternal line. There were no sequelae. No pneumococci were cultured from the sputum, but pneumococci were obtained

in cultures of the biopsy material. Histologically there were masses of fibrin with frequent well preserved polymorphs; macrophages and transitional cells were present in fair numbers; pneumococci were very scanty. The picture was that of late red hepatisation.

He was started on penicillin 200,000 units and sulphatriad four tablets and then received 100,000 units and two tablets respectively four hourly. That evening his temperature rose to 103 degrees but came down by crisis and from the fifth day he was apyrexial. Resolution proceeded rapidly and after five days there was clinical resolution and X-ray resolution was complete after 19 days. His Wassermann reaction was negative. The somatype rating was 1 . 7½ . 1½ .., that is a mesomorph.

Discussion:

This patient presented with gross radiological consolidation but with few physical signs and a poor leucocyte response. Pneumococci were grown from the biopsy material but not from the sputum. Resolution occurred normally.

CASE 68.

Q. VAN N. COLOURED MALE. 4 MONTHS. PULMONARY TUBERCULOSIS.

History:

Troublesome cough at night, gradually becoming worse; slight diarrhoea but no feverishness for two weeks. No contact with tuberculosis.

Examination:

Well nourished, not obviously ill infant, temperature 99 degrees; rhonchi all over both sides of the chest.

Course:

No chemotherapy was given for the first five days as the temperature remained at about 99 degrees. On the 6th day there was a pyrexia of 102.6 degrees. Penicillin 100,000 units eight hourly was started and in addition sulphadiazine 0.5 gm. (and then 0.25 gm. eight hourly) was given. X-ray chest showed consolidation of the whole of the right upper lobe. After a week the penicillin dosage was doubled but the temperature remained between 100 and 102 degrees. A month later there was no change on the X-ray and Terramycin half a capsule for four doses six hourly then quarter of a capsule six hourly was started. There was no response and five days later penicillin given four hourly was added. The temperature was often normal but not

infrequently 99 to 100 degrees. The child looked well but in spite of all this antibiotic therapy the X-ray appearance remained constant. This regime was continued for a month. At this stage the child still appeared well; over the right upper lobe there was dullness and diminished air entry. It was suggested that this might be an encysted emphema and it was decided to try aspiration and if there was no fluid then a lung biopsy would be attempted. Aspiration was attempted through the 4th interspace in the right midaxillary line. No fluid was obtained. A lung biopsy was then performed using a No. 20 intramuscular needle and a 5 c.c. syringe. The needle was inserted to a depth of about 1 cm. and the lung felt abnormally firm. The material obtained was white and macroscopically resembled caseous material. The child had been given ½ gr. of nembutal half an hour before and the biopsy was uneventful. There were no sequelae and X-ray a few hours later showed no pneumothorax. The biopsy cultures in serum broth and on blood agar were sterile but there was a good growth of tubercle bacilli on the Lowenstein medium. Histologically most of the material was of a structureless nature with small areas of fibrin; cells were scanty and difficult to identify but some appeared to be polymorphs; fairly frequent acid and alcohol fast bacilli were identified in the slide stained by the Ziehl Neelsen method.

Streptomycin was started (0.25 gm. twice daily) but six weeks later there was little change in the X-ray appearance. The tuberculin jelly test was positive.

Discussion:

This case presented a fascinating diagnostic problem and there was no doubt that tuberculosis was the answer. Sanderson (1936) in a discussion on chronic pneumonia in young infants, stated that the original tuberculous focus became rapidly surrounded by an exudative infiltrate which varied in size within wide limits, sometimes occupying almost an entire lobe, commonly the right upper lobe. The tuberculin reaction was said to become positive at this stage. This description was probably what is termed "epituberculosis". This type of lesion would fit in well with the X-ray picture and clinical state of the present case. His Mantoux test was positive. It was very unlikely that this was a true tuberculous lobar pneumonia as the child would have been extremely ill. If this case was one of epituberculosis then it was likely that the biopsy needle had entered the primary focus.

CASE 69, 69-1 AND 69-2.

S.G. COLOURED MALE, 38 YEARS. CHRONIC LOBAR PNEUMONIA.

History:

Pleuritic pain over lower part of right chest laterally and cough with yellow white sputum for four days. Seven years previously he had had a similar pain on the right side and had been kept in bed for two weeks. Worked as a casual labourer at the flower market. He slept on the mountain in good weather and in a stable when it was wet. Drank about a bottle of wine daily for years.

Examination:

Not toxic, not dyspnoeic, temperature 102 degrees; over right upper lobe diminished movement, increased vocal fremitus and resonance, relative dullness, bronchial breathing and numerous medium crepitations; urine normal; white cells 16,000 with 85 per cent neutrophils.

Course:

X-ray showed consolidation of the right upper lobe (see Figure 138). Lung biopsy was performed (soon after admission) through the second interspace about 3 cm. to the right of the right sternal border. There were no sequelae. Pneumococci were cultured from both the sputum and the lung biopsy material. The slides showed a fair amount of fibrin with

innumerable well preserved polymorphs; occasional small macrophages and transitional cells not infrequent; occasional polymorphs were seen within macrophages; pneumococci were scanty. The picture was that of red hepatisation.

He was given penicillin 200,000 units and sulphatriad four tablets and then penicillin 100,000 units and sulphatriad two tablets four hourly. His temperature fell by crisis and from the second day onwards he was apyrexial. Resolution at first appeared to be rapid and four days after admission there was only increased vocal fremitus and resonance with medium and fine crepitations and X-ray showed definite clearing of the consolidation. Lung biopsy (69-1) was repeated through the same site as before. Shortly afterwards he coughed up a little blood stained sputum and blood streaking of the sputum persisted for about half an hour. The biopsy material was sterile and the mucoid sputum grew salivary organisms. Histologically there was a fair amount of fibrin with very many small macrophages and a fair number of transitional cells; polymorphs were scanty and well preserved and only very occasionally seen within macrophages. This was advanced resolution. Fourteen days after admission the chest was normal on physical examination and X-ray showed further resolution. Penicillin therapy was stopped.

Radiological resolution proceeded slowly and another lung biopsy (69-2) was done through the same area 33 days

after admission. The biopsy was followed by cough and haemoptysis of about five tablespoonfuls of blood and blood staining of the sputum continued for about an hour. The biopsy cultures were sterile and the sputum grew mixed organisms. The slides showed scanty fibrin, a fair number of small macrophages and some of the larger "chronic pneumonia" macrophages; transitional cells were not infrequent; polymorphs were present in proportion to the amount of blood. The slides showed very advanced resolution. Complete X-ray resolution was seen after 46 days in hospital. No bronchogram could be done because of iodine sensitivity. The Wassermann reaction was positive. Somatype rating was 1 . 6 . 2. that is a mesomorph.

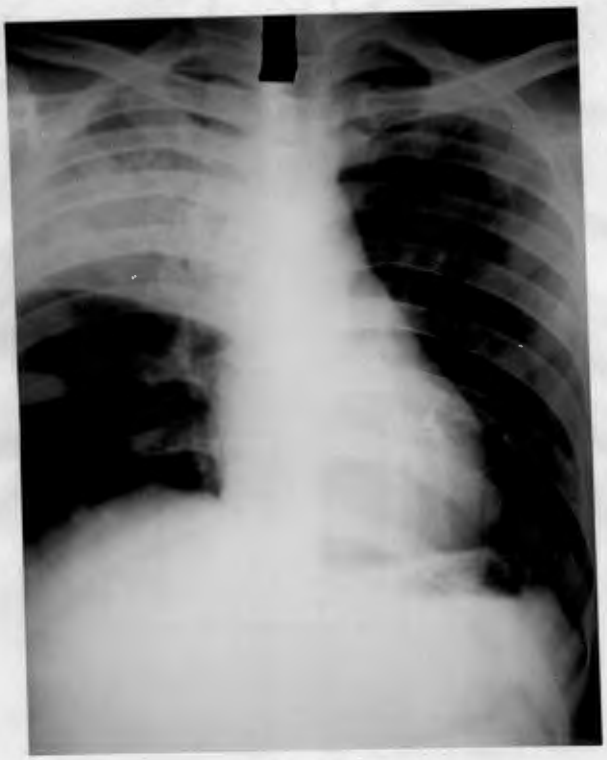


Figure 138. Case 69.

X-ray Chest. PA.
(On admission).

Discussion:

This patient had a proved pneumococcal lobar pneumonia which took 46 days to resolve completely. The serial biopsies showed the progressive changes from red hepatisation to advanced resolution to very advanced resolution. The cause of the slow resolution was uncertain but possibly might be related to the old attack of what was possibly pneumonia, to his consumption of alcohol and his abode on the mountain.

CASE 70 AND 70-1.

J.N. COLOURED MALE. 31 YEARS. CHRONIC LOBAR PNEUMONIA.

History:

Pleuritic pain laterally in right lower chest, dry cough, feverishness and dyspnoea for four days. He received an intramuscular injection from his doctor (probably penicillin) about 10 hours before admission. Two years before admission he had had a stone removed from his right kidney and a year later his left kidney was removed also because of calculi. His wife had died of tuberculous meningitis.

Examination:

Toxic, dyspnoeic, temperature 102.5 degrees, sputum rusty; over almost the whole of the right lung diminished movement, increased vocal fremitus and resonance, relative dullness, bronchial breathing and a few medium crepitations; urine one plus albumin; red cells 5.0 million; white cells 6,000 with 89 per cent neutrophils (but this count was done about 12 hours after admission).

Course:

Soon after admission lung biopsy was performed through the 7th interspace just below and lateral to the angle of the right scapula. There were no sequelae. Pneumococci were not cultured from either the sputum or the biopsy

material. Histologically small areas of fibrin were present; polymorphs were numerous and many were small and showed signs of early degeneration; small macrophages were fairly common and in many cases had ingested polymorphs; transitional cells were not frequent; no definite organisms were seen but many of the polymorphs contained small Gram positive dots which might have been pneumococci in the process of being digested. The picture was that of very late red hepatisation or very early grey hepatisation.

He was started on penicillin 100,000 units four hourly. His temperature came down by crisis on the third day but intermittent temperatures up to about 100 degrees continued for about two weeks and there were occasional peaks to 99 degrees for a further week. X-ray showed consolidation of most of the right lung.

Five days after admission he was much improved in his general condition but the physical signs were little altered and the sputum was still rusty. Extensive herpes febrilis of the nose and right ear appeared. Lung biopsy (70-1) was repeated through the same site as before and again the biopsy material was sterile and the sputum grew mixed organisms. The slides showed many macrophages, many of which were of the larger "chronic" type, but no fibrin was seen; transitional cells were infrequent and polymorphs scanty. This picture was that of very advanced resolution. X-ray showed little change in the consolidation.

The physical signs changed quite rapidly and after eight days there was dullness, increased vocal fremitus and resonance and harsh vesicular breathing chiefly over the right lower lobe. A few days later crepitations again appeared. About three weeks after admission X-ray showed a small basal effusion but the area of consolidation was little altered. About 100 c.c. of sterile exudate was aspirated. By the fourth week there was only slight dullness and diminished air entry at the right base and X-ray showed some resolution but some fluid was still present.

After 35 days there was only a little dullness at the right base and after 46 days X-ray showed complete resolution with a little pleural thickening in the right costo-phrenic angle.

The patient's Wassermann reaction was negative. His somatype rating was 1 . 6 . 2½., that is a mesomorph.

Bronchogram showed a very mild dilatation of the bronchus to the posterior basal segment of the right lower lobe.

The patient also had a neurological condition characterised by nystagmus, ankle and knee clonus and some posterior column sensory loss in the legs. This was still under investigation when the present paper was completed.

Tests for renal function were normal.

Discussion:

This patient showed the classical course of a chronic lobar pneumonia. Factors contributing to the slow resolution might have been the renal operations and his neurological condition. The biopsy was interesting as being the only one which resembled the pathology of grey hepatisation. This was the only case in the chronic pneumonia series which showed a mild residual dilatation of a bronchus.

CASE 71 AND 71-1.

F.P. COLOURED MALE. 35 YEARS. ACUTE LOBAR PNEUMONIA.

History:

Cough with white sputum, shivering and feverishness, and pleuritic pain over the left lower chest anteriorly for six days. He drank about a bottle of sherry daily.

Examination:

Toxic, dyspnoeic, temperature 101 degrees; sputum mucoid with rusty areas; over left lower lobe increased vocal fremitus and resonance, relative dullness, numerous medium crepitations and diminished vesicular breathing; urine normal; red cells 4.0 million; white cells 18,450 with 90 per cent neutrophils.

Course:

Shortly after admission, lung biopsy was done through the 8th interspace just below and lateral to the angle of the left scapula. There were no sequelae. X-ray showed a left lower lobe consolidation with a small associated pleural exudate obscuring the left costo-phrenic angle and seeping along the oblique fissure. The biopsy culture showed a pure growth of pneumococci and from the sputum there grew mixed organisms including pneumococci but there was no predominance of any one organism. The slides showed fibrin

which was not prominent but there were fairly numerous well preserved polymorphs; small macrophages and transitional cells were not infrequent and occasional ingested polymorphs were seen; dust cells were quite common; pneumococci were fairly frequent and seen within both polymorphs and macrophages. The picture was that of late red hepatisation probably just preceding the natural crisis.

The patient was started on penicillin 200,000 units and sulphatriad four tablets and then received 100,000 units and two tablets respectively four hourly. His temperature fell by crisis but he continued to run occasional peaks to 99 or 99.5 degrees for fifteen days. The physical signs remained unaltered except that crepitations became fewer in number. The sputum was mucoid with small purulent areas. Five days after admission lung biopsy (71-1) was done through the same site as before and again there were no sequelae. From the sputum there grew mixed organisms and the biopsy material was sterile. Histologically fibrin was not prominent; there were numerous small macrophages, many dust cells and scanty polymorphs. The pulmogram was that of advanced resolution.

Resolution proceeded normally but not very rapidly and the chest was normal on physical examination and clear radiologically (except for obliteration of the left costo-phrenic angle) 29 days after admission.

The somatype rating was 2½ . 6 . 1., that is a meso-morph. His Wassermann reaction was negative.

Discussion:

This patient had an ordinary acute lobar pneumonia which resolved rather slowly and at one time it seemed probable that he would fall into the chronic group. The biopsies showed the progressive changes from late red hepatisation to resolution.

CASE 72 AND 72-1.

A.V. COLOURED FEMALE. 29 YEARS. ACUTE LOBAR PNEUMONIA.

History:

Feverishness for six days; cough with brownish sputum, and pleuritic pain over the right lower chest laterally for five days. Seven years previously she had "pleurisy" and she was kept in bed for about three weeks.

Examination:

Toxic, dyspnoeic, alae nasi working, temperature 103 degrees, rusty sputum; over right lower lobe increased vocal fremitus and resonance, relative dullness, bronchial breathing and many medium crepitations; urine one plus of albumin and one plus urobilin; red cells 4.2 million; white cells 12,000 with 78 per cent neutrophils.

Course:

Lung biopsy was performed soon after admission, the needle being inserted through the 7th interspace just below and medial to the angle of the right scapula. There were no sequelae and X-ray showed consolidation of the right middle and lower zones with a small area of consolidation in the left upper zone; there was no pneumothorax. Pneumococci were grown from the sputum and the biopsy cultures. The slides showed masses of fibrin with innumerable well preserved

polymorphs; macrophages and transitional cells were infrequent and very occasionally an ingested polymorph was seen; numerous pneumococci were seen and these were being actively ingested by the polymorphs. The picture was that of red hepatisation.

She was started on penicillin 200,000 units and sulphatriad four tablets and then was given 100,000 units and two tablets respectively four hourly. Her temperature fell by crisis and from the fourth day she was apyrexial. After six days her general condition was excellent, the sputum was purulent and on examination the physical signs were as before except that there was only one small area of bronchial breathing in the area where the biopsy had been done; X-ray showed slight resolution. Lung biopsy (72-1) was repeated through the same site as before and this was followed by a small haemoptysis which continued with slight blood streaking of the sputum for 21 hours. There was no significant growth from the sputum and the biopsy material was sterile. Histologically fibrin was not prominent but there were innumerable small macrophages, fairly frequent transitional cells and scanty well preserved polymorphs. This was obviously advanced resolution.

Resolution proceeded rather slowly and the chest was clinically normal after 25 days. The X-ray showed almost complete resolution after 29 days. Her Wassermann reaction

was negative. The somatype rating was 1 . 3½ . 5 that is a mesoectomorph.

Discussion:

This patient was a straight forward case of severe pneumococcal lobar pneumonia, the biopsies showing the changes from red hepatisation to resolution.

CASE 73.

G.T. COLOURED MALE 37 YEARS. PNEUMONIA OF UNCERTAIN ETIOLOGY.

History:

For three days he had felt "out of sorts", had no appetite and complained of a slight cough with white sputum. The night before admission he sweated profusely and felt feverish.

Examination:

Not toxic, not dyspnoeic, ?early clubbing of the fingers; apyrexial but pulse 92/minute; over left side of chest anteriorly diminished movement, slight dullness, vesicular breathing with fine crepitations, vocal fremitus and resonance unaltered; few fine crepitations over right lung anteriorly at the base; urine normal; blood - P.C.V. 36 per cent, smear normal, white cells 21,000 with neutrophils 51 per cent, lymphocytes 41 per cent, monocytes 5 per cent and eosinophils 3 per cent; E.S.R. 115 m.m. in one hour (Westergren).

Course:

An X-ray done on the day of admission showed signs of chronic pulmonary fibrosis at the lung bases but the striking feature was that the antero-lateral and postero-lateral segments as well as the lingula of the left upper lobe

showed a peculiar stippled non-homogeneous opacity. This was present to a lesser degree on the right side. The patient was started on penicillin (500,000 units twice daily) and his subjective feeling of malaise diminished. He remained apyrexial. The Wassermann reaction was negative. His sputum was greenish yellow and purulent but five examinations of 24 hour specimens were negative for tubercle. Eight days after admission his physical signs were unaltered except that crepitations had diminished in number and he felt perfectly fit; the sputum was still frankly purulent but odourless.

At this stage lung biopsy was performed through the third interspace about 5 cm. to the left of the midsternal line. A small drop of dark brown material was obtained. There was no cough or pain but some time later there was a small amount of blood in the sputum. The biopsy material was sterile and the sputum grew mixed salivary organisms only. The histology was unusual; there were small areas of fibrin with a fair number of associated polymorphs which showed a shift to the right; there were a fair number of whorled areas consisting of thread-like material which consisted probably of collagen and elastic fibres with some fibroblasts; associated with these areas there were many small black particles; alveolar cells were not infrequent and groups of ciliated bronchial epithelial cells were seen; no organisms were observed.

X-ray done the day after the biopsy showed very marked clearing of the consolidation.

About two weeks after admission his E.S.R. was 46 m.m. in one hour (Westergren) and the white cell count 12,000.

He was discharged after having been in hospital for 22 days. He returned to the outpatient department for a final check two weeks later and physical examination showed no abnormality. Unfortunately no further X-rays were done.

Discussion:

It was very difficult to interpret this case. The patient was not very ill but showed a quite extensive consolidation of the lung and in addition he had a high leucocyte count with a rather high percentage of lymphocytes. It was difficult to decide whether his response was due to penicillin or was unrelated to therapy. The lung biopsy showed a mixture of a rather chronic lesion associated with a subacute inflammatory lesion. The cultures were sterile but he had been on chemotherapy. The sputum was frankly purulent. Neither the clinical, radiological nor biopsy appearances were that of a virus pneumonia. The type of consolidation remained a mystery. It was a pity that he was not more fully investigated with further X-rays and a bronchogram. The relationship of the two broken ribs on the right side remained obscure as there was no history of trauma.

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Abrahams, A., et al. (1917): Purulent bronchitis: its influenzal and pneumococcal bacteriology, Lancet 2 377.

Alston, J., and Stewart, D. (1930): Incidence of the serological types of the pneumococcus in lobar pneumonia, Brit. M.J. 2 860.

Blady, J. (1939): Aspiration biopsy of tumours in obscure or difficult locations under roentgenoscopic guidance, Am. J. Roentgenol. 42 515.

Blake, F., and Cecil, R. (1920): Studies on experimental pneumonia - production of pneumococcus lobar pneumonia in monkeys, J. Exper. Med. 31 403.

Blake, F., and Cecil, R. (1920): Pathology and pathogenesis of pneumococcal lobar pneumonia in monkeys, J. Exper. Med. 31 445.

Bloomfield, A. (1922): The mechanism of elimination of bacteria from the respiratory tract, Am. J. M. Sc. 164 854.

Bönniger, M. (1907): Quoted by Craver and Binkley (1938).

Boyd, W. (1938): A Textbook of Pathology, 3rd Ed., London: Henry Kimpton.

Boys, F., and Harris, I. (1943): The effect of heparinization on experimental post-irradiation tissue changes in the lung, Am. J. Roentgenol. 50 1.

Briscoe, J. (1908): An experimental investigation of the phagocytic action of the alveolar cells of the lung, J. Path. and Bact. 12 66.

Bullowa, J.G.M. (1936): Quoted by Sappington and Favorite (1936).

Cecil, R., Baldwin, H., and Larsen, N. (1927): Lobar pneumonia - a clinical and bacteriological study of 2,000 typed cases, Arch. Int. Med. 40 253.

Clayden, E. (1951): Practical Section Cutting and Staining 2nd Ed. London: J. and A. Churchill Ltd.

Colby, T.J. (1909): Quoted by Craver and Binkley (1938).

Collins, I. (1947): Unresolved pneumonia, M.J. Australia 2 68.

Coope, R. (1948): Diseases of the Chest 2nd ed. Edinburgh: E. and S. Livingstone Ltd.

Cooper (1929): Quoted by Reimann (1938).

Craver, L. (1940): Diagnosis of malignant lung tumours by aspiration biopsy and by sputum examination, Surgery 8 947.

Craver, L. and Binkley, J. (1938 - 39): J. Thoracic Surg. 8 436.

Cruikshank, R. (1931): Quoted by Sappington and Favorite (1936).

Curphey, T.J. (1935): A preliminary report on intra vitam biopsy studies of the pathogenesis of pneumococcus lobar pneumonia, Am. J. Path. 11 861.

Ellis, E.B. (1922): Quoted by Craver and Binkley (1938).

Eyre, J. (1910): The bacteriology of broncho-pneumonia - a statistical analysis, J. Path. and Bact. 14 160.

Faber, J., Carpenter, R., and Pellicano, V. (1942): Lipoid pneumonia - diagnosis by aspiration biopsy, Am. Rev. Tubero. 45 453.

Felton (1924): Quoted by Reimann (1938).

Fernandez and Tobias (1931): Quoted by Craver and Binkley (1938).

Fitz - Hugh (1924): Quoted by Weinstein and Goodman (1934).

Foot, N. (1927): Studies on endothelial reactions: On the origin of the pulmonary "dust cell", Am. J. Path. 3 413.

Fortescue-Brickdale, J. (1909): Letter to the Lancet 2 1469.

Fränkel, A. (1896): Quoted by Craver and Binkley (1938).

Fried, B. (1934): The lungs and the macrophage system, Arch. Path. 17 76.

Gaskell, J. (1927): Bradshaw lecture on the pathology of pneumonia, Lancet 2 951.

Gay, F. (1931): Tissue resistance and immunity, J.A.M.A. 97 1193.

Geever, E., et al. (1943): The pulmonary alveolar lining under various pathologic conditions in man and animals, Am. J. Path. 19 913.

Geever, E., et al. (1951): Atypical pulmonary inflammatory reactions, Dis. of Chest 19 325.

Gibson, M., and Belcher, J. (1951): Primary staphylococcal pneumonia, Quart. J. Med. 20 43.

Gladhill, E., Spriggs. J, and Binford, C. (1949): Needle aspiration in the diagnosis of lung carcinoma, Amer. J. Clin. Path. 19 235.

Gleichman, T., Leder, M., and Zahn, D. (1949): Am. J. M. Sc. 218 369.

Glynn, E., and Digby, L. (1923): Quoted by Sappington and Favorite (1936).

Godlowski, Z. (1949): Cellular analysis of the aspiration lung biopsy from normal and some pathological conditions, J. Clin. Path. 2 49.

Greenwald, H., et al. (1936): Chronic pneumonia associated with nutritional disturbances in infants, Am. J. Roentgenol. 35 454.

Grier, G. (1944): Importance of bronchography in cases of unresolved pneumonia, Arch. Int. Med. 73 444.

Gunther (1883): Quoted by Thomas and Parker (1920).

Hadfield, G. and Garrod, L. (1942): Recent Advances in Pathology 4th ed. London: J. and A. Churchill Ltd.

Hadfield, G. and Garrod, L. (1947): Recent Advances in Pathology 5th ed. London: J. and A. Churchill Ltd.

Hamburger, H. (1912): Abstract supplied by Stein (1951).

Head, G. and Seabloom, J. (1919): Arsphenamin in pneumonia with delayed resolution in syphilitic soldiers, J.A.M.A. 73 1344.

Hellendall, H. (1899): Quoted by Craver and Binkley (1938).

Hirsch, E., and Russel, H. (1945): Chronic exudative and indurative pneumonia due to inhallation of shellac, Arch. Path. 39 281.

Holinger, P. (1938): So called "Unresolved Pneumonia", Clin. North. Amer. 22 97.

Holmes, A. (1936): Unresolved pneumonia, Clin. J. 65 111.

Horder, T. (1909): Lung puncture: a new application of clinical pathology, Lancet 2 1345.

Horder, T. (1909): Letter to the Lancet 2 1539.

Jacobson (1899): Quoted by Craver and Binkley (1938).

Jorpes, J.E. (1947): The origin and physiology of heparin; the specific therapy in thrombosis, Ann. Int. Med. 27 361.

Kampmeier (1932): Quoted by Weinstein and Goodman (1934).

Keil, P., and Schissel, D. (1950): The differential diagnosis of unresolved pneumonia and bronchiogenic carcinoma by pulmonary angiography, J. Thoracic Surg. 20 62.

Klassen, K.P., et al. (1949): Biopsy of diffuse pulmonary lesions, Arch. Surg. 59 694.

Lamar and Meltzer (1912): Quoted by Gaskell (1927).

Lambert, T.H. and van Ordstrand, H.S. (1941): The value of aspiration lung biopsy in diagnosis - with illustrative cases - Cleveland Clin. Quart. 8 175.

Lanari, A. and Pavlovsky, A. (1937): Quoted by Craver and Binkley (1938).

Lanza, A.J. (1938): Silicosis and Asbestosis, Oxford University Press, New York, Inc.

Lavalle, C. (1937): Treatment of tuberculosis by needle puncture of the lung, Lancet 2 1299.

Leyden (1883): Quoted by Craver and Binkley (1938).

Lister, F.S. (1916): Quoted by Sappington and Favorite (1936).

Loeschcke, H. (1931): Quoted by Robertson and Uhley (1936).

Loosli, C. (1942): The histogenesis of cells in experimental pneumonia in the dog, J. Exper. Med. 75 657.

Loosli, C. (1942): The pathogenesis and pathology of experimental Type I pneumococcal pneumonia in the monkey, J. Exper. Med. 76 79.

Lord, F. (1919): Factors influencing recovery and resolution in lobar pneumonia, J.A.M.A. 73 1420.

Lyon, A. (1922): Bacteriologic studies of 165 cases of pneumonia and post-pneumonic empyema in infants and children, Am. J. Dis. Child. 23 72.

Macklin, C. (1936-7): Pulmonic alveolar epithelium - a round table conference, J. Thoracic Surg. 6 82.

Maclachlan, W., et al. (1937): Clinical observations on the treatment of pneumonia and empyema by some quinine derivatives, especially hydroxyethylapocupreine, Am. J. M. Sc. 194 474.

Mallory, F.B. (1920): Quoted by Robertson and Uhley (1936).

Martin, H., and Ellis, E. (1930): Biopsy by needle puncture and aspiration, Ann. Surg. 92 169.

Martin, H., and Ellis, E. (1934): Aspiration biopsy, Surg., Gynae. and Obst. 59 578.

Martin, H., and Stewart, F. (1936): The advantages and limitations of aspiration biopsy, Am. J. Roentgenol. 35 245.

Massachusetts General Hospital Case Records (1942): Case 28211, New Eng. J. Med. 226 861.

Menetrier, P. (1886): Quoted by Craver and Binkley (1938).

Menkin, V. (1940): Dynamics of Inflammation, New York: The Macmillan Company.

Metzlar (1915): Quoted by Craver and Binkley (1938).

Milanovic,R. (1948): My experiences with Calgluquine, Praxis 37 156.

Moore, F., et al. (1940): Pneumococcic pneumonia - analysis of the records of 1469 patients treated at the Los Angeles County Hospital from 1934-1938, Arch. Int. Med. 66 1290, 1317.

Morris, R.W. and Jacobs, L.M. (1950): On the application of somatyping to the study of constitution in disease, S.A. Journal of Clinical Science 1 347.

Muir, R. (1941): Textbook of Pathology, 5th ed. London: Edward Arnold and Co.

Nathanson, L., et al. (1943): Diagnosis of lipoid pneumonia by aspiration biopsy, Arch. Int. Med. 72 627.

Naunyn (1889): Quoted by Craver and Binkley (1938).

Netter, A. (1918): Quoted by Sappington and Favorite (1936).

Nuzum, J.W. et al. (1918): Quoted by Sappington and Favorite (1936).

Ott, R. (1937-38): Über pneumoniebehandlung mit Chinin - Calcium, Deutch. Arch. Für Klin Med. 181 658.

Patella (1888): Quoted by Thomas and Parker (1920).

Permar, H. (1920): An experimental study of the mononuclear phagocytes of the lung, J. Med. Research 42 9.

Permar, H. (1923): The mononuclear phagocytes in experimental pneumonia, J. Med. Research 44 27.

Pickhardt, O. (1928): Unresolved pneumonia - a surgical analysis, Arch. Surg. 16 192.

Pratt, J.H. (1900): Quoted by Robertson and Uhley (1936).

Rajaram, S.R. (1946): Chronic Pneumonias, The Antiseptic 43 723.

Reimann, H. (1938): The Pneumonias, Philadelphia and London: W.B. Saunders Company.

Repetto, E. (1947): Prevention and treatment of post-operative pulmonary complications with quinine and calcium, Abstract in South African M.J. 25 125 (1951).

Rigdon, R.H., and Schrantz, F.S. (1942): Effect of heparin on phagocytosis by the cells of the reticulo-endothelial system, Ann. Surg. 116 122.

Robertson, O. (1938): Recent studies on experimental lobar pneumonia - pathogenesis, recovery and immunity, J.A.M.A. 111 1432.

Robertson, O. (1941): Phagocytosis of foreign material in the lung, Physiol. Rev. 21 112.

Robertson, O., and Coggeshall, L. (1938): Local recovery in experimental pneumococcus lobar pneumonia in the dog, J. Exper. Med. 67 597.

Robertson, O., and Loosli, C. (1938): A study of the macrophage reaction in the pulmonary lesions of dogs with experimental pneumococcus lobar pneumonia, J. Exper. Med. 67 575.

Robertson, O., and Uhley, C. (1936): Changes occurring in the macrophage system of the lungs in pneumococcus lobar pneumonia, J. Clin. Investigation 15 115.

Rosenow, E. (1911): Quoted by Thomas and Parker (1920).

Russel, A. (1909): Letter to the Lancet 2 1539.

Sanderson, S. (1936): Chronic pneumonia in young infants, Am. J. Roentgenol. 36 757.

Sandoz: Treatment of pneumonia and other acute respiratory infections with "Quinine - Calcium - Sandoz".

Sappington, S. and Favorite, G. (1936): Lung puncture in lobar pneumonia, Am. J. M. Sc. 191 225.

Scadding, J.G. (1939): The chronic pneumonias, Proc. Roy. Soc. Med. 31 1259.

Scadding, J.G. (1946): Pneumonia, The Practitioner 157 333.

Schneider, L. (1948): Chronic benign pneumonitis - its discovery in older individuals with diminished or absent gag reflex, New York State J. Med. 48 520.

Sharp, G. (1931): The diagnosis of primary carcinoma of the lung by aspiration, Am. J. Cancer 15 863.

Shibley, G., and Rogers, E. (1932-33): Occurrence of rough pneumococci in lungs of patients with lobar pneumonia, Proc. Soc. Exper. Biol. and Med. 30 6.

Smeall, J. (1948): A short history of the pneumococcus with special reference to lobar pneumonia, Edinburgh M. J. 55 129.

Sokolowsky (1898): Quoted by Craver and Binkley (1938).

Solis-Cohen, M. (1933): Quinine in the pneumonias of infancy and childhood, M. Clin. North America 17 787.

Stähelin, F. (1919): Quoted by Craver and Binkley (1938).

Stein, P. (1951): Personal communication.

Sternberg, G.M. (1880): Quoted by Smeall (1948).

Stewart, D. (1930): Lung puncture in acute lobar pneumonia, Lancet 2 520.

Stewart, F. (1933): The diagnosis of tumours by aspiration, Am. J. Path. 9 801.

Talamon, L. (1883): Quoted by Thomas and Parker (1920) and by Smeall (1948).

Tchistovitch, N. (1904): Quoted by Thomas and Parker (1920).

Terrell, E., Robertson, O., and Coggeshall, L. (1933): Experimental pneumococcus lobar pneumonia in the dog, J. Clin. Investigation 12 393, 433, 467.

Thatcher, J.S. (1913): Quoted by Pickhardt (1928).

Thomas, H., and Parker, F. (1920): Results of antemortem lung punctures in lobar pneumonia - their bearing on the mechanism of crisis, Arch. Int. Med. 26 125.

Ulbrich, E. (1936): Contribution to the Quinine-Calcium prophylaxis and therapy of post-operative pneumonia, Zentralbl.f. Chir. 63 2244.

Waddell, W., et al. (1949): Chronic pneumonitis: its clinical and pathologic importance, J. Thoracic Surg. 18 707.

Waldvogel (1906): Quoted by Craver and Binkley (1938).

Weinstein, A. and Goodman, M. (1934): Delayed resolution in lobar pneumonia and its relationship to preëxisting syphilis, Am. J. M. Sc. 188 716.

Wilson, T.E. (1945): Aspiration biopsy, M. J. Australia 1 268.

Wood, W. (1946): Surface phagocytosis - its relation to the mechanism of recovery in pneumococcal pneumonia, Science 104 28.

Wood, W. (1947): The mechanism of recovery in acute bacterial pneumonia, Ann. Int. Med. 27 347.

Wood, W. and Irons, E. (1946): Studies of the mechanism of recovery in pneumococcal pneumonia: the effect of sulphonamide therapy upon the pulmonary lesion of experimental pneumonia, J. Exper. Med. 84 365.

Wood, W., McLeod, C., and Irons, E. (1946): Studies of the mechanism of recovery in pneumococcal pneumonia: factors influencing the phagocytosis of pneumococci in the lung during sulphonamide therapy, J. Exper. Med. 84 377.

Wood, W., Smith, M., and Watson, B. (1946): Studies of the mechanism of recovery in pneumococcal pneumonia: the mechanism of phagocytosis in the absence of antibody, J. Exper. Med. 84 387.

Wrenn, F., Feder, J., and Anderson, S. (1942): Aspiration biopsy - further observations with an improved instrument, Surgery 2 456.

Youmans, J., and
Kampmeier, R. (1927): Preëxisting syphilis as cause of unresolved pneumonia and a factor in the production of certain other postpneumonic complications,
Am. J. M. Sc. 174 750.

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