

L O B A R P N E U M O N I A

A Bacteriological and Clinical Investigation

of 100 Cases

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INTRODUCTION

The work on which the following thesis is based was carried out in Knightswood Hospital, Anniesland, during the later months of 1929, and in the Spring of 1930. The work comprises a short resume of the types of pneumococci at present recognised. A clinical analysis of one hundred cases of lobar pneumonia with special reference to the type of pneumococcus present. An investigation into the persistence of pneumococci in the sputum of patients during convalescence, and, finally, a study on the significance of a bacteraemia in cases of lobar pneumonia in relation to prognosis.

I N D E X

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SURVEY of the WORK on the PNEUMOCOCCAL TYPES

The organism which is now regarded as the *Diplococcus Pneumoniae*, was first isolated by Pasteur from the saliva of a case of rabies. To this organism which produced a fatal septicaemia in rabbits he applied the term 'microbe septicémique du salive'. At the same time, though quite independently, Sternberg detected a similar organism in the mouths of healthy individuals. But it was not till 1886 that Weichselbaum established its importance as a cause of pneumonia. Since then, the characteristics of the pneumococcus have been widely investigated, and chiefly through the early work of Neufeld and his associates the serological differences were recognised. This latter work was extended by the research workers of the Rockefeller Institute, who demonstrated, that the pneumococcus could be classified into two groups. The former of these consisted of pneumococci of Types I, II and III, which represented between 70% and 80% of the strains met with in disease, and which represented three apparently fixed types of highly parasitic organisms. The second and smaller group was composed of a collection of organisms, morphologically pneumococci, which gave no reaction with the type sera prepared against the other fixed strains.

In 1915 in an investigation on Type II, Avery found that certain strains gave what he described as an atypical reaction with the antipneumococcal serum of Type II. As a result of his work, he divided these atypical strains into three groups, namely, Group IIA, IIB, and IIX. The first two sub-groups he found were characterised by the possession of immunity-reactions identical with those of all other strains of the homologous sub-groups, and that these reactions were specific only within the sub-group. The sub-group IIX. was peculiar, in that it seemed to consist of a heterogeneous series of independent strains, which did not cross in their immunity reactions with the members of the other two sub-groups, or with each other. By absorption and protective tests he further demonstrated the specificity of his sub-groups especially IIA, and IIB. Stillman, who examined 204 atypical Type II strains classified them into twelve distinct groups on the basis of agglutination. According to this worker atypical groups are occasionally met with in normal mouths. In more recent work on these sub-groups, doubt has been cast on the reliability of the precipitin formation as a basis for subdivision, and in this country there is the tendency to classify such strains as variations of Group IV.

As attempts have been made to demonstrate sub-groups in Type II, so attempts have been made from time to time to

subdivide Group IV. In 1928 Cooper, Edwards and Rosenstein, carried out an investigation of 120 strains from cases of lobar pneumonia which did not agglutinate or react atypically with any of the diagnostic antisera. Monovalent antisera were prepared and agglutination tests carried out. By this means the 120 strains were divided into 10 groups. These groups of organisms were all in turn investigated as regards virulence, and it was found that certain strains tended to be much more virulent as tested on mice than some of the other strains. Further, protection tests were carried out with a concentrated antibody preparation of Types I, II and III, and a homologous antiserum prepared for the particular strain. In all cases, the protection afforded by the homologous serum was much greater than that produced by the antibody preparations of Types I, II and III, which were almost always negligible. Cooper, Edwards and Rosenstein, further showed that their Groups V. and VI. corresponded to Avery's Sub-groups IIA and IIB. The identity of several of the strains has been confirmed by other workers.

Thus there are at present three fixed types for which agglutinating sera are available, and a Group IV, the members of which so far as they have been isolated react only with their homologous serum.

TECHNIQUE EMPLOYED for the DETERMINATION of the
PNEUMOCOCCAL TYPES

For the isolation and identification of the pneumococcus mouse inoculation was almost solely employed. By this method, the presence of associated organisms is not so well demonstrated as by primary plate culture, but as this latter aspect was not under consideration, mouse inoculation was the method adopted. As far as possible white mice were used but occasionally they had to be replaced by coloured mice.

In the great majority of cases the material used was sputum obtained from patients either on admission or during convalescence. In other cases purulent fluid from pleural cavities, or fluid obtained by lung puncture was used to obtain the organisms. Specimens of blood were generally inoculated directly into suitable fluid media.

The following were the methods employed for the isolation of the pneumococci and determination of the specific types.

(I) Collection and preparation of:-

A. Sputum.

The specimen of sputum was collected in a sterile cup and immediately sent to the laboratory. A small portion was chosen, preferably rusty, and with reasonably sterile

precautions was washed in several changes of normal saline. To carry out these washings, a portion of the sputum was placed in a small glass mortar and gently mixed with a little saline. By means of a glass pipette the undissolved sputum was removed to a clean mortar where the process was repeated. In this way, the specimen was as far as possible freed from contamination with mouth organisms. Altogether about 5ccs of saline were used in the process of washing. To complete the emulsifying, the washed sputum was repeatedly drawn up into a small syringe and expelled through a medium sized needle. In this way an emulsion sufficiently fine to pass through a hypodermic needle was obtained. Finally, about 5ccs of the emulsion was drawn up into a syringe for injection into a mouse. In cases where the sputum was very thin the number of washings was reduced to one or two.

B. Empyema Pus.

Direct smears were first made in every case and the presence of gram positive diplococci ascertained. In positive cases, the pus was emulsified in a little saline and used for mouse injection.

C. Lung Juice Culture.

In cases where sputum was not available, usually on account of the age of the patient, lung puncture was adopted as a means of obtaining the organisms. To carry this

out, the skin of the patient over the affected area was rendered surgically clean. The syringe which was used was a 5cc syringe fitted with a medium sized needle, about No.18 gauge. Before the needle was inserted 1cc of sterile normal saline was drawn up into the barrel. The needle was then thrust into the consolidated area and the saline slowly injected. Steady suction was then applied and a varying amount of blood stained fluid was drawn into the syringe. This fluid was transferred to a small sterile test tube and taken to the laboratory where a mouse was immediately injected.

D. Blood.

To obtain blood, the usual procedure of inserting a needle into the median basilic vein and drawing the blood into a syringe was adopted. Only 2ccs of blood were withdrawn, and it was immediately injected into 15ccs of a 1% Glucose broth. The method of preparing the broth was as follows:-

To 1 lb. of fresh ox flesh finely minced, and free from fat 1000 ccs of distilled water were added. This was kept in a cool place for 24 hours, when the fat which had risen to the surface was removed. The meat juice was then filtered through muslin into a flask, care being taken to express as much of the fluid from the meat as possible. The resulting fluid was boiled for three hours, by which process the albuminous material present was coagulated. When cool,

it was filtered through Chardin filter paper, made up to 1000 ccs with distilled water and .1% of glucose added. As the media at this stage had a very acid reaction, the P.H. was standardised to 7.8 by the addition of deci-normal sodium hydrate solution, phenol red being used as an indicator. The media was then put into tubes and sterilised at 100°C on three successive occasions.

(II) Mouse Inoculation and Autopsy

To carry out the inoculation the mouse was held in the left hand in such a way that the abdominal wall was freely exposed. The part was then cleaned with spirit, and .5ccs of the infected material injected. Thereafter the mouse was isolated in a special jar.

In practically every case the mice were dead, or sufficiently ill for one to expect a profuse growth of pneumococci inside eighteen hours. At the autopsy, the dead mouse was pinned out and the abdomen singed with a spatula. The skin was then reflected exposing the whole of the peritoneal surface. A small opening was made in the abdominal wall and by means of a pipette and rubber teat the abdominal cavity was washed out with 5ccs of sterile normal saline. To get rid of any gross material in the washings the fluid was centrifuged at low speed for a few minutes. The supernatant cloudy fluid was then pipetted off into another tube and centi-

fruged at high speed for 15 to 20 minutes. After removing the clear supernatant fluid, normal saline was added to the deposit of organisms to form a fairly heavy emulsion. This emulsion was used for typing with antipneumococcic serum and for the bile solubility test.

(III) Determination of the Types of Pneumococci.

The first step in the determination of the type was the preparation of a film from the saline emulsion. This was stained by grams method and the presence of gram positive diplococci verified. If the film showed a fair number of diplococci the following tests were carried out.

A. Agglutination method

The antipneumococcic serum used throughout the experiments was supplied by Mulford & Co. of Philadelphia. The dilutions which were used are shown in the table below.

TABLE I.

10 drops of undiluted				Type I. serum plus 10 drops of				emulsion.
10	"	"	1:5 dilution	"	I.	"	"	10
10	"	"	undiluted	"	II.	"	"	10
10	"	"	1:5 dilution	"	II.	"	"	10
10	"	"	undiluted	"	III.	"	"	10
10	"	"	1:5 dilution	"	III.	"	"	10

(Following their directions the tubes were incubated in a

water bath for one hour at 37 C.)

From time to time controls with sera produced by the Lederle Antitoxin Laboratories New York were used and the results in all cases conformed with the results obtained with Mulford & Co's sera. Further, in a number of cases the Type I. serum prepared by Burroughs Wellcome & Co. was used as a control. This latter serum was found to be much more potent than the American preparations.

B. Bile Solubility Test.

The bile solubility test was carried out in the same rack and at the same time as the agglutination test. The preparation used was a 2% solution of sodium taurocholate. The method adopted is shown in Table II.

TABLE II.

2	drops	of	2%	sol.	sod.	taurocholate	plus	8	drops	emulsion.
2	"	"	saline	"	"	"	"	8	"	"

OBSERVATIONS on the IDENTIFICATION of the
PNEUMOCOCCUS

The following interesting points were observed during the work on the identification of the pneumococcus.

(I) Time between injection and mouse autopsy

As illustrating the susceptibility of mice to inoculation with sputum containing pneumococci, it was found that the average time for the mice to die or to appear sufficiently ill to give a good growth, varied between 16 and 30 hours. These figures are of course for the injection of sputum obtained from patients at the height of the disease, for, when sputum from convalescent cases was injected, the mice in some cases survived for a slightly longer period. Glynn and Digby in their report to the Medical Research Council gave as an average period for the mice to die after injection as 27.7 hours for the fixed types, and 31.1 hours for Group IV.

(II) Growth of pneumococci obtained from the mouse
peritoneal cavity.

Since the same amount of fluid was used for washing out the peritoneal cavities of the mice, a rough estimate of the growth could be obtained from the appearance of the fluid.

In the great majority of cases the emulsion was quite milky and ample for typing and the bile solubility test. There were those cases, however, where the washings were only slightly coloured. These, on microscopic examination were found to consist, either of a pure but scanty growth of pneumococci, or were due to a mixed infection. The latter were met with occasionally when the sputa from convalescent cases were examined.

(III) Bile Solubility.

This test was applied to every strain of pneumococcus and was definitely positive in all but a few cases. In these few cases examination of the tubes showed that partial clearing had occurred. Two strains however, the identity of which was confirmed by Burrough Wellcome's serum in a dilution of 1 in 30, were insoluble in the sodium taurocholate solution.

(IV) Macroscopic Agglutination.

As previously stated the serum used was prepared by Mulford & Co. of Philadelphia. The reactions which occurred were always quite definite, though the time for agglutination to take place and the amount of agglutination varied slightly according to the age of the serum. When fresh batches of serum were used the reactions occurred immediately the

emulsion of organisms was added to the serum. At no time did cross agglutination occur even though pure serum was used in certain of the tubes.

(V) Stained slide, "Microscopic Agglutination Test".

In addition to the foregoing, a microscopic agglutination test was carried out in conjunction with the macroscopic test. This slide method has recently been advocated by workers in America, who hold that it is equally as accurate as the older method. The procedure in carrying out the test is as follows:-

A glass slide was marked off into four parts with a blue pencil. On to each a loopful of the bacterial emulsion to be tested was placed. The first space was then smeared with a loopful of Type I. antipneumococcal agglutinating serum, the second with Type II. serum, the third with Type III. serum and the fourth with saline as a control. The smear was made thin so that it dried rapidly. It was then stained for half a minute with a 10% solution of carbol fuchsin, washed in water and dried. Extra care had to be exercised in the washing of the slide as the films were very easily washed off. On examination, the specimen if positive for any one of the fixed types showed agglutination for the corresponding anti-serum, as evidenced by close clumping together of the organisms. Sometimes in the saline control the organisms showed a certain

amount of gathering together, but at no time did it cause any difficulty in the recognition of the presence or absence of specific agglutination. In no instance did cross agglutination occur as evidenced by the appearance of clumping in more than one section of the slide. When compared with the macroscopic method it was found to agree in every case. The method has the advantage of being simple and little serum is required.

CLINICAL INVESTIGATION of the
SEROLOGICAL TYPES

(A) Type Incidence

In the present series 100 cases were investigated. These were not confined to any particular age group, save, that no case over sixty years of age was included, but were selected according to the distribution of the pneumonic condition in the lung. As far as possible, only cases with a lobar distribution were included. All cases clinically pneumonia, but where tubercle bacilli were found in the sputum were excluded. As there was no influenza prevalent at the time when the investigations were made the difficulty in differentiating the pneumonic consolidation occurring in that condition did not arise. Further, cases where the pneumococcus could not be isolated were excluded from the series, so that all the cases chosen for examination were pneumococcal in origin.

As a result of the serological tests pneumococci belonging to the three fixed types were found to be present in the majority of the cases. In the remainder, pneumococci were obtained which gave no reaction with the agglutinating sera of the fixed types and which were accordingly regarded as Group IV. organisms. The incidence of these various strains

of pneumococci in the present series is shown in Table III.

TABLE III.

Incidence of the types in 100 Cases
of Lobar Pneumonia

<u>Type I.</u>	<u>Type II.</u>	<u>Type III.</u>	<u>Group IV.</u>
38	35	4	23

As stated above, these figures include all age groups, so that for comparison with other figures where adults alone were examined all cases occurring in children will have to be excluded. If therefore, all ages up to fifteen years are excluded, then the percentage incidence of the various types among adults will be as shown in Table IV.

TABLE IV.

(Type incidence among Adults)

<u>Type I.</u>	<u>Type II.</u>	<u>Type III.</u>	<u>Group IV.</u>
33.8%	38.4%	4.6%	23%

When these figures are compared with the average British figures it will be found that there is a diminution in Type I. and Group IV, and an increase in Type II. This difference is not so marked however, when the average British figures are compared with the figures in Table III.

TABLE V.

Average British figures for Incidence
of the Types

<u>Type I.</u>	<u>Type II.</u>	<u>Type III.</u>	<u>Group IV.</u>
38.2%	30.8%	3.9%	27%

In 1920 Dr Grant in the City of Glasgow Hospital, Ruchill, examined a series of cases and found that Type II. organisms were present in about 50% of cases. Davidson and McLachlan in Edinburgh found that in their cases Type I. predominated, being present in 64% of cases. Griffith in 1920, in a district in England investigated the presence of the pneumococcal types, and at a later date he investigated a further series of cases in the same district. He found, that while Type I. remained fairly constant in the two occasions, Type II. and Group IV. showed a marked alteration. On his first examination Type II was present in 32.6% of cases, while at the second examination the incidence had fallen to 7.4%. There was a corresponding alteration in the incidence of Group IV. Armstrong in 1921 in a small series of cases found Types I. and II. present in a very high proportion, while Group IV. was markedly reduced.

Turning now to the cases of 15 years and under, which were not included in Table IV, it was found that there was

quite an appreciable difference in the incidence of the types, compared with the figures for the later years of life. As will be seen from Table VI. there was an increase in Type I. and a fall in Type II, while Group IV. remained very much the same.

TABLE VI.

Incidence of Types in 35 children
(15 years and under)

	<u>Type I.</u>	<u>Type II.</u>	<u>Type III.</u>	<u>Group IV.</u>	(Total)
No. of cases.	16	9	1	9	35
%	45.7	25.7	2.8	25.7	

The high incidence of Type I. in Table VI. may be related to the fact that in about 30% of the cases the organisms were obtained by lung puncture.

It would therefore seem that variations in the prevalence of the fixed types may occur in different districts though the figures for the whole country remain fairly even, and that in any one district a variation in the type may occur from time to time.

(B) Clinical Analysis.

As shown in Tables III and IV, the cases in the present series could be classified into four groups, according to the serological reaction of the organisms present. An

attempt was therefore made to discover if this classification could be distinguished by clinical examination.

Age Group

The first point to be investigated in this analysis was the incidence of the types in the various age groups.

TABLE VII.

<u>Age</u>	<u>Type I.</u>	<u>Type II.</u>	<u>Type III.</u>	<u>Type IV.</u>	<u>Total</u>	<u>Mortality</u>
1 - 5	5	-	-	3	8	1
6 -10	5	5	1	4	15	-
11-15	6	4	-	2	12	-
16-20	6	9	1	7	23	-
21-25	2	6	1	2	11	2
26-30	6	4	-	2	12	3
31-35	-	4	1	-	5	3
36-40	4	-	-	2	6	-
41-45	1	1	-	-	2	-
46-50	1	1	-	1	3	-
51-55	-	1	-	-	1	-
56-60	2	-	-	-	2	-

As will be seen from Table VII. the greatest number of cases occurred between the ages of 16 and 30, that is, in the second fifteen years of life. The next largest age group was that

from 1 to 15 years. These figures are slightly lower than the results given in the Medical Research Council Report in 1923 where the greatest incidence was placed between the 20th and 40th years. When each five years was separately considered, the greatest number occurred between the ages of 16 and 20. As regards the incidence of the various types, it was found that under the age of five years Type I. and Group IV. organisms predominated. Thereafter the only point of interest was the predominance of the fixed types over Group IV. for any of the age groups, save in the age group 16 to 20 where a fairly large number of Group IV. cases were met with.

Time elapsing between onset and admission to hospital.

The next point investigated was the period of time elapsing between the onset of the condition and admission to hospital, with a view to finding if the onset of any one of the types, being more severe than another, would be indicated by a shorter time elapsing before admission to hospital. When worked out it was found that only a very slight difference existed between the types. But, small as the difference was, it shewed that in Group IV. cases a slightly longer period elapsed than in the cases due to the fixed types. The actual figures are shown in Table VIII.

TABLE VIII.

Average number of days between onset and
admission to hospital

	<u>Type I.</u>	<u>Type II.</u>	<u>Type III.</u>	<u>Group IV.</u>
Days.	3.73%	3.5%	4%	4.2%

Previous History

The number of cases in the present series giving a history of previous attacks of respiratory disease was relatively small. As will be seen from Table IX, 12% gave a history of previous attacks of pneumonia, 8% a history of bronchitis, 1% a history of influenza and 1% a history of pleurisy, giving a total of 22% with a history of previous respiratory disease.

TABLE IX.

Incidence of Previous Respiratory
Disease

	<u>Type</u> <u>I.</u>	<u>%</u>	<u>Type</u> <u>II.</u>	<u>%</u>	<u>Type</u> <u>III.</u>	<u>%</u>	<u>Group</u> <u>IV.</u>	<u>%</u>	<u>Total</u>
Pneumonia.	6	15.7	2	5.7	-	-	4	17.3	12
Bronchitis.	2	5.2	3	8.6	-	-	3	13	8
Pleurisy...	-	-	1	2.8	-	-	-	-	1
Influenza..	-	-	1	2.8	-	-	-	-	1

When separated out according to the various types, it was observed, that while there was little difference in the total incidence of previous respiratory disease in Types I. and II, there was a slightly greater incidence in Group IV. When the individual diseases were separately considered, it was found that pneumonia occurred less frequently in Type II. than in the other types and that bronchitis occurred with greater frequency in Group IV.

It is of interest too, that of the cases in Group IV. in which a history of pneumonia was obtained, all had had two or three previous attacks, while in the fixed types no case had more than one previous attack of pneumonia.

As it was difficult in many instances to obtain an accurate history in the case of children, the incidence of previous respiratory disease was calculated in the adults alone, and it was found that a greater proportion of these had suffered from previous respiratory disease than the figures in Table IX. would indicate. In Types I. and II. the incidence was 27.2% and 30.7%, and in Group IV. 42.8%. These latter figures are in keeping with the results of the Johns Hopkins Hospital where the incidence in Group IV. cases was likewise much greater than in any of the other types. There was only a slight difference in their figures between the fixed types.

From these figures it would seem that where there is

a history of previous respiratory disease, especially a history of several attacks of pneumonia, individuals are more likely to be affected by a Group IV. organism.

Initial Symptoms.

In eliciting the history, the patients were allowed as far as possible to relate the facts in their own words. When they were too ill on admission to give a complete account, the facts were amplified as soon as convalescence had begun. In the case of children who were often too young to give an accurate history the details were obtained from relatives.

Taking first the symptoms of patients under sixteen years of age, it was found that the commonest symptoms were vomiting, pain in the side, cough, headache and shivering. The incidence of vomiting and pleuritic pain was slightly greater in the fixed types than in Group IV. With these exceptions the initial symptoms showed little difference between the various types. Among the adults, the order of frequency of the initial symptoms was slightly different from that under sixteen years of age. In the adult age group pleuritic pain and shivering were the commonest symptoms and vomiting occurred less frequently in this than in the younger age group. These symptoms in the order of their frequency are shown in Table X.

TABLE X.
Incidence of initial symptoms

	Under 16 years per cent	Adults per cent	Incidence in adults according to type			
			Type I.	Type II.	Type III.	Group IV.
Pleuritic pain.....	48.5	63	63.6	68	100	46.6
Shivering...	31.4	60	72.7	56	66	53.3
Vomiting....	68.2	44.4	50	40	-	53.3
Cough.....	42.8	36.9	40.9	40	33	26.6
Headache....	40	36.9	36.4	40	66	40
Abdominal pain.....		4.6	9.1	4		
Pain in shoulder..		4.6	-	8		6.6
Pain in back		7.2	9.1	8		6.6
Dyspnoea....		4.6	9.1	4		
Epistaxis...		3	4.5			

When the various types were compared, shivering, pleuritic pain and cough were found to occur more frequently in the fixed types than in Group IV. The only one symptom which was definitely more frequent in one type than another was shivering, and this as shown in Table X. occurred in 72.6% of the cases in Type I.

There is thus little or no evidence, apart from the

incidence of shivering in Type I, that any train of symptoms is more characteristic of one type than another.

Temperature.

As all the cases were treated in hospital a few days had to elapse in most cases ere the patients came under observation, so it was impossible to ascertain the temperature at the onset of the illness. It was found however, that at the time of admission fully 70% of the cases had a temperature over 102°F. Between the types there was little or no difference, even the cases in Group IV. had temperatures equally as high as the fixed types. When the temperatures during the course of the illness were examined, it was found that in Type I. cases, the temperature showed less tendency to remissions and maintained a slightly higher level than in the other types.

With regard to the termination of the pyrexia 58% ended by crisis and 39% by lysis. In the former group the majority of the cases reached the normal level within twelve hours, in the remainder the crisis extended over twenty four hours. Of the cases ending by lysis the majority reached the normal level in from three to four days. When the individual types were examined, no marked difference existed as to the frequency with which crisis occurred.

The day on which the crisis occurred was next investigated, and it was found that the greatest number

occurred on the seventh day. Of the other days, the sixth and ninth had a slightly higher incidence than the fifth and eighth. As will be seen from Table XI. the cases in Type II. tended to terminate by crisis earlier than in the other types.

TABLE XI.

Time of Crisis

<u>Day of Crisis</u>	<u>Type I.</u>	<u>Type II.</u>	<u>Type III.</u>	<u>Group IV.</u>	<u>Total</u>	<u>Percentage</u>
4						
5		6		1	7	12.1
6	6	4		1	11	19
7	3	5	2	6	16	27.5
8	4	3		2	9	15.5
9	6	2		3	11	19
10	3	1			4	6.9

From an examination of the temperature charts there was no outstanding difference between the various types. Cases were met with in all types where the temperature ran a high and continuous course and ended by crisis in a few hours. But as previously stated, over all cases, there was a greater tendency for remissions to occur in the temperatures in cases in Type II. and Group IV. than in cases belonging to Type I.

Pulse Respiration Ratio.

The pulse respiration ratio is usually held to be about 1:3 in cases of lobar pneumonia. In the present series fully 70% of the cases had a pulse respiration ratio between 1:2.6 and 1:3.7. Only 7% had a ratio greater than 1:2.6. Abraham in his series of cases found that the ratio varied between 1:3 and 1:4.5 . In only 12% of his cases did he meet with a ratio of 1:2 or 1:1;5.

The only point of note between the types was a slightly greater percentage of Type I. cases with a ratio of 1:3 or greater.

Distribution of Pneumonic Areas.

The distribution of pneumonic areas was next considered and it was found that the right lung was involved in 53% of the cases and the left lung in 47%. These figures differ slightly from those published by Osler, who found at 100 autopsies that the right lung was involved in 51%, the left lung in 32% and both lungs in 17%. Jaugensin, in a series of 6,666 cases found the right lung involved in 53.7%, the left lung in 38.2% and both lungs in 8%.

Though little difference existed as to the particular lung involved there was a considerable variation in the lobar involvement. In the left lung the upper lobe was involved in 2% of the cases while the lower was involved in 45% of the

cases. In the right lung the upper lobe was involved in 23% and the lower lobe in 30%.

When the age groups 1-15 and 16-60 were considered, it was found that in both groups the left lower lobe was more often involved than the right lower lobe, and that the right apex was much more commonly affected than the left apex. It was also observed that the upper lobes were more often affected in the younger age group than in the older age group. The actual incidence in the two groups was 31.5% and 20.1% respectively.

Between the various types there was no marked difference as to which lung was involved. In Type I. cases the left lung was slightly more often affected than the right. In Type II. the reverse was the case, while in Group IV. cases the lungs were involved with the same frequency.

Sputum.

The presence or absence of sputum in cases of pneumonia varies to a considerable extent with the age of the patient. Among the adults in the present series no difficulty was met with in obtaining sputum; but, among the children, where the sputum was often very slight and they were unable to expectorate, considerable difficulty was experienced in obtaining material, for, in a number of initial experiments where the saliva from young children was used, the mice which were

injected invariably survived. However, with a good deal of persuasion it was often possible to get the children to cough, when more suitable material was obtained. This however was not always so, for in one case, where, after persuasion a small pellet of muco-purulent material was coughed up examination showed the presence of a Group IV. organism. The sputum was examined one week later and a Group IV. organism was again obtained. When however, the case was again examined, this time when convalescence was well established and material for mouse inoculation was obtained by lung puncture, a Type I. organism was obtained. In one other case, initial examination of the sputum from a child gave a negative result on mouse inoculation. During convalescence the child developed a second attack of pneumonia, and when lung puncture was performed Type I. organisms were obtained. It would seem therefore that the examination of the sputum especially in children is not an entirely reliable method of isolating the pneumococcus. In Table XII. there are shown the varieties of sputum which were met with and the incidence in which they occurred. As will be seen, blood stained sputum was obtained in 63% of the cases. This compares closely with the figures given in the Medical Research Council Report 1923, where in the series of cases examined 63.9% had blood stained sputa. The remaining 37% in the present series were made up of cases where the

sputum was either muco-purulent or mucoid, or where no sputum was available.

TABLE XII

Incidence of Blood stained Sputum

<u>Nature of sputum</u>	<u>Type I.</u>	<u>Type II.</u>	<u>Type III.</u>	<u>Group IV.</u>	<u>Total & %</u>
Blood stained.....	23	27	4	9	63
Muco purulent.....	9	6		8	23
Mucoid.....	1	2		5	8
No sputum.....	5			1	6
Total	38	35	4	23	100
Percentage of Blood stained sputum....	60.5	77.1	100	39.1	

Between the different types considerable variation existed in the incidence of blood stained sputa. In Type III. all the cases had blood stained sputa. In Type I. and Type II. the incidence was 60.5% and 76.4% respectively, while in Group IV. the incidence was 41.6%. When the adults of the series were alone considered the incidence of blood stained sputa was 80%; of this number 67.9% were associated with cases belonging to Types I, II and III, while only 12.3% were associated with cases belonging to Group IV.

The duration of the rusty sputum was found to be very variable, in some cases it lasted for only one day, in other cases it lasted for five or six days after admission.

From these figures it would seem that a blood stained sputum occurs much more frequently among adults than among children, and that it is more often associated with pneumococci of the fixed types than with pneumococci belonging to Group IV. Further, that the presence of a Group IV organism in the sputum need not necessarily indicate that the pneumonic condition in the lung is due to that particular strain of pneumococcus, and not to one of the fixed types.

Herpes Labialis.

Herpes labialis was present in 10% of the cases. This figure is low compared with those given by Osler who found that herpes occurred between 12% and 40% of his cases. Geissler in a series of 421 cases found herpes present in 43.2% of the cases. Of the 10 cases in the present series 8 belonged to Type I, 1 to Type II, and 1 to Group IV. It is of interest that herpes did not occur in any of the cases which had a fatal termination.

Complications.

The first important complication met with was empyema and it occurred in 3% of the cases. Compared with the previous winter in this hospital the figure was very low, for, over a similar number of cases admitted as pneumonia,

thirty cases of pneumococcal empyema were met with. The incidence, however, in the present series approximates closely to the published figures of different workers. Mackenzie in his series placed the percentage of cases with empyema at 3.4%. Meeson and Moris in a fairly large number of cases found that empyema occurred in 2.2% of the cases.

With regard to the type of pneumococcus giving rise to the complication two of the cases were due to a Type I. pneumococcus and one to a member of Group IV. In all three cases the organism present in the pus from the empyema cavity was the same as that obtained from the sputum. These cases after initial aspiration had all to be operated on and a portion of rib resected. They all made a good recovery.

Though there were too few cases of empyema to express any opinion regarding the mortality in such cases, it is of interest that no deaths occurred among the thirty cases which were met with in the winter 1928-29. The treatment in these cases consisted of aspiration and where this did not suffice rib resection was performed. In only one or two cases was aspiration sufficient, the great majority having to be operated upon.

The next complication which was met with was meningitis. This occurred in two cases. The first case was a man aged 35 who was admitted on the fourth day of illness.

The initial history was of a sudden attack of shivering, followed by headache and pain in the side. When admitted to hospital his chief complaint was of severe pain in his head. On examination, there was in addition to the pneumonic condition in the lung evidence of meningeal involvement. From the sputum which was blood stained a Type III pneumococcus was obtained. When lumbar puncture was performed very turbid fluid under pressure was withdrawn. This was inoculated into a mouse and the same type of organism as was present in the sputum was obtained. The blood culture in this case showed the presence of a definite bacteraemia. The condition of the patient gradually became worse and he died three days after admission.

The second case was a patient aged 22, who was admitted on the fourth day of illness. The history which he gave was of a sudden attack of shivering, followed by headache and pain in his side. On examination, there was evidence of a pneumonic condition with a considerable amount of pleurisy in the upper part of the right lung. From the sputum which was muco purulent in appearance a Group IV. pneumococcus was isolated. The illness ran a typical course and the temperature fell by crisis on the seventh day. Two days later the temperature began to rise, and as the patient had no complaint the onset of an empyema was considered as a possible explanation

of the temperature. When the chest was examined the physical findings were not at all confirmatory of this as the cause of the temperature. On the following day slight headache developed, which in spite of treatment became more severe. This, along with the elevated temperature suggested involvement of the nervous system, so that lumbar puncture was performed, when 30ccs of faintly turbid fluid under pressure were withdrawn. The operation was again performed on the following day when the fluid was found to be more definitely turbid. Examination of the fluid showed the cells present to be polymorpho nuclear leucocytes, and when a mouse was inoculated Group IV organisms were obtained. The condition of the patient rapidly became worse in spite of repeated lumbar puncture, and death ensued some days later.

The third complication was meningismus, and this like the previous complication occurred in only two cases. The first case in this group was a man aged thirty who was admitted to hospital on the second day of illness. When examined he appeared acutely ill and there was evidence of a commencing pneumonia in the lower lobe of the right lung. The sputum was a typical rusty sputum from which after mouse inoculation a Type I pneumococcus was obtained. On the following day the pneumonic condition in the lung was quite definite, and was associated with a considerable amount of pleurisy.

During the fourth day of illness he had several attacks of sickness and complained of slight headache. In spite of treatment the headache became very much worse, and when a slight amount of rigidity of the posterior muscles of the neck developed, meningitis was suspected. He was in consequence lumbar punctured and 40ccs of clear fluid under considerable pressure were removed. This gave temporary relief to the patient, but with the recrudescence of the severe headache he was lumbar punctured on the following day. On this occasion 40ccs of fluid still under increased pressure were withdrawn. Next day the temperature which had maintained a fairly even level at about 103°F fell by crisis. Thereafter the patient made an uninterrupted recovery.

As previously stated examination of the sputum revealed a Type I organism as the cause of the pneumonic condition. Blood culture in glucose broth gave a negative result as did also injection of the spinal fluid into a mouse.

The second case was a man of thirty, who was admitted on the third day of illness. He appeared acutely ill, and examination revealed definite consolidation in the lower lobe of the right lung with a certain amount of pleural involvement. In addition to pain in his side he complained of slight headache. On the following day the headache became so severe that he could not lie still in bed. He had no sickness, and

the rigidity of the nucelial muscles was only very slight. When lumbar puncture was performed, 35ccs of clear fluid under very marked pressure were removed. This temporarily relieved his headache, but on the following day the lumbar puncture had to be repeated when 45 ccs of clear fluid still under increased pressure were withdrawn. After this the headaches began to diminish in severity. During the succeeding day and a half, the temperature, which had maintained a high level fell to normal. To find if any change in the spinal fluid had occurred coincident with the rapid lysis, the patient was again lumbar punctured when the temperature had reached the normal level. It was found that the pressure as estimated by the rate of out flow from the needle had practically returned to normal. In this case like the former one, mouse inoculation with the spinal fluid gave a negative result.

These cultural results are of interest when compared with those in the cases of meningitis where positive cultures were obtained from the spinal fluid in both cases and from the blood in one of the cases. Further, of the four cases showing involvement of the nervous system, either as meningitis or as meningismus, two were due to organisms of the fixed types, while two were due to organisms belonging to Group IV.

Delirium.

The fourth complication met with was delirium and it occurred in varying degree in 19% of the cases. For purposes of description the degree of delirium has been classified as severe, moderate, and slight. In the severe cases the patients were very noisy and had to be forcibly restrained in bed. In the moderate cases they were talkative and at times tried to get out of bed. In the third group are classified those cases which were subject to a low muttering and were restless. Based on this classification of severity it was found that 3% of the cases were severe, 6% were moderate and 10% were slight. While all the cases in the first group ended fatally there were no deaths in the other two groups.

Between the various types slight differences existed. In Type I. there were seven cases of delirium, one of these was severe, four were moderate and two were slight. In Type II two cases were severe, one was moderate and five were slight. In Type III only one case showed slight delirium. In Group IV there were no cases with severe delirium, only one had moderate delirium and two slight delirium.

From these figures it will be seen that while slight differences existed between Types I. and II. there was a diminution both in the number of cases affected and the severity of the delirium in Group IV compared with the fixed types.

Mortality

The death rate from lobar pneumonia in this country has been shown by Glynn and Digby and others, to correspond fairly closely to that in America. Even the rates for the individual types roughly correspond. In the American figures Type III, though giving rise to the smallest number of cases is yet associated with the greatest fatality compared with the other types. As this particular strain occurs much less frequently in this country its importance is consequently not so great. Type II. in both countries gives rise to a slightly higher death rate than Type I, while the lowest rate is caused by members of Group IV.

In the present series the death rate irrespective of type incidence was only 9%. This figure is much lower than the average either for this country or America. But it resembles fairly closely the mortality in a series of cases examined by Abrahams who found that in 558 cases there was a death rate of 10%.

When the death rate was subdivided according to the incidence in the various types, it was found that the greatest percentage occurred in Type III, while as will be seen from Table XIII, the percentage rate for the other types was practically equal.

TABLE XIII.

Percentage Death rate

<u>Type</u>	<u>Total No. of Cases</u>	<u>No. of deaths</u>	<u>Percentage death rate.</u>
I.	38	3	7.9
II.	35	3	8.6
III.	4	1	25
IV.	23	2	8.6

The death rate was next applied to the various age groups, and it was found that in the age group 1 to 15 there was one death, in the age group 16 to 30 there were five deaths, and in the age group 31 to 45 there were three deaths. When each five years was separately considered, the greatest number of deaths occurred in the two age groups 26 to 30 and 31 to 35. As there were twelve cases of pneumonia in the first of these age groups, and five in the second, and as three deaths occurred in each group it was found that the greatest mortality lay in the age group 31 to 35. When other age groups were considered for the purposes of comparison, it was found that in the age group 21 to 30 the death rate was 21.7%, while for the age group 31 to 40 the death rate was 27.3%. These figures compare closely with those of Osler, who placed the death rate in the first of these age groups at 20% and in the second at 30%. In the Medical Research Council

Report in 1923 the death rate for these two age groups is given as 22.8% and 28.5% respectively. While the death rate for pneumonia normally increases as age advances there were in the present series no deaths among the eight cases over forty years of age, even although 87% of these were associated with either a Type I or a Type II pneumococcus.

The time of death and its relation to the fall of the temperature was next investigated, and it was found that in three cases death occurred before the crisis, in three cases it occurred a few days after the crisis, and in two cases death occurred during lysis. Between the types, the only point of interest was that all the uncomplicated cases terminating before crisis belong to Type II. In addition it was found that in many of the cases terminating fatally there was a history of previous respiratory disease or other debilitating factor. Of the cases in Type I, one had been gassed during the war and had had a previous attack of pneumonia, and another a female had been confined seven weeks before. In Type II, one case gave a history of bronchitis while in the case of the other two there was no such history present. In Group IV, one case had a history of an attack of pneumonia in the previous year. The two remaining cases died of meningitis. Thus the only two uncomplicated cases, in which there was no previous history of disease, were affected by Type II organisms.

From the above observations it will be evident that the pneumonia met with during the present investigation was of a relatively mild nature. Though there were only a few deaths, it is interesting that for any one type the greatest incidence occurred in Type III. This incidence would have been still greater if all the cases of lobar pneumonia over sixty years of age had been included; for as pointed out later two of the three cases of lobar pneumonia over the age of sixty were due to Type III organisms and both had a fatal termination.

TYPES of PNEUMOCOCCI PRESENT in CASES of LOBAR
PNEUMONIA over 60 YEARS of AGE and in OTHER
RESPIRATORY CONDITIONS

In this chapter are described a number of respiratory conditions associated with the presence of pneumococci in the sputum, which could not be included among the preceding 100 cases of lobar pneumonia. The first three cases in this series, were cases of lobar pneumonia occurring in patients over sixty years of age. The actual ages of the patients were 61, 65 and 75 years respectively. When admitted to hospital they were very sharply ill, though their temperatures were only moderately elevated. The sputum in each case was typically blood stained and revealed on examination a Type I pneumococcus in the case of the patient aged 61, and Type III pneumococci in the other two cases. Blood culture in the Type I case was positive. The course of the illness in each case was very severe and terminated fatally in the two cases due to Type III pneumococci.

The next case in the series was a patient aged 65 years who was admitted to hospital suffering from broncho pneumonia. She appeared very sharply ill and examination showed that a considerable amount of consolidation had occurred in the right base. The temperature varied between 102.5°F.

and 103.5° F. for about nine days and then fell by a prolonged lysis. The sputum which was blood stained was examined twice and a Group IV. pneumococcus isolated on both occasions. Convalescence in this case went on quite uninterrupted.

The remaining cases when admitted were only moderately ill. Examination in each case revealed the presence of a considerable amount of chronic bronchitis in association with a small area of pneumonic congestion. This latter was usually located at the base of the lungs. In two of these cases a diagnosis of bronchiectasis was ultimately made. The course of the illness was invariably mild though in certain cases somewhat prolonged. The sputum too was always mucopurulent and tended in some cases to have a nummular appearance; in no case was it blood stained. When examination was made for the organism present Type II pneumococci were obtained in three cases and pneumococci belonging to Group IV. in the other four cases.

TABLE/

TABLE XIV.

<u>No.</u>	<u>Case</u>		<u>Type</u>	<u>Result</u>
1.	Lobar pneumonia		I.	Recovered
2.	Lobar pneumonia		III.	Died
3.	Lobar pneumonia		III.	Died
4.	Broncho-pneumonia		IV.	Recovered
5.	Bronchiectasis		II.	do.
6.	Bronchiectasis		II.	do.
7.	Chronic bronchitis (with area of consolidation)		II.	do.
8.	do.	do.	IV.	do.
9.	do.	do.	IV.	do.
10.	do.	do.	IV.	do.
11.	do.	do.	IV.	do.

From the above facts it will be seen that Type III pneumococci not only occurred more frequently but gave rise to a higher death rate among cases of lobar pneumonia over the age of sixty than any of the other types of pneumococci. When these cases due to Type III organisms were taken together with the cases occurring under the age of sixty years, it was found, that of the six cases met with 50% ended fatally. It is of interest too that among the cases with chronic disease of the

chest Type II organisms occurred in 43% of the cases, and as will be shown later the organisms were still present in the sputum in a number of the cases at the time of dismissal from hospital.

THE PERSISTENCE during CONVALESCENCE of the TYPE
of PNEUMOCOCCUS CAUSING the DISEASE

It has frequently been demonstrated that pneumococci may exist as harmless saprophytes in the mouths of healthy people. Avery and his co-workers found that pneumococci were present in 39% of a series of 297 cases in whom there was no history of any contact with patients suffering from pneumonia. They also showed that the great majority of those organisms belonged to Group IV. and not to the fixed types. When, however, healthy people who had been in contact with cases of pneumonia were examined a greater incidence of Types I. and II. was met with. The type present in the sputum was invariably the same as that of the case with which they had been in contact.

That such people could harbour the virulent types, raised the question of the existence of possible carriers. To investigate this possibility, a number of cases of pneumonia were examined at varying periods during convalescence, in order to find whether the virulent types disappeared from the sputum or whether they persisted and the patients were dismissed from hospital with virulent organisms still in the sputum.

To determine the presence of pneumococci in the convalescent sputum the ordinary method of mouse inoculation was adopted. According to Sharpe and Urbantki in America this

method may fail when the fixed types in the sputum are very scanty. They therefore advocated the plating of the sputum in blood agar and after incubation, likely colonies were picked off and grown in broth. To this culture was added a few drops of bile and after sufficient time had elapsed the tubes were centrifuged and the supernatant fluid removed. This was then tested against antipneumococcal serum. By this method they held that the antigen for any of the fixed types present was precipitated by the corresponding serum.

As previously stated, the cases were examined at varying periods during convalescence and it was found in a number of cases that after the sixteenth day of illness there was a tendency for the type present at the height of the disease to disappear from the sputum. At the mouse autopsy in such cases the amount of peritoneal fluid present was invariably very slight, and a smear preparation revealed the presence of a variety of organisms other than pneumococci. In a few cases pneumococci were obtained which gave no reaction with the type sera. These were accordingly classified as Group IV organisms. At no time during convalescence were fixed types met with different from that present at the height of the disease, that is, Type II organisms were not met with in the convalescence of Type I cases and similarly Type I organisms were not met with in the convalescence of Type II cases. It

was also observed that the fixed strains isolated during convalescence were apparently as virulent for mice as were the types at the onset of the disease.

As will be observed from Table XV. the shortest period during which the organisms could be detected was 16 days and the longest was 29 days. This latter period was much shorter than that given by Sittman, who was able to keep patients under observation for a much longer period and was able to detect the presence of the organisms up to the eightieth day after the onset of the illness. Avery in his series was able to isolate the organisms up to the ninety-fifth day after the onset. In certain cases in the present series the persistence of the organism in the sputum was in association with definite chronic disease in the chest. In the two cases classified as bronchiectasis Type II organisms were obtained on the twenty second and twenty third days of illness. As previously mentioned a case was met with in which a Group IV. organism was obtained on two occasions from the sputum at the onset of the illness and yet a virulent Type I organism was obtained by lung puncture on the twenty-fifth day of illness.

TABLE/

TABLE XV.

Presistence during convalescence of the type
of pneumococcus causing the disease

No.	Type of pneumococcus at height of disease	Day of disease reckoned from the onset	Type of pneumococcus during convalescence
1.	IV	13	IV
		25	I
2.	I	10	I
		17	No pneumococci
3.	I	21	No pneumococci
4.	I	12	I
		17	I
		23	No pneumococci
5.	I	22	I
6.	I	18	No pneumococci
7.	I	9	I
		19	No pneumococci
8.	I	17	No pneumococci
9.	I	17	I
10.	I	13	I
11.	I	16	IV
12.	II	22	IV
13.	II	9	II
14.	II	36	IV
15.	II	29	II
16.	II	7	II
		24	No pneumococci
17.	II	12	II
18.	II	16	No pneumococci
19.	II	16	II
		26	II
20.	III	24	No pneumococci
21./			

TABLE XV. (Contd)

No.	Type of pneumococcus at height of disease	Day of disease reckoned from the onset	Type of pneumococcus during convalescence
21.	III	16	IV
22.	IV	7	IV
23.	IV	9	IV
24.	II	12	II
		22	II
25.	II	14	II
		23	II

From the above observations it will be seen that the fixed types of pneumococci tended to disappear from the sputum at varying periods after the onset of the illness. In certain cases where the organism persisted there was definite chronic disease of the chest. It is of interest too, that though cases were dismissed from the hospital with virulent strains of pneumococci still present in their throats there were no "return cases" as are met with in scarlet fever. Further, in obtaining the history from the cases in the present series there was no instance of any case having been associated with known cases of the disease.

LUNG PUNCTURE

As a means of obtaining the pneumococcus especially in children where the sputum is often absent, lung puncture affords a simple and accurate method. Many workers in America have availed themselves of the method with, according to their reports, little or no injury to the patient. The possible risks as recorded in the Medical Research Council Report of 1923 are air embolism, haemorrhage, and pneumo-thorax, but, as pointed out, their incidence where reasonable care has been taken is very slight. In spite of the small risk attached to it, workers in this country have not made very wide use of the method and in consequence much of the data regarding lung puncture has to be drawn from American results. From their statistics it has been shown, that where lung punctures are positive the pneumococci are usually obtained in pure culture, and are only occasionally associated with other organisms such as streptococci or bacillus influenza. Further, that the fixed types are more frequently met with in lobar-pneumonia and Group IV organisms in broncho-pneumonia.

In the present work, lung puncture was performed in ten cases all of which were children. Of these, six had lobar-pneumonia and five had broncho-pneumonia. As will be seen from Table XVI. five of the lobar-pneumonias were due to

Type I pneumococci. To confirm the serological results given by the serum of Mulford & Co. in these cases, tests were carried out with the serum prepared by Burroughs Wellcome & Co. in a final dilution of 1 in 30. In the cases of broncho-pneumonia, pneumococci were obtained in only one case and were found to belong to Group IV. The other cases gave a negative result as evidenced by the survival of the injected mice. The punctures, save in three cases were all performed on admission or very soon thereafter. As will be seen from Table XVI. organisms were obtained on the fourth, third and first day before the crisis. In three cases organisms were not obtained till the second, fourteenth and fifteenth day after the crisis. Thomas and Parker who examined seventy-three cases of lung puncture found that as the crisis approached the number of organisms present diminished. Rosenow and Tchistovitch however, were able to obtain positive lung punctures after the crisis and from that concluded that the crisis in pneumonia was not due to the sudden disappearance of the organism.

TABLE/

TABLE XVI.

Lung Puncture

<u>Case</u>	<u>Clinical diagnosis</u>	<u>Day of illness</u>	<u>No. of Days before crisis</u>	<u>No. of Days after crisis</u>	<u>Type</u>	<u>Termination</u>
1.	Lobar-pneumonia	4	4		I	Recovered
2.	do.	4	3		I	do.
3.	do.	6	1		IV	do.
4.	do.	11		2	I	Died
5.	do.	22		14	I	Recovered
6.	do.	23		15	I	do.
7.	Broncho-pneumonia	6			IV	do.
8.	do.	7			Nil	Died
9.	do.	7			Nil	Recovered
10.	do.	8			Nil	do.

As all the cases in which lung puncture was performed were under the age of seven it is of interest that only Type I. and Group IV. pneumococci were met with. This is in contrast to the greater incidence of Type II in the adult age group. It is also of interest that those cases from which Type I. pneumococci were obtained were clinically lobar pneumonia. In the cases of broncho-pneumonia pneumococci were obtained in only one instance.

THE SIGNIFICANCE of BACTERAEemia in
LOBAR PNEUMONIA

The presence of pneumococci in the blood of cases of lobar pneumonia has been extensively investigated. From the reports published, considerable variation seems to exist as to the frequency with which it is possible to obtain the pneumococcus from the blood. These differences are in part explained by differences in technique, and the severity of the cases examined. Prochaski obtained positive results in 100% of his cases. Dochez in 1912 obtained positive blood cultures in 50% of his cases. Cole, out of 728 cases only obtained 27% of positive blood cultures. In Monograph No.7 of the Rockefeller Institute for Medical Research the incidence of positive blood cultures is given as 30.3%. Rosenbluth, in an investigation carried out at Harlem Hospital, New York, in 1929, obtained positive blood cultures in an even smaller percentage, viz:- 22.4% in a series of 500 cases. In this last instance, the small percentage of positives was probably due to the fact that only one or two ccs of blood were used, also that cases giving a negative result were not again examined unless some circumstance arose suggesting a bacterial invasion of the blood.

As a result of these and other varied reports,

divergent opinions have been brought forward as to the significance of a bacteraemia in lobar pneumonia. Those who have reported a high percentage of positive cases, lay little or no stress on the presence of bacteraemia as an aid to prognosis. There again, those who have obtained only a small percentage of positive blood cultures, consider the presence of bacteraemia as of considerable value from the point of view of prognosis, and they find too, a close relationship between the presence of the organism in the blood and the mortality of the cases. Sittman detected organisms in four cases out of sixteen, that is in 25%, three of the four cases died. Dochez, in a series of thirty-seven cases found that of those giving a positive blood culture 77% died, while only 4% of the negatives proved fatal. From their series of 448 cases Avery and his Co-workers placed the mortality of cases with positive blood cultures, at 55.8%. Rosenbluth in his work likewise found a marked increase in the deaths among cases with a positive blood culture compared with those giving a negative culture. He found that 81% of the patients belonging to Type I. with a positive blood culture, died, while only 16% of those giving a negative result, died. In Type II, 75% with a positive blood culture died, while 21% with a negative culture, died. Likewise the number of deaths among patients in Type III and Group IV with a positive blood culture

was much higher than those with a negative blood culture. Sutton and Sevius in their work in the bacteraemia in pneumonia found, that all cases giving more than five colonies per c.c. of blood when grown in solid media, had a fatal termination. Avery and his Co-workers met with a somewhat similar result, for they found that when the number of the colonies in solid media per c.c. of blood was above 15, a fatal result invariably ensued.

In the present investigation the presence of organisms in 2 c.cs of the patients blood was taken as an indication of a definite bacteraemia as distinguished from the invasion of the blood by a few organisms and which would be detected if a large amount of blood were used. As a rule the blood was obtained on admission so that, in relation to the illness, the time of the culture varied between the third and fifth day of illness. This as pointed out by Rosenow is the most favourable period, as cultures made within the first twenty four hours of the illness or at the time of the crisis are invariably negative. As will be seen from Table XVII, thirty cases were examined for the presence or absence of a bacteraemia, and as will also be seen only 16% showed the presence of organisms in 2 c.cs of blood. This low figure is probably related, not only to the small amount of blood used, but also to the general absence of very severe cases of

pneumonia as indicated by the percentage mortality over all the cases examined of only 9%. In the examination of the cultures, where negative results were obtained at the end of twenty-four hours, the tubes were incubated for another twenty-four hours and again examined. If no growth was then obtained the cultures were declared negative.

Of the five cases in which a positive result was obtained three terminated fatally and two recovered. In the former, death occurred in two instances on the day after the blood culture was taken, in the third case, death occurred four days after the blood culture. In the latter cases which recovered, blood cultures were repeated twelve hours after the crisis with negative results, which would indicate that at the time of the crisis the organisms rapidly disappear from the blood stream. But as previously stated organisms can be obtained from the lung tissue itself many days after the crisis. In this connection Dochez and others have shown that in some cases, organisms can be obtained from the blood stream after the crisis. From this they conclude that the crisis is not due to the sudden disappearance of the organisms from the circulation.

TABLE/

TABLE XVII

Result of single blood cultures from 30 cases of pneumonia.

Cases	<u>Blood Cultures</u>			<u>Mortality</u>		
	No. made	Positive No.	per cent	Positive cases No.	per cent.	Negative cases %
LOBAR PNEUMONIA	30	5	16.6	3	60	4

From the clinical point of view all the cases with a positive culture ran a very severe course. Even the two cases which recovered were in the period before the crisis as ill as those which terminated fatally. Among the cases with a negative blood culture there was only one death, but in this case the fatal termination was not due to the severity of the pneumonia per se but to the onset of meningitis later in the disease. So that, if this case is excluded from the series it will be found, that while 60% of those with a positive blood culture died, there were no deaths among the cases with a negative culture.

Between the different types there was very little difference in the incidence of positive cultures probably accounted for by the small number of cases examined. In Types I. and II. there were two cases with positive cultures and in each case there was one death. The fifth case belonged to

Type III. and terminated fatally.

From these observations it will be seen that the presence of a bacteraemia in a case of lobar pneumonia as estimated by the finding of pneumococci in 2 c.cs of the patients blood is of great importance, for as shown above, 60% of those with a positive culture had a fatal termination.

S U M M A R Y

The following is a summary of the observations which were made during the course of the present investigation.

(I) Isolation and identification of the pneumococcus

- A. The intraperitoneal inoculation of mice proved an excellent method of obtaining pneumococci in sufficient quantity for purposes of identification.
- B. The sodium taurocholate solution gave good results in most cases, but two strains of Type I. organisms were met with which were insoluble in the taurocholate solution.
- C. The microscopic agglutination test which was carried out in conjunction with the macroscopic test was found to give results which were in perfect agreement with the results obtained by the older method.

(II) Incidence of the serological types.

The percentage incidence of the different types is shown in Table III. From Tables IV. and VI. it will be seen that in the age group 16 to 60 the greatest number of cases were due to Type II organisms, while in the 1 to 15 age group the greatest number were due to Type I organisms.

(III) Clinical investigation of the cases.

- A. In the clinical examination of the cases there was no evidence that any train of symptoms existed by which one type could be distinguished from another. Certain minor differences did however exist between the various types. In Type I. cases the onset of the condition was more often associated with shivering. The temperatures in these cases tended to run at a slightly higher level and were less liable to remissions than in the other types. In Group IV. cases, more especially among the adults there was a greater percentage of cases giving a history of previous respiratory disease.
- B. In the present series of cases, blood stained sputa were met with in 63% of the cases. Among the adults 80% had blood stained sputa, and of this number 67.9% were met with in cases due to the fixed types, and 12.3% in Group IV. cases. Between the fixed types there was a slightly greater incidence in Type II. than in Type I.
- C. Complications.
- The number of cases which developed complications was relatively small. Of the four cases mani-

festing involvement of the nervous system 50% were due to Group IV organisms.

(IV) Mortality

The mortality rate in the present series was only 9%. This is in contrast to the high death rate of 50% in cases due to Type III. pneumococci.

(V) Lung puncture

Lung puncture affords an accurate means of obtaining the organism in cases where sputum is not available. In one case, the type of pneumococcus isolated from the lung juice differed from that isolated from the sputum.

(VI) Significance of a bacteraemia in lobar pneumonia

The presence of a bacteraemia in cases of lobar pneumonia, as estimated by finding the pneumococcus in 2 c.cs of blood, is of grave significance. In the present series 60% of the cases with a bacteraemia terminated fatally.

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