OBSERVATIONS

ON THE CLINICAL DIFFERENTIATION OF

TYPED LOBAR PNEUMONIA.

By

John Fleming, M.B., Ch.B., F.R.F.P.S.G.

ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

EXPLANATORY NOTE.

The thesis is accompanied by two appendices:-

A, consisting of summaries of case histories, and

B, consisting of analyses of clinical data.

I N D E X.

INTRODUCTION: HISTORICAL.

Lobar pneumonia has been recognised to be a specific disease since the earliest recorded medical observations. In the writings of Hippocrates and Aretaeus are clinical descriptions of pneumonic patients which could not be improved upon, and which indicate that the writers recognised the identity of this disease complex. This is not to be wondered at, for few diseases have so clearly defined a clinical sequence as a typical case of lobar pneumonia. The dramatic onset and acute course to the day of crisis present a classical picture which belongs almost as much to literature, and the lay mind, as to medicine and the medical mind.

Until the medical renaissance during the seventeenth and eighteenth centuries nothing was added to the knowledge of pneumonia, but with the age of Valsalva (1704), Morgagni (1766) and at the beginning of the modern era, Laennec (1819) and Rokitansky (1842), the correlation of symptoms with physical signs and post-mortem appearances was accomplished. From the time of Laennec clinical descriptions of acute lobar pneumonia have undergone little or no modification, so accurate were the observations of the pioneers. The infectious nature of the disease was recognised from early times due to its frequent occurrence in barracks and other crowded communities, but

further advance had to wait the birth of bacteriology as a science. The organism was actually recognised by Pasteur (1881) about three years before Fraenkel identified it as the cause of lobar pneumonia, but the modern knowledge of lobar pneumonia dates from Fraenkel's discovery in 1884. For a time the identity of the organism was in doubt owing to its cultural variability and its close resemblance to the streptococcus group, but the possession of characteristic features such as bile solubility, diplococcus form and possession of a capsule demarcate the pneumococcus and gave it a separate identity.

A small proportion of all cases of pneumonia (less than one per cent.) are due to the pneumobacillus isolated by Friedländer in 1883, but it is better to include these cases with the heterogeneous group of lung infections due to the streptococci, gonococci, micrococci rheumatici, etc. (a group including most of the common pathogenic organisms) and to regard as quite separate the group of pneumonias due to the various types of pneumococcus.

Weichselbaum (1886) completed the association of the clinical picture of lobar pneumonia and the diplococcus of Fraenkel. For about twenty years little was added to our knowledge, but in 1910 Neufeld and Händel discovered that there are several serological strains of pneumococci each having a separate identity. This work was amplified by Dochez and Gillespie (1913) and Cole (1913) of the Rockefeller Institute.

These workers made it clear that three strains were principally concerned with production of lobar pneumonia. These they named Type I, II, III and the other strains were called collectively Group IV. About the same time Lister (1913) at the South African Institute of Medical Research made a similar classification which agreed with the American work, except that the relative prevalence of individual strains did not correspond. In 1917 Dochez and Avery discovered that the capsule of the pneumococcus contains a substance which is specific for each type of organism and further that this substance is shed from the organism during its active growth. Analysis of this specific substance (s.s.s.) revealed that it was a carbohydrate (Heidelberger and Avery, 1923) and moreover that the substance was specific for each pneumococcal strain. The total specificity of the individual type of pneumococcus seems to reside in this capsular substance for when the organism is deprived of its capsule it ceases to have any feature differentiating it from the other strains. This fundamental or R strain would appear to form a core common to all strains of the pneumococcus added to which an enclosing capsule of carbohydrate substance conveys antigenic specificity.

Apart from Types I, II and III additional types have been identified in Group "X", but clinically none of these in this country or in America at least, are of numerical importance. For this work the credit goes mainly to Cooper (1932) and her

coworkers who subdivided Group "X"* into 29 further strains, making a total of 32 Types. The majority of these gave very slight cross-agglutination. Some of these Types appear to occur more frequently in certain types of pneumococcal infections such as lobar pneumonia in children (Types V, VI and XIV) and pneumococcal meningitis (Type XVIII); with more experience this may have a bearing on treatment but meanwhile in this country at least, the clinical problem of lobar pneumonia is concerned mainly with Types I and II.

Although the frequent occurrence of Types I, II and III makes these of more importance, a few strains of Group "X" occur with sufficient frequency to call for consideration, in particular Type V and Type VIII (Winkler and Finland, 1934) which have serological affinities to Types I and II. Further, it had been demonstrated that there is remarkable antigenic similarity not only between certain pneumococcal types but between also certain strains of pneumococci and other bacteria morphologically and culturally dissimilar. Avery, Heidelberger and Goebel (1925) showed that there is similarity of the type specific substances in the case of Type II pneumococci and a strain of Friedländer's bacillus. These writers suggested that there are specific antigens, not identical but sufficiently similar in chemical structure to give cross-agglutination and

*In 1930 Dr. John Cowan suggested that for convenience and to avoid confusion with Type IV, Group IV should be called Group "X".

cross-absorption in some degree. Eyre, Sarah and Stovell (1936) reported experiments which demonstrated the antigenic similarity of two strains of organism classified as streptococcus viridans and Type XXIX pneumococcus. This similarity appears to reside in the type specific carbohydrate fraction. Recently (Enders, Shaffer and Chaogen Wu, 1936) it has been demonstrated that variation in the virulence of Type III organisms depends on the resistance of the capsules to disintegration. Older cultures tend to lose their capsules so that the strains of different virulence sooner or later are all decapsulated.

Not only are the capsular substances serologically different for each type, but the sizes of the capsules vary. Type III organisms have a very large capsule so that in colonies they produce a spreading mucoid appearance which gave origin to the name 'streptococcus mucosus'. The difference in amount of capsular substance is not so striking in the case of Types I and II, but it is frequently possible to note the larger size of Type II in a direct smear. Cruickshank (1933) has shown that the difference is quite striking when the respective colonies are compared, the Type I colony is smaller and more compact, the Type II colony is larger, the organisms being more separate one from another owing to the presence of larger amounts of capsular substance.

Search for a Therapeutic Serum.

Since the end of last century attempts have been made to use the bacteriological knowledge about lobar pneumonia to obtain a suitable antiserum. These attempts met with little success at first since the sera were prepared without regard to the various strains of pneumococcus. But in 1913 Cole, making use of the new knowledge of types, prepared antiserum against Types I and II. This preparation met with some success but the large quantities required made the treatment both difficult and dangerous, and the same criticisms applied to Huntoon's antibody solution (1921).

In 1924, Felton by using the method of precipitation in distilled water managed to concentrate the protective substances while reducing nitrogenous material to minimal quantities. This method was found to give an antiserum of high potency against Type I and Type II and to a lesser extent with the other types. The possession of so valuable a therapeutic weapon brought the obligation to make the greatest use of it. This implied the need for early recognition of the infecting type.

The differentiation of type is primarily a bacteriological problem but it has become important to investigate the clinical picture of lobar pneumonia afresh in the light of this bacteriological discrimination. This paper deals with an examination of some of the main symptoms and signs

of lobar pneumonia as they appeared in a series of cases typed I, II, III and Group "X" including the remaining types. Interest centred mainly round Types I and II which were found to be the infecting types in much the largest number and to be associated with the highest mortality, and further since effective serum was at that time only available against those two types.

Scope of this Paper.

The clinical data here analysed were collected during the course of an investigation into the use and value of Felton's pneumococcic antiserum in Glasgow Royal Infirmary. Early in 1930, following a visit to Glasgow of Dr. Bullowa of New York, Dr. John Cowan initiated the investigation which was continued in the wards of Professor A.W. Harrington. The cases were admitted by arrangement with Dr. A.S.M. MacGregor as soon as they were notified to the Public Health Department after the notification officer had ascertained that they were suffering from definite lobar pneumonia in its early stages. Few unsuitable cases were admitted. From time to time the results of the serum treatment, especially with regard to its effect on morbidity and mortality, have been communicated to various journals (Lancet, Glasgow Medical Journal, Report of Medical Research Council, Lancet (Cruickshank, Milroy Lectures), Proceedings of Pathological Society, Transactions of Glasgow Medico-Chirurgical Society). The use of serum entailed the necessity for complete bacteriological and clinical investigation of each case. Special investigations were carried out in varying numbers of the series, including examination of the blood with special reference to the variations in the leucocyte count, secondary anaemia and degenerative changes in the leucocytes: the incidence and severity of jaundice: the blood chemistry with regard to pH and the calcium and phosphorus content and the acidity of the urine. The investigation was

carried out by a team comprising bacteriologist, biochemist and clinician, and collaboration was maintained as far as possible throughout.

This paper consists of portions of the work for which the writer was personally responsible.

The object has been (1) to classify the cases into the various type groups as soon as possible after admission; (2) to examine the clinical course of each type of infection in an endeavour to discover what differences, if any, there might be.

Two hundred and thirty three cases have been included in the present series and the subjects dealt with are as follows:

(1) Clinical.

(a) The onset symptoms in relation to Types I, II and III and Group "X".
(b) The influence of exposure on susceptibility in Types I, II and III and Group "X".
(c) The occurrence of faucial congestion in Types I, II and III and Group "X".
(d) Previous respiratory illnesses in Types I, II and III and Group "X".
(e) The occurrence of jaundice, including examination of the serum bilirubin by the method of Meulengracht.
(f) The blood: (1) red blood corpuscles, haemoglobin Arneth count, toxic degeneration in a small series of cases; (2) a detailed investigation into the variation in the leucocyte count from day to day during the febrile period (published in the Quarterly Journal of Medicine).
(g) The blood pressure curves and their relation to morbidity.

(2) Bacteriological.

The value of the direct method (Neufeld) of pneumococcal typing. (This method was introduced about halfway through the investigation; previously all the cases were typed by mouse inoculation (Blake).)

IDENTIFICATION OF THE INFECTING TYPE

with special reference to the

DIRECT METHOD.

Until recent years the routine method of typing the pneumococci in pneumonia depended on the high pathogenicity of the pneumococcus for the mouse. In typing by this method some fresh sputum diluted with saline is injected into the peritoneal cavity of the mouse. Usually within 24 hours the predominant pneumococcus can be recovered in pure culture from the peritonitis which develops. The introduction of serum therapy and the need for early diagnosis led to a search for a method which would shorten this relatively lengthy period. Sabin in 1929 described a method of observing microscopically the agglutination of a stained preparation from the peritoneal exudate. It was found possible to make a diagnosis from fluid withdrawn a few hours after inoculation. Thirty years ago Neufeld described the capsular swelling which occurs when pneumococci are mixed with homologous antiserum. In 1932 Armstrong, and Logan and Smeall simultaneously described a method of typing directly from the spit by mixing with undiluted serum and examining for capsular swelling. This method has been used extensively with the cases in the Glasgow Royal Infirmary (Fleming, 1933).

Procedure for Direct Typing.

A clean slide is marked off into two sections. A small fleck of sputum is added to each section. To the first, a drop of Type I and to the second, a drop of Type II serum is added. Each sample is thoroughly emulsified, after which cover glasses are applied and the slide is left undisturbed for a few minutes. In the case of a Type I infection the pneumococci in the slide section treated with Type I antiserum will show a large clear encircling zone (which is the swollen capsule) containing the darker staining organism which has the appearance of a nucleus in a cell. Sputum containing Type II organisms will show a similar appearance in the homologous section of the slide.

Type II pneumococci have by this method larger capsules than Type I. This appears to correspond with the larger amounts of s.s.s. which is obtained from the former and with the wider separation of the individual organisms when growing in colonies, described by Cruickshank (1933). Usually the swelling of the organisms takes place in a few minutes but the actual rate depends on the consistency of the spit and consequently on the intimacy with which the test serum can reach the organisms. A thin mucous spit can be typed more rapidly than a tough glutinous one assuming that similar numbers of organisms are present. It is important that the samples of sputum and testing sera should be thoroughly mixed together.

The quantities of sputum and sera should be sufficiently small to flow evenly to the edge of the coverglass but not beyond, otherwise the preparation tends to float about under the pull of the oil-immersed lens and examination is rendered difficult.

If the sputum is mucoid and the organisms numerous there may be seen, in addition to capsular swelling, a certain tendency to agglutination. This provides useful corroboration of the diagnosis but when present the diagnosis is usually easy to make as the organisms are present in large numbers and 'swelling' is easily seen. Even with carefully prepared specimens the semifluid nature of the preparation makes it difficult to 'hold' the organisms in a particular field. These sputa are usually aerated and contain numerous small bubbles which, instead of being a nuisance, can aid in the examination. By focusing the floor of a bubble it is possible to examine any pneumococci present without any tendency for them to slip out of the field. In this case the organism appears as a small yellow body surrounded by a much paler capsule. The bubble evidently forms a dome over the organisms which lie free from fluid on the floor and are illuminated by reflected light. It is possible to aid in demarking the capsules by mixing a little stain with the preparation. Sabin suggests alkaline methylene blue but a much better result is obtained with a drop each of 0·5 per cent. methyl violet and dilute carbol-fuchsin (Colquhoun described by

Cruickshank, 1933).

The difficulty however is not in distinguishing the swelling of the organisms which is easy to the practiced eye, but in finding them when they are scanty in number, so that there is no great gain in staining the preparation. A pair of pneumococci in the ordinary state are about 1μ in length and 0·25μ in breadth. The capsule is either not visible or present as an ill-defined and very narrow halo. When treated with anti-serum the dimensions of the organisms themselves do not alter but the huge capsules give to each a combined length of 2μ - 2·5μ and a breadth of 1μ. The sputum must be typed soon after expectoration and certainly not later than one hour, otherwise the results may be poor since the pneumococci autolyze very rapidly.

Early Results.

When the direct method was first tried in this investigation the following results were obtained with sputa from cases in Belvidere Hospital (Table I).

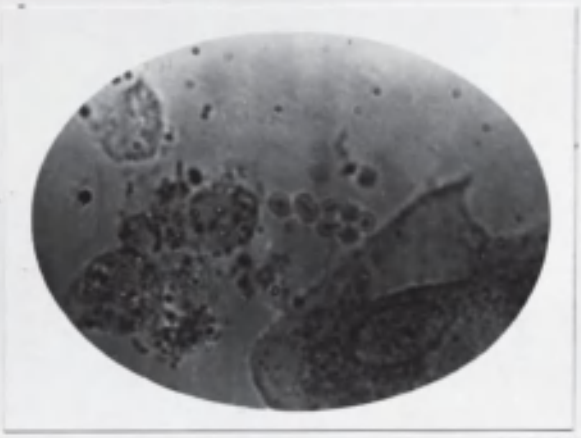
TABLE I.

Direct Typing: 15 Cases.

Direct	Type	"X"	"X"	"X"	"X"	I
Mouse Inoculation	"	I	I	I	I	I
Direct	"	"X"	"X"	"X"	II	II
Mouse Inoculation	"	II	II	II	II	II
Direct	"	"X"	"X"	"X"	"X"	I
Mouse Inoculation	"	"X"	"X"	"X"	"X"	"X"

This 50 per cent. of error consisted of failure to type rather than errors of typing and was later realised to be due to the 24 hours' delay caused by collection and transportation to the Glasgow Royal Infirmary. In such sputa the capsules of the organism, which are first to disintegrate, fail to react to the typing serum so that in the absence of swelling a diagnosis of Group "X" is made, i.e. a strain other than Types I and II.

It is essential that actual expectoration should be obtained for examination. In the early stages of the illness the patient may have little cough and does his best to restrain it lest it aggravate his pleuritis pain. In such cases the sputum consists mainly of upper respiratory mucus and saliva which usually contain Group "X" organisms in any case and so may suggest an erroneous diagnosis. It is thus preferable that where a first sample is doubtful a second specimen should be obtained personally. With a little encouragement, even very ill patients will do their best to produce a sputum well coughed up. In this connection I have found it of great help to give a small dose of morphine (gr.1/6 - 1/8) which is sufficient to make cough comfortable enough for effective expectoration and is usually harmless at this early stage (Blake, 1930), if not beneficial (Davis, 1928; Dawson of Penn, 1931). The organisms are more numerous in the typical rusty sputum of the well developed case, but they are usually present in sufficient numbers to make diagnosis possible in the aerated mucous spit of the onset and frequently they are profuse.



Sputum smear from a lobar pneumonia Type II showing Neufeld "Quellung" reaction with Type II antiserum. x 1,000.

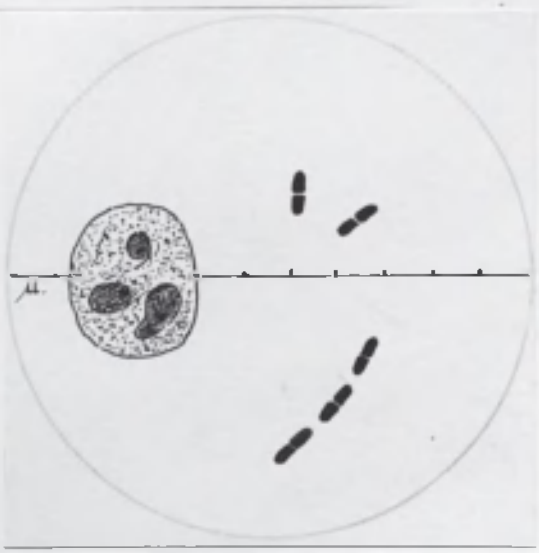


Fig. I.

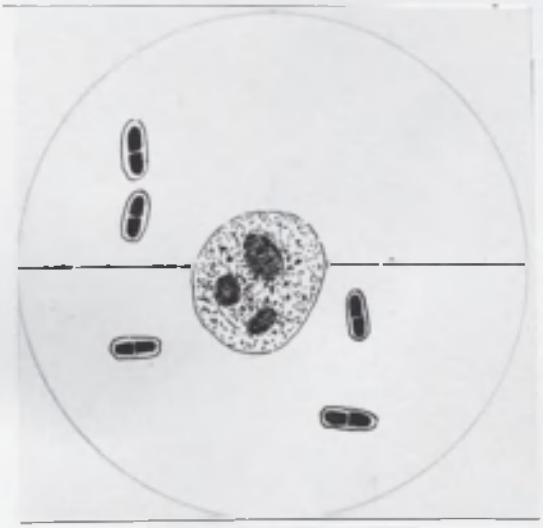


Fig. II.

Diagrams representing the appearance of pneumococci before (Fig. I) and after (Fig. II) adding homologous antiserum.

Horse and Rabbit Antiserum.

Sabin gives as a reason for his early failure with this method that antiserum prepared from horses, which he had been using, does not give the reaction, whereas antiserum prepared from rabbits does give it. Such a distinction seems unlikely on the face of it and has not been borne out by our experience. A small series, three Type II and three Type I sputa were each put up with antiserum of horse and rabbit origin. The rabbit serum was prepared by Dr. Cruickshank in the Glasgow Royal Infirmary Bacteriological Laboratory, while the horse serum was therapeutic serum prepared by Burroughs Wellcome & Co. The swelling was well marked in all the preparations and in the case of the Type II specimens the swollen capsules were especially well defined in the horse serum series.

Disadvantages of the Method.

The disadvantages of the method have been stressed by Logan and Smeall who think it too difficult for persons inexperienced in bacteriology and that it should be confined to the bacteriological laboratory. They suggest that starch grains and the various particulate debris of the spit may have the appearance of swollen organisms and may lead to unreliable diagnosis. The swollen organisms have, however, a very characteristic appearance and recognition is easy with a little

experience. Considerable difficulty may be experienced when the infecting organisms are scanty, as Group IV strains are frequently present in addition to Types I, II and III but if definite 'ballooning' is observed even in a few scattered organisms it may be taken with confidence that they represent the infecting type. This difficulty can be diminished by making sure that a good specimen of spit is obtained and by obtaining a fleck from a suitable portion.

The Direct as compared with the Mouse Method.

Allowing for the difficulty of acquiring experience in recognising the capsular swelling (and there is no doubt that this is much more difficult than recognising agglutination), the direct method is probably not less accurate than the usual procedure with mice. In the earlier stages of the Glasgow Royal Infirmary investigation 10 per cent. of the first sputa examined by mouse inoculation were incorrectly typed but the correct type was identified at a second or subsequent examination. Davies, Hodgeson and Whitby (1935) had 12 cases showing anomalous or mixed infection as judged by examination of the sputum. Six of their cases were diagnosed pneumococcal pneumonia but later developed a streptococcal complication; two proved to be due to a type different from the one at first diagnosed, while in four there was indisputable evidence that

two distinct types were concerned in the pneumonic process.

Sputum in the Early Stages.

During the first 24 hours the sputum is usually scanty and sometimes absent, but if the infection is of average severity a little is usually forthcoming, especially with the cooperation of a helpful nurse. The value of these early sputa for diagnostic purposes varies greatly, but it is usually possible to tell from the appearance whether one is dealing with the exudate from the smaller bronchi or with tracheal and laryngeal mucus. It is unusual to fail in obtaining adequate sputum from a case of lobar pneumonia 24 hours after the onset. The direct method, therefore, makes it possible to administer serum very early in the illness if the case is promptly diagnosed. In Abernethy's (1936) Type I series it was possible to commence treatment at an average of 53·8 hours after the onset of the disease. The importance of this is shown by a series of 185 cases of Type I pneumonia reported by Rosenbluth and Bloch (1936) with 44 deaths (23·7 per cent.). Of the fatal cases only 9 per cent. were treated in the first three days. The details were as follows:-

Mortality among	74	cases	admitted	before	3rd. day	5·4	per	cent.
"	"	80	"	"	3rd. - 7th.	"	26·0	" "
"	"	25	"	"	7th. - 14th.	"	56·0	" "

Langley, Mackay and Stent (1936) stress the importance of treatment before the third day as serum is likely to be helpful from ages 16 - 60, especially if continued till agglutinins persist in the serum. Since it has been shown by Tilghman and Finland (1932) that intravenous administration of antiserum gives the highest and most sustained concentration of agglutinins it is possible, if sputum can be obtained for examination, to bring a proved therapeutic weapon into action within an hour of diagnosing the complaint. While the disease remains active the organisms are present in large numbers during the first few days but thereafter rapidly disappear from cases which do well. The presence of organisms in pure culture in the sputum seven or eight days from the onset usually indicates a serious infection which is still progressing. Where facilities are available the other methods should be used as a check on the direct method even when the result seems definite.

During the present investigation the direct results have all been checked by mouse inoculation and blood culture but increasing experience has confirmed the reliability of the method in experienced hands.

TYPE I CASES.

Case No.	Direct Diagnosis		Mouse Inoculation		Remarks
	Type	Day	Type	Day	
156.	"X"	2nd.	I		
	I	3rd.			
160.	"X"	1st.	I		
	I	2nd.			
162.	I	4th.	I		
164.	"X" "X"	3rd.	I	4th.	Mouse alive.
	I	4th.	I	6th.	Sabin, 110 organisms.
			I	7th.	Mouse died.
166.	I	2nd.	I		
169.	I	2nd.	I		
173.	I	2nd.	I		
175.	I	5th.	I		
179.	II	2nd.	"X"	2nd.	
	I	4th.	I	5th.	
181.	I	4th.	I		Died. Sputum loaded with organisms.
182.	"X"	2nd.	"X"	2nd.	Corrected by blood culture
	"X"	3rd.	"X"	3rd.	2nd. day + Type I.
			"X"	4th.	
183.	"X"	2nd.	I		
	I	3rd.			
184.	I	2nd.	I		Abundant in sputum till
	I	3rd.			6th. day.
185.	I	2nd.	I		
187.	I	5th.	I		
193.	I	2nd.	"X"	2nd.	
			I	3rd.	

TYPE I CASES. (Cont.)

Case No.	Direct Diagnosis		Mouse Inoculation		Remarks
	Type	Day	Type	Day	
197.	I	5th.	I		Pneumococci +++ till 10th. day, then "X" and streps. +++ a "creeping pneumonia".
	I	6th.			
	I	7th.			
	I	8th.			
	I	9th.			
	"X"	10th.			
198.	"X" I	5th.	I	5th.	
			I	6th.	
204.	I	2nd.	I		
	I	3rd.			
	I	4th.			Died.
205.	"X"	2nd.	"X"	2nd.	"X" from pus on 19th. day.
	"X"	3rd.	"X"	3rd.	P.M. on 25th. day gave
	"X"	4th.	"X"	4th.	Type I. Complete failure of typing.
212.	"X"	3rd.	I		
	I	4th.			
215.	I	6th.	I		
182.	"X"	2nd.	"X"	2nd.	Blood culture on 2nd. day
	"X"	3rd.	"X"	3rd.	Type I.
	"X"	4th.			

Type I Cases: Analysis of Results.

At the first examination the direct method failed to reveal the type in ten cases (43 per cent.), but a second examination, usually done twelve hours later gave a correct result in six of these, so that complete failure occurred in only four cases or 17·3 per cent. Of the ten first examination failures, one was a first day sputum, six were of the second day, two were of the third day and one was of the fifth day. In all of these the sputum was scanty and the organisms seen were probably from the normal flora of the pharynx. All were diagnosed Group "X", that is, no swollen organisms were seen. In one second day case, a first diagnosis of Type II was made as definite 'ballooning' was observed in a few organisms with Type II antiserum. By the following day, numerous Type I organisms were seen with no evidence of Type II. In this case mouse inoculation corrected the first diagnosis, but not till the death of the mouse two days later. For the fourth case the mouse on the fourth day was alive and showed 'no organisms', by the Sabin rapid method, and the correct result could not be given till the mouse died on the sixth day. In the ninth case erroneously diagnosed Type II by the direct method, the mouse result on the same day was Group "X" and was not corrected till the fifth day. In three cases there was complete failure to type by both methods.

Complete Failure of Typing Methods.

Case No.	Direct Method		Mouse Inoculation Method		Final Result
	Type	Day	Type	Day	
82.	"X"	2nd.	"X"	2nd.	Blood Culture +
	"X"	3rd.	"X"	3rd.	Type I 2nd.
			"X"	4th.	
205.	"X"	2nd.	"X"	2nd.	P.M. Empyema,
	"X"	3rd.	"X"	3rd.	Pus.
	"X"	4th.	"X"	4th.	Type I.
182.	"X"	2nd.	"X"	2nd.	Blood Culture +.
	"X"	3rd.	"X"	3rd.	
	"X"	4th.			

Conclusions.

There is difficulty in making an accurate diagnosis in many early Type I cases either by the direct or the mouse inoculation method. The mouse inoculation method is probably more accurate finally, but the longer time required gives the direct method precedence.

TYPE II CASES.

N.B. Unless where indicated the direct diagnosis was corroborated by mouse inoculation.

Case No.	Direct Diagnosis		Mouse Inoculation		Remarks
	Type	Day	Type	Day	
171.	II	2nd.	II		
161.	II	4th.	II		
163.	"X"	5th.	"X" and coliform	5th.	
	II	6th.	"X"	6th.	Blood culture "indefinite".
165.	II	6th.	II		
172.	II	2nd.	II		
232.	"X"	3rd.	II	3rd.	No explanation for failure, fairly acute illness, sputum very scanty but seemed typical.
	"X"	4th.			
173.	II	3rd.	II		Died. Abundant organisms.
174.	II	2nd.	II		
176.	II	4th.	II		
177.	II	? 3rd.-6th.	II		
192.	II	2nd.	II		Died. Abundant organisms.
195.	II	4th.	II		
199.	II	3rd.	II		
200.	II	7th.	II		Typed with difficulty.

TYPE II CASES. (Cont.)

Case No.	Direct Diagnosis		Mouse Inoculation		Remarks
	Type	Day	Type	Day	
201.	II+++ II++ II+ II very scanty "X"	2nd. 3rd. 4th. 5th. 6th.	II		This case was specially tested against horse and rabbit antiserum: 3rd. day 'ballooning' with rabbit serum was only fair with horse serum very large; on 4th. day 'ballooning' with rabbit serum was only fair with horse serum very large. The case made a very rapid recovery with serum (60,000 Felton units of Type II); although the blood culture was positive and he was acutely ill at the onset, he was 'well' by 3rd. day, but the lung infection as usual took a few more days to clear.
202.	"X"+ II+ II scanty	2nd. 3rd. 4th.	II		
203.	II II "X"	4th. 5th. 6th.	II		
206.	II II	2nd. 3rd.	II		This patient had a Type I infection 2½ years before with empyema. On this occasion his illness was acute, terminated rapidly but had a serous effusion.
214.	II ?	4th. 5th.			Died 24 hours later.

TYPE II CASES. (Cont.)

Case No.	Direct Diagnosis		Mouse Inoculation		Remarks
	Type	Day	Type	Day	
216.	"X"	2nd.	II		
	II	3rd.			Died. Failure to type meant no serum till 3rd. day.
219.	II	3rd.	II		
	II	6th.			
221.	II	7th.	II		
222.	II	1st.	II		
223.	"X"	4th.	II	4th.	Serum given on mouse finding
	"X"	4th. later.	Sabin		and, although blood positive, rapid recovery with
	II	5th.			100,000 units of serum.
225.	II	3rd.	II		
	II	4th.			
226.	II	2nd.	II		
227.	II	2nd.	II		Organisms +++ in sputum.
228.	II	3rd.	II		
229.	II	4th.	II		
230.	II	4th.	II		
194.	"X"	4th.	"X"	4th.	
	II	5th.	II	5th.	

Type II Cases: Analysis of Results.

At the first examination the direct method failed in six cases, 19 per cent. The second examination gave the correct result in six of these cases. There was complete failure in one case only, 3·2 per cent.

First Examination Failures.

Two of the first examination failures were second day cases; in one a diagnosis was made on the third day with difficulty owing to scanty organisms, and on the fourth day no 'ballooning' was seen, the other was a very virulent infection with a very delirious and debilitated patient from whom satisfactory specimens of spit were difficult to obtain. One was a third day case in which the spit, though scanty, seemed typical. Mouse inoculation isolated a Type II pneumococcus from this third day spit but the direct method failed with the fourth day sputum also. Two were fourth day cases; in one the direct method did not give a correct result till the following day, but the Sabin method established Type II on the fourth day. In the other both methods failed on the fourth day, but both were correct on the fifth day. One fifth day case was diagnosed Group "X" at first but correctly Type II next day, on the fifth day the mouse result was 'Group "X" and coliform organisms', on the sixth day Group "X". The blood

culture was 'indefinite' but post mortem Type II was isolated in pure culture from the spleen. Thus in the Type II series the direct method failed completely in one case only, but the mouse method also failed in one case.

While testing a number of Type II cases against rabbit and horse antiserum respectively the spit was examined daily by the direct method till the organisms disappeared from the spit. In these cases the illness was observed from the second day. Organisms were most numerous on that day and quickly diminished but were still present for a few days after defervescence. Fig. III shows a typical case.

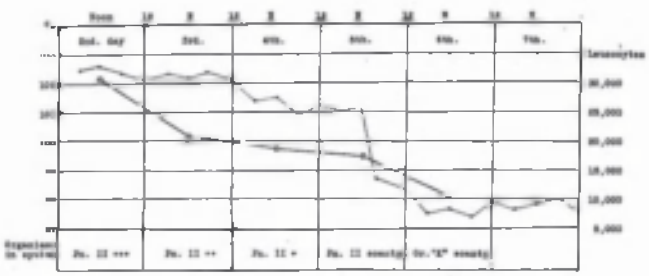


Fig.III. Chart of a case of Type II Lobar Pneumonia, to draw the relations between temperature curve, leucocyte curve, and pneumococci in the sputum.

GROUP "X" CASES.

Case No.	Direct Diagnosis		Mouse Inoculation	
	Type	Day	Type	Day
159.	"X"	2nd.	"X"	-
167.	"X"	3rd.	"X"	-
168.	"X"	4th.	"X"	-
178.	"X"	5th.	"X"	-
180.	"X"	3rd.	"X"	-
186.	"X"	2nd.	"X"	-
188.	"X"	6th.	"X"	-
189.	"X"	6th.	"X"	-
190.	"X"	6th.	"X"	-
194.	"X"	4th.	"X"	-
196.	"X"	4th.	"X"	-
204.	"X"	3rd.	"X"	-
207.	"X"	4th.	"X"	-
208.	"X"	2nd.	"X"	-
209.	"X"	4th. and 5th.	"X"	-
210.	"X"	5th.	"X"	-
211.	"X"	1st.	"X"	-
217.	"X"	2nd.	"X"	-
218.	"X"	5th.	"X"	-
220.	"X"	1st. 5th. and 6th.	"X"	-

Group "X" Cases: Analysis of Results.

Since the introduction of the direct method all the Group "X" cases have been correctly diagnosed, and therefore no serum has been given uselessly. In most of these cases only one specimen of sputum was examined, a minute examination lasting about 30 minutes. It is now realised that the scarcity of I and II organisms may lead to a fallacious diagnosis of "X" by both methods if only one specimen is examined, so that repeated examinations are indicated in all cases where absence of 'ballooning' compels a diagnosis of "X".

Discussion.

In this investigation the fact that Type III cases were very few limited the diagnostic problem to the differentiation of Type I from Type II and Group "X" cases. Seven cases of Type III infection were encountered but of these only one has been treated since the introduction of the direct method of typing. In this case the patient was a young woman of 20 who had a severe spreading infection with a pink sputum resembling that seen in influenzal pneumonia. Direct typing showed only Group "X" organisms but mouse inoculation indicated a combination of Type III and Group "X".

If the organisms are present in reasonable numbers

(e.g. 2 or 3 in the field of a 1/12 objective), there is no difficulty in recognising a Type II infection. Type II pneumococci have large capsules which swell in a few minutes to twice their previous size. The apparent increase is more than this since an unswollen capsule is indistinct in the fresh preparation, whereas the swollen capsule is more refractile and therefore more obvious. Type I organisms present the same characteristics except that the swollen capsules are much smaller than is the case with Type II. It is thus much easier to fail in identifying Type I pneumococci when the numbers are small. In this series the first examination of the sputum failed to reveal the infecting organism in 43 per cent. of the Type I cases examined, but in only 19 per cent. of the Type II cases. These figures give a fair idea of the relative difficulty in identifying the two types. It is fortunate that the most serious of the common infecting strains should be the most easily identified. A delay of 24 hours may not interfere much with the usefulness of Type I antiserum but in the case of Type II may prevent any therapeutic benefit. By this method of typing, antisera are employed only against Types I, II and III so that pneumonia due to Group "X" strains is diagnosed by the absence of 'ballooning' in any of the three test preparations. This constitutes the greatest difficulty of the method, for whereas the presence of swollen organisms is definite evidence of the particular strain be it I, II or III, the absence of such

swelling does not permit of a diagnosis of Group "X" till a very thorough examination has excluded the possibility of scanty organisms belonging to the other strains being present. This difficulty is most frequent in early cases where cough is shallow and sputum scanty. The direct method failed in eight Type I cases and in six of these mouse inoculation also failed; it failed also in one Type II case and one Group "X". In a total of 74 cases the error in direct typing was 17·3 per cent. of 23 Type I cases, 3·2 per cent. of 31 Type II cases, and 0 per cent. of 20 Group "X" cases. It is a good thing that accuracy is high in Type II where early diagnosis is so necessary but the error is still considerable in the Type I series. Since in six of 88 Type I cases, mouse inoculation also failed and in two cases the direct result gave a correct result while mouse inoculation was still indefinite, it is likely that the error is very similar with both methods.

It is difficult to explain the failure to type certain Type I cases, e.g. R.M. aged 25, was admitted 24 hours after the onset with a severe pneumonia involving the whole right lung. On the second, third and fourth days the pneumococcus in the sputum was diagnosed Group "X" both by direct and mouse inoculation methods. On the 19th. day pus from an empyema was still diagnosed Group "X" but he died, and a culture from the spleen gave a pure Type I. In this case, through complete failure of the typing he was deprived of the help of serum.

Such a case makes one very apprehensive of the diagnosis Group "X" even after extensive investigation in cases which are acutely ill.

Conclusions.

The direct method of typing pneumococci is simple and accurate when some experience has been acquired. It is probably rather less accurate than mouse inoculation but compensates for this by requiring much less time. The error in typing Type I cases is greater than with Type II cases and is due mainly to the relatively smaller size of the Type I capsular swelling and to the fact that the organisms tend to be present in smaller numbers in Type I than in Type II infections.

The organisms, in all types, are usually scanty during the first 24 hours, are most plentiful on the second and third days and remain so till resolution commences, after which they rapidly diminish in numbers. Thus difficulty in typing is found at the onset and again at the termination of the fever. In less acute cases the Group "X" inhabitants of the upper respiratory tract may obscure the bacteriological diagnosis and there is some evidence that organisms of more than one type may be present.

THE CLINICAL ANTECEDENTS OF PNEUMONIA.

An analysis has been made of the clinical histories of previous respiratory affections and of the symptoms and signs which immediately preceded the development of consolidation. An attempt has been made to consider each type separately.

The data are classified as follows:-

(1) Previous Respiratory Illnesses.
(2) Upper Respiratory Infections preceding the Onset.
(3) Faucial Congestion.
(4) The Influence of Exposure on Susceptibility.
(5) The Symptoms of the Onset.

Previous Respiratory Illnesses.

Respiratory illness evidently impresses itself on the memories of most patients, for very good histories were obtained from a large number of the total series.

TABLE II.

PREVIOUS RESPIRATORY ILLNESS.

	Pneumonia	Pleurisy	Chronic Bronchitis	Influenza	Other	Total	% of all Cases
Type I	13	-	7	-	1 asthma 2 gassed	23	31·43
Type II	14	4	3	3	1 gassed	25	31·25
Type III	1	-	-	1	-	2	25·00
Group "X"	5	2	6	3	1 pl. pericard. 1 sinusitis	18	24·00
Total	33	6	16	7	6	68	29·22

CASE ANALYSES.

Type I.

Past History	Present Age	Present Illness
Pn. L. aged 31. Bronchitis ++	38	Pn. L.2.
Pleurisy aged 23. Pn. aged 28	38	Pn. L.12.
Pn. aged 15	17	Pn. R.1.
Br. Emphys. Dry Pleurisy R.L.	63	Pn. R.3. Br. and Emph.
Chr. Bronchitis. Pn. aged 37	38	Pn. L.2. Br. ++
Pn. L. aged 16	31	Pn. L.2.
Pn. R. aged 16	24	Pn. R.3.
As. Bronchitis	38	L.2.
'Gassed' aged 22	36	R.3. Bronchitis +
'Gassed' aged 24	37	R.1.
Chr. Bronchitis	24	R.3.
Chr. Bronchitis	15	R.3.
Pn. aged 21	33	R.12. Bronchitis ++
Chr. Bronchitis	60	R.3.
Bronchitis several weeks aged 24	55	R. 123. Bronch. ++ Pleur. ++
Pn. L. aged 37	54	L.2.
'Gassed' aged 18. Bronch.Pleur.20	33	R.3.
Pn. aged 10	17	L.2.
'Double Pn.' aged 23	30	L.2.
Asthma	25	L.2.
Pn. aged 22	20	L.2.
Pn. L. aged 29	49	R.23.

CASE ANALYSES.

Type II.

Past Lesion, with age (when obtainable)	Present Age	Site of Present Lesion
As. Bronchitis	16	R.3.
Pn. L. aged 25; Pn. L. aged 18	44	R. 123. Died.
Bronchitis aged 14	22	R.1.
? Pn. aged 19	33	R. 3. Bronch. +++
Pn. L. aged 19	26	L.12.
Pn. aged 11/12. 2½. 7. 13	14	L.2. R.3. Bronch. +++
'Pn.' aged 2	17	L.2.
Pleurisy aged 32	46	L.2.
Pn. aged 5	29	L.2.
Influenza aged 24	37	L.2. Empyema.
Pn. R. 3 times previously	59	R.3. Bronch. +++ Died.
Bronchitis As.	41	R.1. Bronch. +++ Died.
Pn. childhood	30	L.2. Bronch. +
'Gassed' aged 41	56	R.3. Bronch. ++
Pleurisy aged 16	19	R.3. L.2.
Pn. L.2. aged 18	43	L.12. R.3. Died.
Pn. aged 14	27	R. 123
Recurrent colds	28	R.3. L.12.

CASE ANALYSES.

Type II.(Cont.)

Past Lesion, with age (when obtainable)	Present Age	Site of Present Lesion
Pn. aged 6	22	R.123
Influenza and Pleurisy 19	20	L.2.
Pleurisy L. aged 46	49	L.2.
Pn. in childhood	21	L.2.
Pn. L.2. Type I Aug. 1931	21	L.2. Type II Dec. 1931
Pn. R. aged 24	29	R.3.
Influenzal attacks	22	R.3.

CASE ANALYSES.

Type III.

Past History	Present Age	Type of Illness
Influenza 6 weeks 1929	47	Pneumonia 1930 L.2. Bronch. +++
Pneumonia aged 7 and 10	20	Pneumonia R.123.

CASE ANALYSES.

Group "X".

Past History	Present Age	Type of Illness
Pneumonia aged 14. Frequent colds	34	Pn. mild.
Pleurisy L. aged 22	23	Pn. R.3;R.2;R.1;L.2. Died.
Chr. Bronchitis	42	Pn. R.13. Bronch. +
Op. Turbinates removed 2/3/30	20	Pn. 27/3/30. Consolid. L.12.
Chr. Bronchitis	14	Pn. L.2.
Influenza aged 22	24	Pn. R.3.
Pleurisy R. aged 42	62	Pn. R.3.
Pn. L. aged 14	22	Pn. L.12.
Pn. R. aged 33	34	Pn. R.13.
Influenza aged 20	21	Pn. R.13. L.2. Bronch. ++
Asthma. Bronch. Pn.I. aged 17; Pn.II.aged 41	42	Pn. Bronch. ++
Pn. L. aged 32	34	Pn. R.1.
Chr. Bronchitis	59	Pn. R.3. Bronch. +++
Influenza aged 22	32	Pn. R.3.
Chr. cough Bronchiectasis	18	Pn. L.2.
Pericarditis aged 28	31	Pn. R.3. Pleurisy ++
Chr. Bronchitis	42	Pn. R.1.
Chr. Bronchitis	38	Pn. L.1.

Discussion.

Less than one third of all the cases gave a definite history of previous acute or chronic respiratory infection. Thirty three of the total number (233) and 27 of the 150 Type I and Type II cases had previously been treated for pneumonia. This supports the generally accepted view that an individual who has had a pneumonia is on the whole more liable to have a second attack. Chronic chest conditions were not commonly found and were fairly evenly distributed between the types. There is therefore probably no special tendency for such cases to develop lobar pneumonia, their occurrence in such a series as this being due simply to their chance scatter in the general population. Where the previous attack had occurred during adult life the patient could frequently state definitely which lung had been affected.

TABLE III.

Situation of a Second Consolidation.

		Same Side		Opposite Sides	
	Cases	L.	R.	Previous attack	Present attack
Type I	6	4	1	L	R
Type II	7	4	2	L	R
Group "X"	3	1	1	L	R
Total	16	9	4	3	

i.e. nine had two attacks in the left chest and four had two attacks in the right chest, while three who had had previously a left-sided pneumonia had on the second occasion a right-sided consolidation.

Evidence is accumulating to show that, although a first attack predisposes to a second, some immunity is acquired, e.g. an individual who has had a Type I pneumonia is more prone to develop a second attack, but the infecting organism is likely to be Type II, Type III or Group "X".

W.M. aged 42, was admitted to Belvidere Hospital in October 1930 to the ward of Dr. Montgomery who was in charge of the control investigation. He then had a Type II infection from which he made a slow recovery and was in indifferent health till his admission to Glasgow Royal Infirmary in February 1931. The illness was on this occasion more broncho-pneumonic and a pneumococcus Type XVII was isolated.

W.C. aged 21, was admitted to Belvidere in August 1931 with a fairly severe L.2 pneumonia Type I and developed empyema for which he was operated on but made a good recovery. He remained well till December 1933 when he was admitted to Glasgow Royal Infirmary. He was seriously ill and had a complete L.2 consolidation. Type II was isolated. The pneumonic consolidation was very massive and effusion was present on the fourth day.

Cruickshank (Milroy Lectures, 1933) has accumulated a further five cases in which the second attack was due to a different serological type. One case is of exceptional interest: the patient was readmitted a year after an attack of Type II pneumonia and again Type II pneumococcus was recovered

from the spit. He developed, however, an empyema from which a haemolytic streptococcus was recovered. Further, this case had been proved to be a Type II carrier after his first attack, and no doubt was still harbouring this organism when he developed his second attack.

Conclusions.

The cases, though small in number, support the accepted view that a second attack has a predilection for the lobe previously affected and indicate that this holds for each Type. There is some evidence that a second attack of pneumonia is likely to be caused by a pneumococcus different in type from that which caused the first attack.

Upper Respiratory Tract Infections.

The belief that a 'neglected cold' is a frequent precursor of pneumonia is another that is common to the man in the street, and this also receives support from medical opinion. Cecil (1930) goes so far as to say that "the prevention of pneumonia is really dependent almost entirely on the prevention of the milder respiratory infections". He says that a surprisingly high percentage of his patients had a history of sore throat, coryza or influenzal attack, even acute tonsillitis or a sinus infection.

It is difficult to reconcile this view with the fact that the large majority of cases of lobar pneumonia are due to strains of pneumococcous which are rarely found associated with infections of the upper respiratory tract. There is, however, evidence that some epidemics of sore throat and common cold are in a measure due to fixed type pneumococci (Park, 1930). Joppich (1934) relates an interesting account of an epidemic of Type I in a rural area in Germany. In this area there was a home for about 30 children of all ages in charge of domestics and nurses. The first case was a child aged 2, who had a double pneumonia and purulent pleural effusion. He later died, after developing purulent meningitis. Type I pneumococci were isolated from all the exudates. A few days later, three more children were admitted to hospital from the same home. The

clinical and X-ray evidence were indicative of croupous pneumonia and the organism isolated was Type I in all cases. A bacteriological examination of the inmates of the home was made, and of 23 found to be harbouring pneumococci, 15 were Type I. A score of persons examined were more or less ill, suffering from pharyngitis, tracheitis, bronchitis, etc. While some had been febrile for several days, others had escaped more lightly. There was no relationship between the age of the patients and the severity of their symptoms. Among seven persons found to be clinically well were four carrying the pneumococcus. The infectivity of this Type I pneumococcus was almost as great as that of influenza, but the disease took the form of croupous pneumonia in only a few cases. The important point is that in this localised epidemic, more than 60 per cent. of the persons examined were carriers of this special type of pneumococcus. The author compares this with the figures for a healthy population among whom only 12 to 13 per cent. ordinarily show Type I, although this figure may be increased four times in the presence of pneumonia.

A somewhat similar epidemic is related by Gundel and Wallbruch (1935) in a village of three hundred inhabitants. A slight epidemic of influenza occurred two weeks before the appearance of the first case of lobar pneumonia. Nineteen cases of Type I pneumonia occurred. Type I was found in the throats of thirty five out of sixty nine contacts with the

infection, in contrast to the healthy elements of the community who showed only one per cent. of Type I carriers.

Cruickshank (1933) has collected a number of cases where a convalescent carrier was the source of lobar pneumonia in another, but there was no means of investigation for the presence of upper respiratory infection from the same source. The possibility of acute upper respiratory infections being in some cases due to fixed type pneumococci is obviously a problem calling for further investigation.

The Present Series.

The acute cold and the associated upper respiratory infections are very prevalent in Glasgow, especially during the winter months. It would not have been surprising, therefore, to have found that a considerable number of the present series (of which a large majority were investigated during the winter months) had had a cold immediately or some short time preceding the onset of pneumonia. Only one Type I case had an upper respiratory infection immediately preceding the onset of pneumonia, while one patient although subject to 'influenzal colds' was well at the beginning of his pneumonia. In three Type II cases the pneumonia followed an attack of cold; on the other hand, two who were liable to 'colds' and a third who took frequent sore throat were free from these conditions at the time of onset. Since the Group "X" organisms are frequently present

in the exudate of upper respiratory infections, it would not be surprising to find that a 'cold' often preceded a Group "X" pneumonia. However, only one had a definite cold as a precursor, while a second had 'influenzal symptoms' and none had a history of liability to upper respiratory infections.

Conclusion.

No evidence can be adduced from this series to suggest that the common cold is a frequent precursor of lobar pneumonia due to the fixed type pneumococci.

In epidemics where lobar pneumonia and upper respiratory infections occur coincidently, it is possible that a proportion of the latter are due to pneumococci of the same types as the pulmonary cases.

Faucial Congestion.

Although few made any complaint of sore throat either preceding the onset or after admission, a very large number were found to have faucial congestion.

TABLE IV.

Cases showing Faucial Congestion.

Type	Cases	Percentage	Total Cases
I	47	67·14	70
II	58	72·50	80
III	6	75·00	8
"X"	41	54·67	75
Total	152	65·23	233

In nearly all cases this was quite evident on admission and seemed to progress and abate with the pulmonary condition. The congestion involved the posterior pharyngeal wall, faucial pillars, uvula and tonsillar surface, but the tonsils were not specially affected. Occasionally the mucous surfaces became bluish red, smooth and glazed with flecks of mucopurulent discharge, but even in these cases the inflammation was not well marked in the tonsillar regions and the submaxillary glands were either not enlarged or only slightly larger than normal. The impression gained was that the faucial congestion was an

accompaniment of the pneumonia and not an antecedent. In many cases the frequent hard cough of the onset appeared to be the cause; in others there was an actual purulent infection but in all it was mild and easily controlled by adequate mouth hygiene. The faucial congestion occasionally becomes severe and extensive, constituting a serious complication, but in the majority of recorded cases acute pneumococcal pharyngitis occurred in the absence of pulmonary consolidations.

Henderson (1934) has made a survey of the scanty literature and recorded eleven cases which occurred during an epidemic of pneumonia and influenza. Nine of his patients were women and two were men. In all cases the illness was of exceptional severity in which an intense inflammatory reaction in the peritonsillar regions was accompanied by septicaemia. Pulmonary symptoms were present only in one case in which the infecting organism was Type I. This patient had a positive blood culture but made a good recovery. Antipneumococcal serum was used. Four of the remainder were Type III infections and six were Group "X". All of these had an associated septicaemia and all died, but none had signs of lobar pneumonia. It seems that, with the exception of the Type I case which appears to have been a typical case of lobar pneumonia with unusually severe throat symptoms, the other cases belong to a separate group in which typical pneumonia is unusual. The Type III and Group "X"

strains in this series had evidently for these individuals overwhelming invasive power but little tendency to cause pulmonary consolidation. Type III is closely related to the streptococcus group and no doubt certain of the Group "X" strains have similar affinities (Avery, Heidelberger and Goebel, 1925).

Bradbeen (1936) reports two cases of Type I pneumococcal mastoiditis which made good recoveries with small doses of antiserum. The blood cultures were negative. This is interesting in view of the antigenic similarities between strains of the streptococcus and certain pneumococcal types, especially Type III and Type XXIX, since the streptococci are much the most common cause of acute otitis media and mastoiditis. Harris and Yemkomshian (1936) reported a case of pneumococcal meningitis following tonsillectomy.

The Present Series.

In this series, out of 233 patients only 6 gave a history of antecedent sore throat, so that this is not, at least, a common mode of onset. Further, it is a common experience that many patients have recurrent nasopharyngeal catarrh for many years without developing acute pulmonary disease. Cruickshank and Montgomery (1933) while investigating contact and convalescent carriers of Type I and II pneumococci,

found that the majority of these had some abnormal condition of tonsils, nose or sinuses, or a chronic bronchitis. Persistent contact carriers of the type specific I and II pneumococci appear to be rare (Christie, 1932) and when more are recognised will probably be found to resemble the comparable diphtheria and typhoid carriers in having little apparent residual disease. The convalescent carriers, on the other hand, maintain the type specific infection for a varying and often prolonged period because of previously debilitated tissues which are slow to return to normal (Macgregor, 1933).

Conclusions.

It appears that acute membranous pharyngitis, although it may be of pneumococcal origin, is not a common precursor or complication of lobar pneumonia and does not frequently occur as a separate condition following infection with strains which are commonly found associated with lobar pneumonia, i.e. Type I, Type II and the associated Group "X" strains. On the other hand, although Type III and Group "X" strains resembling it do not frequently develop invasive powers they may, in the case of susceptible individuals, gain rapid and destructive entry via the pharynx and kill quickly with septicaemia, or produce a severe local infection originating in the upper respiratory tract and extending beyond it without pulmonary symptoms. A mild

degree of faucial congestion is, however, present in nearly every case during the course of the illness.

The Influence of Exposure on Susceptibility.

Special regard was paid to the circumstances of the onset and the period preceding it, with reference to unusual exposure to the weather or extremes of temperature. Reliable histories were obtained in 224 cases; 63 Type I, 77 Type II, 76 Group "X" and 8 Type III. The numbers in each type have been classified into those who gave and those who did not give a history of chill. Of the remainder, all of whom gave no history of chill, the nature of the occupation has been taken into account.

The Influence of Environment.

The idea that exposure to cold and damp predispose to pneumonia is prevalent in the lay mind and is subscribed to in most medical textbooks. But statistical evidence that these factors have a selective effect on the incidence of cases in a community exposed to the pneumococcal infection, is incomplete.

Cruickshank (1933) discussing the incidence of lobar pneumonia from the epidemiological stand-point, stresses the fact

that a comparison of the death rate in various communities may not be made unless the percentage incidence of the pneumococcus types, the age incidence, the climatic conditions and the constitution of the exposed community are all considered. The first three of these criteria can be ascertained with accuracy; the fourth, which in its widest implications is a consummation of innumerable factors concerning the individual cases, can be roughly compared when the individuals are engaged in the same occupation.

Vernon (1920) found that lobar pneumonia is much more common among steelworkers than in other trades. The characteristics of this occupation are hard physical toil and exposure to alternating extremes of temperature. The present series, although all came from an industrial area containing all the heavy industries, has only a few steelworkers but contains a large number of persons who were exposed to the weather while doing hard work. Among these, the steelworkers illustrate the effect of the exciting factors in an extreme form.

The Present Series.

Type I. Males.

26 gave no history of exposure and were not occupied in exposing occupations. 4 gave definite history of 'chill', one of these at a 'funeral' thus giving evidence of a frequently alleged cause of 'cold'. 14 were engaged in occupations exposing them to change of temperature (bakers 2, labourers 4 and 8 various). One developed pneumonia during a preceding attack of subacute rheumatism for which he had been in the ward for seven days. Thus of the total 45, only 4 gave definite history of 'chill'.

Females.

Of 18 women, only one gave a definite history of 'chill'. One followed tonsillitis, the others had no preceding exposure.

Type II. Males.

25 gave no history of chill; 8 gave a definite history. 28 belonged to 'exposing' occupations and these amplify the Type I list with regard to varieties of occupation. Bakers and general labourers are again specially prominent but the list includes outdoor workers of all sorts. Two were men who took ill on their first day of employment after a long spell on the 'dole', testimony to the debilitating influence of idleness.

Females.

While 11 gave no history of 'chill', 5 gave a definite history; one developed pneumonia as a sequence to influenza.

Type III.

There were only 8 Type III cases and only one of these, a woman, gave a history of 'chill'. All were persons not specially exposed to weather.

Group "X". Males.

28 gave and 3 did not give history of 'chill'. 22 belonged to exposing occupations of the same type as in Types I and II.

Females.

In all 26 female cases no history of 'chill' was obtainable.

Comment.

These figures seem to indicate that sudden chilling of the body is not a frequent precursor of pneumonic infection and in a number it was not clear whether the initial chill experienced was not a rigor introducing the reaction to an already established infection. It is, however, a sufficiently frequent occurrence to justify its inclusion as a predisposing

factor. A large number of cases occurred in persons whose occupation exposed them to the weather; this number is specially large in the Type II series. Evidently a life of physical toil in the open does not increase resistance to infection in these cases. It has to be borne in mind, however, that many had very unsatisfactory social conditions involving poor feeding and overcrowding. A majority, which was large in the Type I but not in the Type II and Group "X" series, belong to sheltered occupations and have not been exposed to notable chill. This is specially true of the female patients who usually had led sheltered lives and had not experienced 'chill'. It appears that the infection may attack any susceptible individual, but when susceptible it is specially dangerous to have to earn a living at a physically tiring outdoor job, while the risk is augmented a little by unusually prolonged or severe chilling.

Symptoms at the Onset of Infection.

In practically all of the cases the onset was well defined and was ushered in by the characteristic symptoms. In order of frequency these were:— rigor, thoracic pain, sickness, malaise and cough. Rigor was the most frequent initial symptom but frequently did not occur if one or two other symptoms introduced the infection. Pain was almost as frequent a first symptom as rigor and was constantly present as one of the first three symptoms. Malaise was a frequent first symptom, while cough was usually later. Nausea was a fairly common early symptom but actual vomiting was unusual except in very young patients who in this series were few. Headache was not very frequent but was apt to be severe. It was usually frontal or general and was notably resistant to treatment.

When the occurrence of these symptoms is analysed under the heading of the Types, it is found that in this series rigor is the most frequent initial symptom in the fixed Types I and II but is a little less frequent than pain in the Group "X" series. Pain remains a constant feature in all groups. There is nothing of note in the distribution of the other symptoms except that malaise, which is fairly prominent in all, is rather more frequent in Type II. Malaise probably occurs much more frequently as an initial symptom than these figures indicate since the patient probably tends to forget an ill-defined feeling

of 'unwellness' with the later occurrence of one of the more dramatic symptoms. Case 137, who was a physician, had an extremely severe Type I pneumonia. The illness developed fairly suddenly with pain and cough in the evening after driving from Edinburgh. During his convalescence he recollected that he had felt the road very 'bumpy' and had stopped twice, thinking a tyre was down. The Edinburgh road is a speed track with a perfect surface and the car was in excellent condition, so that there is little doubt that the 'bumps' were the ordinary mild road vibration felt unduly by a nervous mechanism beginning to be toxically depressed. Case 173, a man of 40 who died of a Type II infection marked by severe toxaemia, had a similar experience while driving from Forfar to Paisley. He, an expert driver, found the journey a great strain, "the car jolted badly" and he felt very tired and uncomfortable. He had a rigor during the night and was acutely ill next morning. General aching of the bones was felt by a few in all groups, but this symptom, so characteristic of the influenzal series of infections, always took a subsidiary place to the symptoms typical of lobar pneumonia.

Seven patients, three Type I, three Type II and one Group "X" had as a prominent early symptom acute abdominal pain and were admitted first to the surgeon, suspected of having appendicitis. All were sufficiently anomalous to encourage the

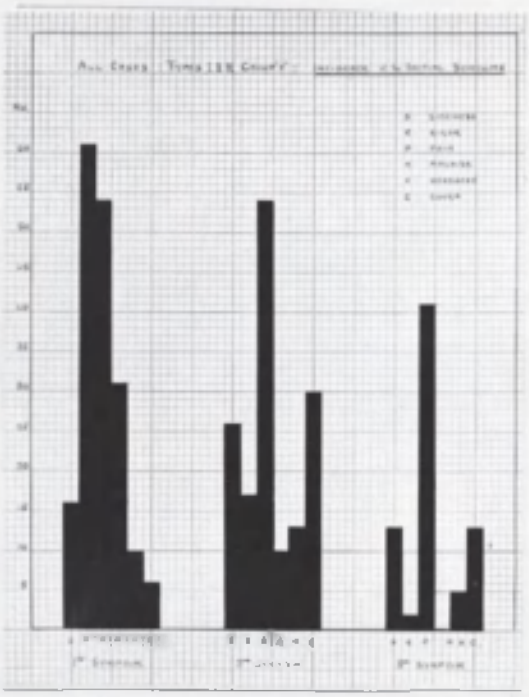
surgeon to delay operation, but in one or two, intrapulmonary signs were in abeyance for 24 or 48 hours and not unusually were poorly defined throughout. In these cases the initial lesion is usually a diaphragmatic pleurisy and it is important to examine at the extreme bases, especially anteriorly and laterally. Cough is frequently very slight but an observant nurse can usually obtain a fleck of sputum sooner or later which greatly simplifies the diagnosis.

Ferguson and Lovell (1928) found in a typical series of 193 cases that rigor occurred in about 90 per cent., malaise in 70 per cent. Pain in the chest was frequent and headache and vomiting were fairly common in the younger patients. They found that preliminary malaise was frequently followed by a severe illness.

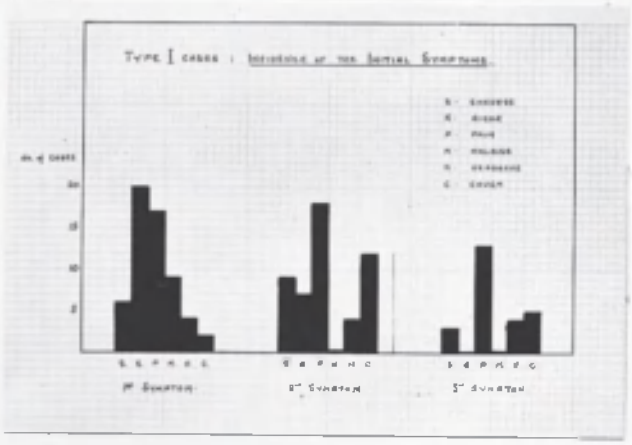
Conclusions.

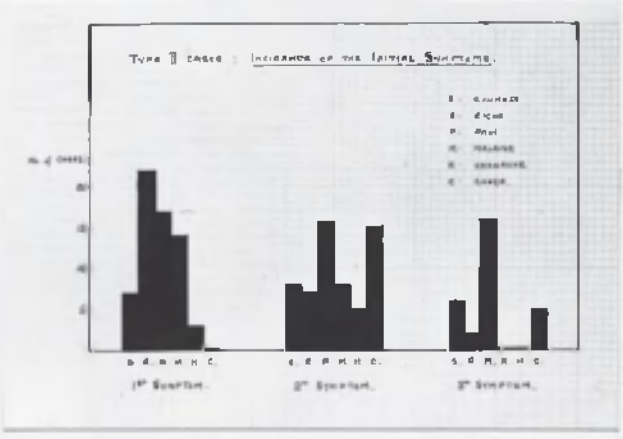
The introduction of a specific remedy in lobar pneumonia has laid on the physician an increased obligation to make a diagnosis at the earliest possible moment, since the efficacy of the Felton Serum is to some extent inversely proportional to the delay in administration. The present investigation confirms the accepted data regarding the incidence of the initial symptoms and shows that with small variations they are similar for all types examined. In the great majority the onset is with rigor followed by pain in the chest, or vice versa. This dramatic

syndrome should in all cases be regarded as the forerunner of lobar pneumonia and be an indication for rest in bed and close observation until later symptoms and signs confirm the diagnosis or till the attack shows itself clearly as an abortive one. During the period of observation every effort should be made to obtain sputum specimens immediately they are available. When we turn from the characteristic symptoms of onset to those more infrequent and poorly defined, such as malaise, sickness, headache and abdominal pain, the diagnosis has to be made from acute cerebral and acute abdominal disease. In these cases the symptoms are usually indeterminate and a period of observation is necessary, but again, no harm is done in treating such cases as lobar pneumonia, while keeping the mind open to other possibilities, and in examining at once any sputum obtained. Only by attempting diagnosis in the early stages before the classical signs of consolidation are present, can we hope to obtain the maximum benefit from antiserum. This is particularly true of the Type II cases where the serum is probably of little use if given after the first 48 hours of illness.



Incidence of the Initial Symptoms:
All cases Types I, II, III and "X".


Type I cases : Incidence of the Initial Symptoms.
1st Symptom
2nd Symptom
3rd Symptom


Type II cases : Incidence of the Initial Symptoms.
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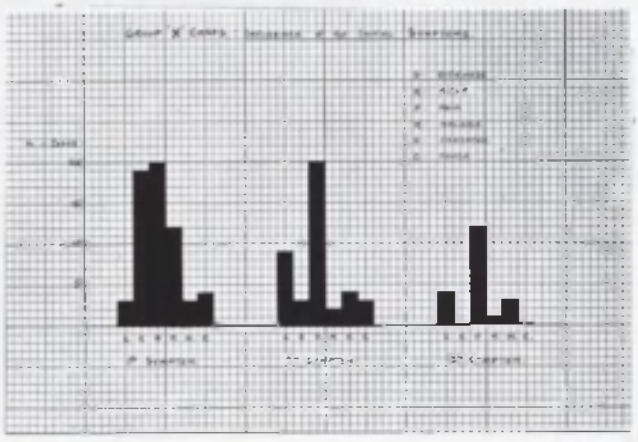
2nd Symptom
3rd Symptom



JAUNDICE IN LOBAR PNEUMONIA.

It has long been recognised that clinical jaundice occurs from time to time in lobar pneumonia and several hypotheses have been offered as to its pathogenesis.

(1) The haemolytic theory according to Banti ascribes to the pneumococcus a direct haemolytic effect and McPhedran (1911) suggested that destruction of the red blood corpuscles occurs in the lung alveoli undergoing hepatisation.

(2) The hepatic theory — that bacterial action on the liver produces hepatitis, cholecystitis, duodenitis and catarrh of the bile passages.

Howard (1936) believes that jaundice arises from a variety of causes: retention of bile; infection of the bile ducts, gall-bladder or liver; hypostatic congestion and haemolysis. This last he believes to be of primary importance.

These theories assume that the presence of jaundice indicates a harmful effect on the tissues. But Elton (1929) has suggested that a high bilirubinaemia is associated with recovery either by crisis or by pleural exudate and that low concentration of bile in the blood are common in fatal cases. Recently, Najib-Farah (1937) has shown that the addition of quantities of bilirubin, comparable to these found in states of

hyper-bilirubinaemia, to normal human serum confers on it powers of agglutination and lysis for pneumococci. Streptococci were not affected nor were avirulent strains of pneumococci, but when streptococci and virulent pneumococci were added, the streptococci flourished while the pneumococci underwent disintegration and lysis.

One case described in detail is that of a boy who had a Type I bacteriaemia associated with severe sore throat and symptoms of subacute rheumatism. The blood showed bilirubinaemia increasing to 2·0 units Van den Bergh. Seven other cases of acute and subacute rheumatism had varying degrees of bilirubinaemia. There is no mention of a pneumococcal infection in these cases, but the author draws the conclusion that the increased bile-content of the serum may be a defensive measure against the pneumococcus, on the assumption that his cases were of pneumococcal origin, although it may have been possible to demonstrate this in the blood only during the initial sore throat phase of the disease. The evidence seems to support little more than a conjecture.

Until the introduction of the Van den Bergh test and the Icteric Index, jaundice was thought to be infrequent in pneumonia although the difficulty of detecting slight icterus in the skin and conjunctivae was known. In one thousand five hundred and one cases Aufrecht (1899) recorded clinical jaundice in only fifteen (1 per cent.); Elton (1929) had three cases of

jaundice in seventy (4·3 per cent.), while in the present series of two hundred and thirty three cases jaundice was detected in seven cases (3 per cent.).

It is now recognised that estimation of the occurrence and intensity of jaundice from the colour of the skin and conjunctivae is as inaccurate as the estimation of anaemia from the skin and mucous membranes. An increase in the bilirubin content of the serum has to be considerable before pigmentation is noticeable. The simplest and most reliable method of estimating the serum bilirubin is by a direct comparison of the colour of the serum or plasma with a standard coloured substance. By the method of Meulengracht (1920) the standard colour is a weak dilution of potassium bichromate: 1/10,000 with a trace of sulphuric acid. This gives a solution closely resembling the colour of normal blood serum or plasma. If protected from light it keeps well and can be used indefinitely. The plasma to be tested is diluted to near the colour of the standard solutions. The two are then compared in a colorimeter. Where R is the reading of the serum being tested and S is the reading of the standard, while D is the degree of dilution, then R/S x D = the Icterus Index of the serum. By this method the normal range is one to two or three which is equivalent to 0·5 - 1·5 mgm. of bilirubin per cent. Jaundice does not usually become evident in the surface tissues till the Icterus Index reaches fifteen to seventeen, so that there is a

considerable interval (Icterus Index 3 — Icterus Index 15) when the jaundice is latent.

An estimation of the Icterus Index makes it possible to observe the progress of a case of jaundice, for it has been found that owing to the slow rate at which the pigment is removed from the tissues, an individual may for several days remain clinically jaundiced although the serum content has returned to normal. The main disadvantage of the method is that to obtain sufficient serum or plasma, about 5 c.c. of blood are necessary.

Clinical Significance of Bile Solubility.

The bile solubility of the pneumococcus is one of its characteristic features and recent work has confirmed the findings of earlier workers in terms of the subdivision into the pneumonic types (Rigobello, 1930; Ziegler, 1930; Neufeld and Ettinger Tulezynska, 1930).

The solvent action in these studies is assumed to be a property of the surface-tension decreasing effect of the bile salts (sodium glycocholate and sodium taurocholate). The investigation of the relation of hyperbilirubinaemia to increase of the bile salts in the serum is a difficult matter. Aldrich and Bledsoe (1928) have devised a method using the Pettenkofer test in a quantitative adaptation. The method is elaborate and owing to the varying colour of the test, solutions at

various concentrations cannot be readily estimated in the colorimeter, although by using standard wedges fairly accurate results can be obtained. The evidence suggests that increase in bile pigment in the blood is usually associated with a comparable increase in the bile salt content. It is unlikely, however, that as Elton (1930) suggests, the bile content of the serum rises to such an extent as to be comparable to the experimental solvent conditions of the bacteriologist. He attempts to show that a high bilirubinaemia is associated with recovery either by crisis or by pleural exudate and that fatal cases tend to have low concentration of bile in the blood. To some extent this is true for his cases because of a time factor. His charts show that the greatest bilirubin content was not reached in the recovery group till after the sixth day of illness, whereas most of the deaths occurred at or about the sixth day.

Mogena (1929) examined a series of cases for hyper-bilirubinaemia by the Hertzfeld method. In five cases of pneumonia he was not able to demonstrate an increase. He states that jaundice occurs more frequently when the right lower lobe is consolidated. Bernheim (1924) states that an Icterus Index of 7·5 is the upper limit to be associated with a favourable prognosis in lobar pneumonia, but that an index of over 15 is compatible with recovery. Schiff (1927) reported on eight hundred and twenty six cases of lobar pneumonia; twenty one

had clinical jaundice while of the whole number eight died, none of these being jaundiced. He concludes that jaundice is not of serious prognostic significance. Milroy (1929) in a general series had eight cases of lobar pneumonia with Icteric Indices ranging between four and ten with an average of 7·5. All of Elton's (1930) fatal cases had indices of less than 17.

The Present Series.

In a number of patients in the present series, an estimation of the Icterus Index was made shortly after admission, and in a few was repeated if the condition of the patient justified it.

Ninety six cases were examined. The average Icterus Index in twenty eight Type I cases was 9·90; in thirty seven Type II cases 9·91; in five Type III cases 9·34; in twenty six Group "X" cases 7·2. The detailed tables show that in every case the Icterus Index was above normal, the figures ranging from 3·5 to 24·5. Both of the extreme figures were found in the Type I cases who recovered. The average indices for each day of admission (Table IV) show that there is a tendency for the figures to be higher in the later stages of illness. The icteric indices show that a hyperbilirubinaemia was present in all the cases examined and that the bilirubin content of the blood was at times found to be at a level where clinical jaundice would be expected but was not recognised. This

finding, however, is common in a variety of congestive conditions (e.g. chronic venous congestion in cardiac disease) and it is understandable that the cyanosis and congestion of the face and conjunctivae which are frequently seen in acute pneumonia, may interfere with the recognition of slight icterus.

TABLE V.

The Average Indices on each Day of Illness.

	1	2	3	4	5	6	7	8	9
Type I	5·7	9·4	10·6	7·6	6·7	5·7	-	-	-
Type II	8·7	6·2	6·0	11·3	9·5	6·7	5·5	-	-
Type III	-	-	5·7	8·5	8·5	15·5	-	-	-
Group "X"	6·7	6·0	7·6	8·9	6·0	7·5	14·0	-	-

ICTERUS INDEX — TYPE I (28 Cases).

Name or No.	Age	Icterus Index	Day	Clinical
MD	22	5·3	4	
JS	46	6·0	4	
3	26	8·5	2	
4	38	7·5	4	Sl. icterus
5	18	8·6	3	
6	31	7·5	2	
7	30	4·9	1	
8	24	7·2	3	
9	32	8·3	2	
10	38	6·8 6·5	2 3	
11	20	4·5	4	
12	37	10·0	2	
13	37	5·3 7·3	4 6	
14	24	3·5	2	
15	24	5·5	2	
16	33	6·5	1	
17	60	24·5	2	
18	10	11·5	2	
19	37	10·5	2	
20	54	8·5	5	Day of crisis

Unless where indicated, the Icteric Index was estimated on the day of admission.

ICTERUS INDEX — TYPE I. (Cont.)

Name or No.	Age	Icterus Index	Day	Clinical
21	24	5·0	4	
22	59	9·0 17·0	2 4	A very acute illness, had thrombosis of leg and clinical jaundice.
23	17	5·0	5	
24	30	10·4	2	Clinical jaundice very slight.
25	57	10·0	4	Died. No P.M.
26	56	9·3	2	Died. No P.M.
27	25	6·5	2	Died. No P.M.
28	46	20·0 24·0	3 6	Slight jaundice.

ICTERUS INDEX — TYPE II (37 Cases).

Name or No.	Age	Icterus Index	Day	Clinical
JM	44	8·7	2	Died. P.M.
HR	64	3·3	6	
JM	20	1·5	3	
MH	42	20·6	5	Clinical jaundice.
JM	26	6·6	4	
DD	23	5·2	3	
7	27	6·7	4	
8	41	10·5	6	Died. P.M.
9	52	6·8	4	
10	44	6·8 7·8	3 5	Died. No P.M. Late clinical jaundice.
11	36	6·5	2	Died. P.M.
12	56	4·2	2	
13	44	4·3	3	Died. No P.M.
14	59	11·5	4	Died. No P.M.
15	28	15·4	3	
16	15	12·0	1	
17	27	5·5	7	
18	17	7·8	5	
19	20	8·5	4	
20	41	4·8 5·0	2 5	Died. No P.M.

ICTERUS INDEX — TYPE II. (Cont.)

Name or No.	Age	Icterus Index	Day	Clinical
21	49	20·0	4	
22	19	6·5	6	
23	21	9·0	2	
24	24	8·7	3	
25	21	8·0	2	
26	17	15·0	4	
27	29	5·3	2	
28	26	8·5	4	
29	21	8·3	2	
30	39	6·4	2	Died. No P.M.
31	21	5·5	1	
32	34	5·0	4	
33	29	5·5	2	
34	19	1·5	2	
35	22	3·0	3	
36	48	5·0 17·0	4 14	Active T.B. long convalescence.
37	30	25·0	4	Gross secondary anaemia.

ICTERUS INDEX — GROUP "X" (26 Cases).

Name or No.	Age	Icterus Index	Day	Clinical
JG	20	10·4	2	Pleural effusion.
WM	19	1·5	2	
AD	14	6·7	1	
D	24	4·0	5	
TA	62	4·5	3	Average 7·2.
P	30	10·5	3	
7	28	7·3	2	
8	49	5·0	2	
9	65	9·5	7	Died. No P.M.
10	28	4·0	4	
11	20	12·5	4	
12	26	10·4	4	
13	21	8·3	2	
14	44	7·3	3	
15	34	6·5	2	
16	46	18·5	7	
17	27	6·4	2	
18	59	10·6	5	
19	17	8·5	3	
20	32	7·4	2	

ICTERUS INDEX — GROUP "X". (Cont.)

Name or No.	Age	Icterus Index	Day	Clinical
21	37	8·0	5	
22	21	7·3	3	
23	19	5·0	2	
24	47	7·5	6	
25	25	3·0	2	
26	46	7·0	2	

ICTERUS INDEX — TYPE III (5 Cases).

No.	Age	Icterus Index	Day	Clinical
1	58	8·5	5	Died.
2	41	5·7	3	Died. No P.M.
3	23	8·5	4	
4	20	8·5	4	
5	38	15·5	6	Died. P.M. — Grey hepatisation; mitral stenosis; nutmeg liver.

ICTERUS INDEX — STREPTOCOCCAL PNEUMONIA.

No.	Age	Icterus Index	Day	Clinical
120	68	10·6	6	Died. No P.M.

Fatal Cases.

Three fatal Type I cases had an average index of 8·6, the highest 10 and the lowest 6·5. Seven fatal Type II cases had an average of 7·2, with 11·5 and 4·3 as the extremes. One Group "X" patient who died had an index of 9·5, while the three fatal Type III cases had respectively 8·5, 5·7 and 15·5.

Cases with High Indices.

The following had an index higher than 17 :—

Type I. Three cases.

Case 122. F. aged 60. Icterus Index 24·5 on second day. A partial consolidation resolved completely during an uneventful convalescence. She was a chronic bronchitic.

Case 173. M. aged 59. A very acute illness involving R.1, 2, 3 and L.2. He had a crisis on the fifth day but convalescence was slow and a month later he had a thrombosis of the calf. The Icterus Index on the second day was 9 and on the fourth day 17. Jaundice of the conjunctivae was noted on the third day. The blood culture was positive and there was a leucopenia.

Case 40. M. aged 46, had a severe 'patchy' pneumonia involving both lungs. He was extremely cyanosed and dyspnoeic on admission and was in a state of low delirium suggesting an alcoholic background. He made a dramatic recovery with serum. He was

jaundiced when admitted on the third day and the Icterus Index was 20 on the sixth day; two days after the crisis the Index was 24, but recovery was rapid and jaundice was quite clear by the ninth day.

All three patients were in the 'over 40' group where the disease tends to be severe and toxic.

Type II. Only three cases had indices over 17.

Case 32. F. aged 42, had a severe toxic illness. After a crisis on the eighth and ninth days, temperature rose to 107°F. on the twelfth day and with this was associated blood and albumin in the urine and pneumococcus Type I was found in pure culture in the urine. She had slight conjunctival icterus when admitted on the fifth day and the Index was 20·6.

Case 229. M. aged 48, was extremely ill on admission and was thought to be moribund until the 17th. day. Convalescence was very slow and he was later found to have an active tubercular lesion with a degree of bronchiectasis; this had been masked by his pneumonia. The Icterus Index was 5·0 on the fourth day and 17·0 on the 14th. day, and there was no jaundice clinically at any time.

Case 230. F. aged 30. She was admitted on the fourth day sharply ill and made a very slow recovery. There was slight jaundice and an Index of 25·0. She was, however, grossly anaemic (R.B.C. 3,200,000; Hb. 30 per cent.), this having followed the birth of a child some months previously.

Group "X".

Case 123. M. aged 46, admitted on the seventh day at the termination of a mild attack. The Index was 18·5 but there was no jaundice.

Although no fatal case in the series had an Index of more than 17 this does not distinguish them in any way from the great majority of cases which recovered, the indices in both groups being quite comparable.

Summary.

Only seven cases had indices of 17 or over; all but one were patients over 40 who had severe illnesses showing other evidence of acute toxaemia and, in fact, are the cases in which liver upset is to be expected. The exception was the girl with post-puerperal anaemia, noted above, whose jaundice was probably of haemolytic origin. There is no evidence here that bilirubinaemia had an association with the mechanism of the crisis. On the other hand, the findings support the generally accepted view that jaundice in pneumonia is an expression of the pneumonic bacteriaemia and toxaemia on the liver cells. This effect appears to be more noticeable in older patients and where the acute illness lasts a week or more.

Post-Mortem Examinations.

Four of the fatal cases came to post mortem, two Type II and two Type III. All had septicaemia and extensive lung lesions, but the Icterus Index was below 11 in all of them and the condition of the livers was normal for their respective ages. This suggests that while the pneumococcus and its toxins invariably disturb the liver to some extent and while this is more marked when the illness is prolonged and severe gross liver damage is not a conspicuous complication of lobar pneumonia.

Conclusions.

(1) The findings, which in this series of typed cases are in agreement with most of the previous work on clinical jaundice and the estimation of bilirubin in untyped series, suggest that a high bilirubinaemia is due to the continued action of pneumococcal toxins on the liver cells.

(2) The longer the duration of the illness, the more likely is jaundice to be present.

(3) A fatal illness of short duration may have a low index while clinical jaundice may be present in a less severe but more prolonged illness ending with recovery.

(4) The evidence is insufficient to support the contention that the presence of bile aids recovery by its action on the pneumococci or that a high bilirubinaemia is associated with termination by crisis.

(5) A subclinical jaundice is nearly always present.

(6) Clinical jaundice is not common.

(7) Jaundice, even when considerable, is not of serious significance.

THE BLOOD IN TYPED LOBAR PNEUMONIA.

Most of the knowledge concerning the blood changes in lobar pneumonia is based on work done antecedent to the differentiation of the fixed type infections. The main features are well recognised and most textbooks contain full accounts. The main interest of the blood in the recent work on pneumonia has been bacteriological — bacteriaemia (the presence or absence of precipitins, agglutinins, opsonins, etc.) — or biochemical — anoxaemia, disturbance of the acid base balance and the effect on the clinical constitution of the plasma and serum. The cellular elements were known to behave in the presence of a pneumococcal infection in a fashion similar to the other acute septic infections.

The toxaemia, which in a serious case of pneumonia may be profound and which is always present to some extent, has long been a matter of clinical observation but until recently there was no explanation for the variability of its occurrence. Segregation of the types has carried us a step further, for it is now clear that in general the varying morbidity and mortality associated with Types I, II and III and Group "X" can be correlated with the toxaemia encountered in these groups.

The bacteriological explanation of this varying toxicity is not yet complete. No specific toxin has been demonstrated but it has long been known that the pneumococcus is

virulent only when its capsule is intact. This fact has directed much attention to the chemical constitution of the capsule. It consists of a soluble carbohydrate substance which in large quantities is harmless to laboratory animals. Nevertheless it has been shown (Sia, 1926) that this specific soluble substance is able to inactivate the natural defensive substances of the blood and enable pneumococci to flourish in conditions where otherwise they would be destroyed.

Earlier investigations (Dochez and Avery, 1917) had shown that specific soluble substance is present in blood and urine during the course of the illness and that the quantity elaborated varies with the type of infecting organism, i.e. it is greater in Type III than in Types I and II. Cruickshank (1933) from a review of the evidence suggests that this variation in the quantity of specific soluble substance may be taken as an explanation of the difference of morbidity and mortality of pneumonia Type I as compared with Type II.

Type II and Type III.

Since the commencement of this investigation an accurate record has been kept of the occurrence of symptoms and rigors and signs associated with toxaemia, headache, restlessness, insomnia, delirium, prostration, incontinence, vomiting, diarrhoea, etc., both for the serum treated cases at

Glasgow Royal Infirmary and the control cases at Belvidere Hospital under Montgomery.

While of extreme value to the experienced clinician, estimation of the progress of the individual case by the correlation of these symptoms is difficult when dealing with large numbers. For this reason the leucocyte count was thought likely to give more comparable information and routine daily counts were made during the course of the illness (Fleming, 1933). It was found that in the infections associated with acute toxaemia (Types II and III) the leucocyte count tended to be lower than in Type I and Group "X" cases in whom toxic symptoms are seldom severe. It was discovered that this depression of the leucocyte count made it uncommon to find Type II and Type III cases with counts above 15,000 cells per c.m. during the first four days of the illness, whereas Type I and Group "X" cases commonly had counts above 20,000 cells in the comparable period. The tendency to depression of the count became greater with increasing age and in the presence of bacteriaemia. It was possible to make the generalisation that where the age of the patient and the day of illness were considered along with the leucocyte count, it is possible to attempt clinically the differentiation of Type II and Type III from Type I and the Group "X" strains. While these findings supported the idea that an antileucocytic substance might be at work, it was insufficient to disprove that the depression of the leucocyte counts was not an expression of

the general depressent effect of the infection on all the body processes including the bone marrow.

In diseases of the blood it is a fairly general finding that when one department of the haematological system is affected profoundly the other departments are also influenced to some, usually lesser, extent. It is usual to find a secondary anaemia associated with the leukaemias, for instance, while the disturbance of the red cell manufacture in pernicious anaemia also disturbs the output of polymorphonuclear leucocytes. If therefore the leucopenia encountered in so many of these cases is due to a direct toxic effect on the leucocyto-poetic mechanism, it is reasonable to expect other evidence of this in both the white cells and the red cells.

With this purpose in view, an examination of the blood picture was made in those cases which showed evidence of severe toxaemia and especially when very low leucocyte counts were found.

Changes in the Blood Cells indicating Toxaemia.

In addition to the total leucocyte count, the two most important methods used to show toxic effect on the blood cells are:- (1) the Arneth index and its modification by Schilling, and (2) the enumeration of the white cells showing toxic changes.

There is much diversity of opinion as to the relative value of these procedures.

Kollman (1933) has investigated fifty cases of pneumonia, using the Schilling index. He agrees that at times it is a distinct aid in assessing the value of clinical findings, but thinks the index of no more value than the total leucocyte count, and that it is not to be given a place of priority among the other clinical findings. Ponder (1926) and Young (1935), while believing that the Arneth differentiation has diagnostic and prognostic value, find that so much variation occurs both in health and disease that it is only accessary to total leucocyte counts. Kugel and Rosenthal (1932) think the comparative number of normal and toxic cells (which expressed as a percentage they call the 'Degenerative Index') of more value than the total leucocyte count as a prognostic indication. This, however, refers to the leucocyte count regarded without reference to age, type or day of illness, criteria which have been shown elsewhere (Fleming, 1933) to give greatly enhanced prognostic value. Sutro and Rosenthal (1933) describe the cytoplasmic changes in the circulating leucocytes in a large number of infective conditions including pneumonia. They conclude that a degenerative index of four plus carries a bad prognosis even when the blood culture is negative. Mendell, Meranze and Meranze (1936) in a comprehensive study of the cytoplasmic and nuclear changes in the neutrophils in severe infectious states describe toxic granularity as the most striking phenomenon of early degeneration and (ibid., 1935)

comment favourably on the value of this study in prognosis. Adler (1921), in an early paper, thought a count of these cells more value than the Schilling index, and Harkins (1934) thinks it an essential portion of the haemogram.

PROTOCOLS OF BLOOD COUNTS.

Case 228
Male, aet. 22
Type II

Days	3	4*	5	6	7†	8
Leucocytes (thousands)	11·0	7·0	14·0	15·0	10	15

	% Toxic	Non-Toxic	Total
*Poly.	33·3	4·6	37·9
Transit.	20·0	12·1	32·1
Lymphs.			24·0
Myelo.			0·7
Mono.			4·6
Eosino.			0·7

	% Toxic	Non-Toxic	Total
†Poly.	36·7	3·3	40·0
Transit.	34·0		34·0
Lymphs.			16·7
Myelo.			0·7
Mono.			8·6

Case 188 ? TB. Moderate Pl. effusion.
Male, aet. 25
Group "X"

	% Toxic	Non-Toxic	Total	
Poly.	20·0	27·5	47·5	only moderate granularity.
Band.		15·0	15·0	
Mono.			26·5	'lymph. and mono. reaction'.
Lymphs.			11·0	

Case 192 Massive consolidation. Died.
Male, aet. 37
Type II

Days	2	3	4	5*	6	7†	8	9@
Leucocytes (thousands)	22·9	28·2	14·6	14·8	15·0	18·8	37·2	15·5

R.B.C. 4,500,000; Hb. 85%.

	% Toxic	Non-Toxic	Total
*Poly.	67·0	7·0	74·0
Band.	13·0	2·0	15·0
Mono.			7·0
Lymphs.			4·0

	% Toxic	Non-Toxic	Total
†Poly.	34·0	4·5	38·5
Band.	45·0	12·5	57·5
Mono.			1·5
Lymphs.			2·5

	% Toxic	Non-Toxic	Total
@Poly.	13·0	1·0	14·0
Band.	70·0	9·5	79·5
Mono.			2·0
Lymphs.			4·5

Vacuolisation was ++.

Case 207 Feeble ch. bronch.++; mild pneum. but N.B. considerable; toxic. Died.
Male, aet. 42
Type "X"

7th. day:-

	% Toxic	Non-Toxic	Total
Poly.	18·0	36·5	54·5
Band.	5·0	23·0	28·0
Mono.			9·0
Lymphs.			8·5

Case 206 — Previous Type I pneumonia with empyema, illness ++; effusion.
Male, aet. 21
Type II

Days	2*	3	4	5	6	8	9
Leucocytes (thousands)	37·0	33·0	29·4	30·5	27·3	17·6	12·0

*R.B.C. 5,050,000; Hb. 90%.

5th. day:-	% Toxic	Non-Toxic	Total
*Poly.	7·6	20·8	28·4
Band.	22·2	36·2	58·4
Mono.			10·4
Lymphs.			2·8

Case 205 — Illness +++; empyema. Died.
Male, aet. 25
Type I

Days	2	3	4	5*	7	8†	9	10
Leucocytes (thousands)	40·0	42·0	39·0		40·0	29·0	19·0	13·0

	% Toxic	Non-Toxic	Total
*Poly.	5·6	1·8	7·4
Band.	43·4	35·5	78·9
Mono.			7·3
Lymphs.			6·4

	% Toxic	Non-Toxic	Total
†Poly.	55·0	—	55·0
Band.	29·1	3·4	32·5
Mono.			6·7
Lymphs.			5·0
Eosino.			0·8

Case 187 Alcoholic: lung abscess.
Male, aet. 33
Type I

5th. day:-	% Toxic	Non-Toxic	Total
Poly.	50·0	15·0	65·0
Transit.	6·0	20·0	20·0
Lymph.			7·5
Mono.			1·0

Vacuolisation was ++.

Case 181 Moribund: Died 28 hrs. later; toxaemia +++.
Male, aet. 57.
Type I

Days		
4th.	Poly.	10,000
5th.	"	8,000
6th.	"	8,600

Polymorphs 6·6%; Band forms 93·6%. All showed intense granularity both of the multilobed and bilobed cells, but vacuolisation was not conspicuous.

Case 182
Male, aet. 19
Type I

Days	2	3	4*	5	6	7	8	9†	10	11
Leucocytes (thousands)	20·4	11·0	6·0	6·4	16.2	12·6	15·8	24·2	17·6	10·0

	% Toxic	Non-Toxic	Total
*Poly.- -	16·5	12·2	28·7
Transit.	37·8	20·7	58·5
Mono.			4·3
Lymphs.-			8·5

	% Toxic	Non-Toxic	Total
†Poly. - - -	6·2	25·5	31·7
Transit. -	17·7	40·3	58·0
Mono. - -			3·3
Lymphs. - -			6.5

Case 106
Female, aet. 19
Type II

3rd. day:-

Poly.	14·1%	Mono.	5·2%	Myelo.	0·6%
Band.	72·1%	Lymphs.	8·0%		

Megalocytosis.

Case 107
Male, aet. 43
Type II

4th. day	12/5/31		13/5/31		
	Poly.	5·4%	Poly.	3·6%	Mono. 4·0%
	Band.	64·8%	Band.	40·5%	Lymphs. 36·1%
			Eosino.	2·8%	

Leucopenia. Died.

Case 109
Male, aet. 44
Type II

4th. day	25/5/31		26/5/31		27/5/31	
	Poly.	70·5%	Poly.	8·8%	Poly.	12·5%
	Band.	—	Band.	77·0%	Band.	60·0%
	Lymphs.	14·0%	Lymphs.	8·8%	Lymphs.	22·5%
	Mono.	4·0%	Mono.	4·0%	Mono.	5·0%

Died.

Case 113
Male, aet. 43
Group "X"

10th. day:-

Poly.	61·0%	Lymphs.	10·0%
Band.	28·3%	Mono.	0·7%

Died.

Case 158
Female, aet. 41
Type II

14th. day:-

Poly.	52·0%	Mono.	0·3%	Myelo.	0·6%
Band.	39·7%	Lymphs.	6·6%	Eosino.	0·6%

Leucocytes +++.

BLOOD COUNTS.

No.	Sex	Age	Type					
115	Male	11	"X"	5th. day:-	R.B.C. 4,400,000			
					Hb. 81 per cent.			
					W.B.C. 17,000			
13	Male	23	"X"	3rd. day:-	R.B.C. 4,750,000			Died.
					Hb. 94 per cent.			
					W.B.C. 4,750			
9	Female	17	"X"	3rd. day:-	R.B.C. 4,080,000			
					Hb. 80 per cent.			
					W.B.C. 32,000			
7	Male	24	"X"	3rd. day:-	R.B.C. 4,400,000			
					Hb. 92 per cent.			
					W.B.C. 18,000			
160	Male	58	III	Poly. 50% (all band forms)				
				Lymphs. 50% 4000 Leucopenia.				
99	Male	36		2nd. day	3rd. day	4th. day	5th. day	
			Poly.	11,000	before serum 7,000. after serum 7,400.	9,500	5,400	Died.
204	Male	56	I	Extremely severe illness in chronic bronchitis.				
				3rd. day:-	R.B.C. 4,000,000			Died.
					Hb. 71 per cent.			
					W.B.C. 12·2			
203	Male	27	II	Massive consolidation.				
				5th. day:-	R.B.C. 4,740,000			
					Hb. 78 per cent.			
					W.B.C. 14·8			

BLOOD COUNTS. (Cont.)

No.	Sex	Age	Type				
116	Male	28	II	3rd. day:-	R.B.C.	5,000,000	
					Hb.	86	per cent.
					W.B.C.	17·4	
109	Male	44	II	4th. day:-	R.B.C.	5,200,000	Died.
					Hb.	75	per cent.
					W.B.C.	9,000	
206	Male	19	II	5th. day:-	R.B.C.	5,050,000	
					Hb.	65	per cent.
					W.B.C.	20,000	
118	Male	41	III		R.B.C.	5,200,000	
					Hb.	75	per cent.
					W.B.C.	16,000	

Analysis of this Series.

Red Blood Counts.

A small number of blood counts were made in the more seriously ill patients, choosing days when the white cell counts were low. The protocols show that the red blood counts were normal in the Type II and Group "X" and Type III cases examined. In one Type II case who died, the count was 4,000,000. On the other hand, there was a slight but definite secondary anaemia in all cases. The numbers are too small to particularise with regard to Type, but the lowest haemoglobin estimation, 65 per cent., occurred in a Type II patient.

Shift to the Left.

Schilling's modification of Arneth's method was applied to the differentiation of the polymorphs and showed a shift to the left in all cases during the acute illness. In the more serious cases normal leucocytes were greatly reduced in number and occasionally, and especially when the leucocyte count was low, were almost completely replaced by 'band' forms.

Again, the numbers were too small to permit an attempt to find differentiating features between the types. The intensity of the 'shift to the left' was well marked in all the seriously ill cases, irrespective of type. Where a moribund patient survived long enough for a series of counts to be made, it was found in two cases that the relative proportion of normal

polymorphs did not alter much but the 'band' forms tended to fall in number while the lymphocytes increased to such an extent as to constitute a lymphocytosis. This was well marked in a severe Type I case, aged 58, who on the third day, with a count of 4,000, had 50 polymorphs (all 'band' forms) and 50 per cent. lymphocytes.

Eosinophils are usually greatly reduced or absent. Mackay (personal communication) had a case of asthma who, while in hospital, developed pneumonia. His blood showed an intense eosinophilia (56·6 per cent. in the differential count, normal leucocyte count) previous to the onset of pneumonia. Shortly after the onset, eosinophils were completely absent and there was a leucopenia with loss of granular cells. In this series eosinophils were seen in three cases. One, a lad aged 25, who died of an intense Type I infection associated with empyema, had on the fifth day a count of 39,000 cells and there were no eosinophils. Thereafter the count fell rapidly but two days before he died with a count of 29,000 there was 0·8 per cent. of eosinophils. A fatal case, a woman aged 41 with a Type II infection, had low early counts which on the last day rose to 51,000. A differential count done at this time showed 0·6 per cent. of eosinophils.

One case was of special interest; a man aged 43 with a fatal Type II pneumonia in addition to a well marked lymphocytic reaction, had 2·8 per cent. of eosinophils the day before

he died. The leucocyte count was 3,000.

Myelocytic reaction has been observed but no such case occurred in this series.

Lymphocytic Reaction.

One patient, a lad of 25, had a moderate Group "X" illness with pleural effusion. Shift to the left was moderate but monocytes were 26·5 per cent. and lymphocytes were 11 per cent. Although the spit was constantly negative, this case was suspected of having a basic tubercular infection.

Toxic Changes in the Leucocytes.

Shift to the left and the associated responses of the other cells of the leucocyte system are indications of the demand for these cells and the inability of the leucocytopoetic mechanism to respond completely to this demand. There is evidence, however, that in the presence of severe infections the blood cells and especially the polymorphs undergo structural changes which seem to indicate damage inflicted after their discharge from the bone marrow and while in the general circulation. The most striking of these changes is an increase in the size of the basophilic granules of the cytoplasm of the polymorphs. In addition to being larger, the granules appear to have an increased affinity for the stain so that the cell has a coarsely granular appearance which is characteristic and

differentiates them sharply fron normal cells. The appearances are seen in most acute toxic infections, especially streptococcaemia, but also in cases of diphtheria and typhoid and I have seen it in the scanty polymorphs of severe pernicious anaemia.

In addition, vacuolisation is occasionally seen in the cytoplasm of the cells. It is rare compared with granularity and is seen only in very toxic cases.

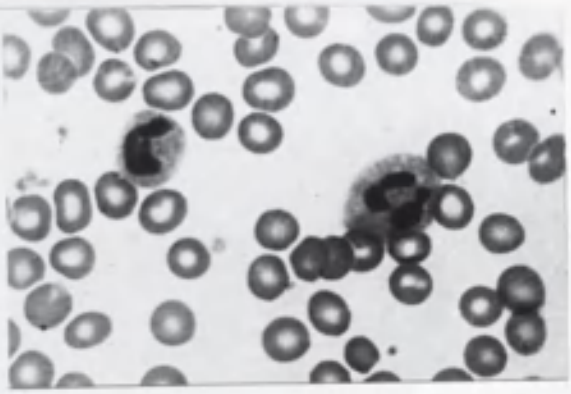


Fig. I.

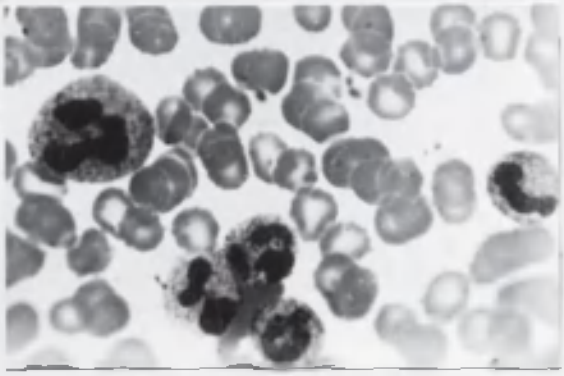


Fig. II.

Fig. I: Normal blood film. x 1,000.

Fig. II: Blood film from a moribund Type II case showing increased granularity of the cytoplasm of the polymorphonuclear leucocytes. x 1,000.

Both films were made at the same time and stained Leishman for similar periods.

A small group of the most acute cases were examined for toxic changes in the cells and the relative percentage estimated in a differential count.

In the earlier stages of a severe toxic infection the typical changes are seen almost entirely in the mature polymorphs, e.g. Case 187. When the shift to the left is slight and band forms are entering the circulation in relatively small numbers, toxic changes are not well marked and will be seen only in an occasional mature leucocyte. On the other hand, when the shift to the left is large, the toxic changes quickly affect the band cells as well and in a critical case (Case 181) there may be no cells of normal appearance present.

Case 192 shows well the progressive effect on the differential percentages. The leucocyte counts here seemed to indicate that some resistance was being maintained since, after an early fall in numbers, the level remained stationary and the day before death showed a preterminal leucocyte crisis. The differential count, however, shows a progressive deterioration from 75 per cent. polymorph count to 14 per cent. and with a corresponding rise in the number of band cells. Signs of degeneracy gradually increase to envelop both groups. In such a case as this the examination for increasing toxic degeneration gives more valuable prognostic information than the leucocyte count alone.

The method involves more personal error than the

ordinary differential count and in any case means so much expense of time that it is probably not suitable as a routine method in pneumonia, but there is no doubt that it has a place in supplementing the information to be derived from daily leucocyte examinations.

Conclusions.

In a small series of severely ill and fatal cases whose blood pictures were examined without reference to Type, it was found that —

(1) A slight but constant reduction in the percentage of haemoglobin was constant, although there was no notable diminution in the red cell count.

(2) A 'shift to the left' of varying degree was found in every case.

(3) Toxic changes in the leucocytes were frequently found and were usually severe in cases showing a severe shift to the left.

From these findings it is inferred that the varying diminution in the total count previously examined is due to a toxic effect on the bone marrow varying with the severity and type of the infection.

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THE LEUCOCYTOSIS IN TYPED LOBAR PNEUMONIA SERUM TREATED CASES.

An attack of lobar pneumonia calls forth changes in the cellular elements of the blood. The most important of these is the sudden increase in the number of the circulating leucocytes. The count begins to rise immediately after infection, and may reach 15,000 - 25,000 even before symptoms have declared themselves. The leucocytosis is mainly due to increase of neutrophil polymorphs, but there may be a shift to the left of varying degree with the appearance of metamyelocytes, and even occasional myelocytes. Lymphocytes and hyaline cells are reduced absolutely, and eosinophils are usually absent. The leucocytosis is maintained until the crisis, when the count rapidly falls to normal figures, the fall usually lagging a little behind the fall in temperature.

While this is the usual response to the infection, in some cases the count may remain low throughout the illness or may rise to very high figures; 100,000 cells per c.mm. has been recorded (Osler, 1909). In many cases these variations can be correlated with the occurrence of complications such as empyema or pulmonary abscess, or with the amount of lung tissue involved, but in others no adequate clinical explanation is available. Leucocytosis is regarded as a favourable sign, leucopenia as unfavourable.

The observations upon the leucocyte count in pneumonia in the past have, with one exception (Clough, 1917), been made in untyped cases, and it has seemed desirable to revise the subject in a series of cases in which the special type of pneumococcous concerned has been determined.

Only typical cases of lobar pneumonia have been considered, the criteria of diagnosis being consolidation of the lung, rusty sputum, and bacteriological detection of pneumococci in the sputum or blood. The onset of illness was estimated by the time of occurrence of the more dramatic symptoms; pleuritic pain, rigor, vomiting, etc. In the majority of cases it was well defined. The blood counts were first made about an hour after admission of the patient to the wards, coincidentally with the first blood cultures, and prior to the administration of serum.

Two counts were made from each blood sample and the mean taken. Subsequent counts were generally made between 9 a.m. and 12 noon. All the patients were given a simple fluid diet, and the effects of digestion upon the leucocyte count can thus be disregarded, although according to the work of Bernard Shaw (1925) this effect can be disregarded in any case. Counts in most cases were made every day until convalescence was established.

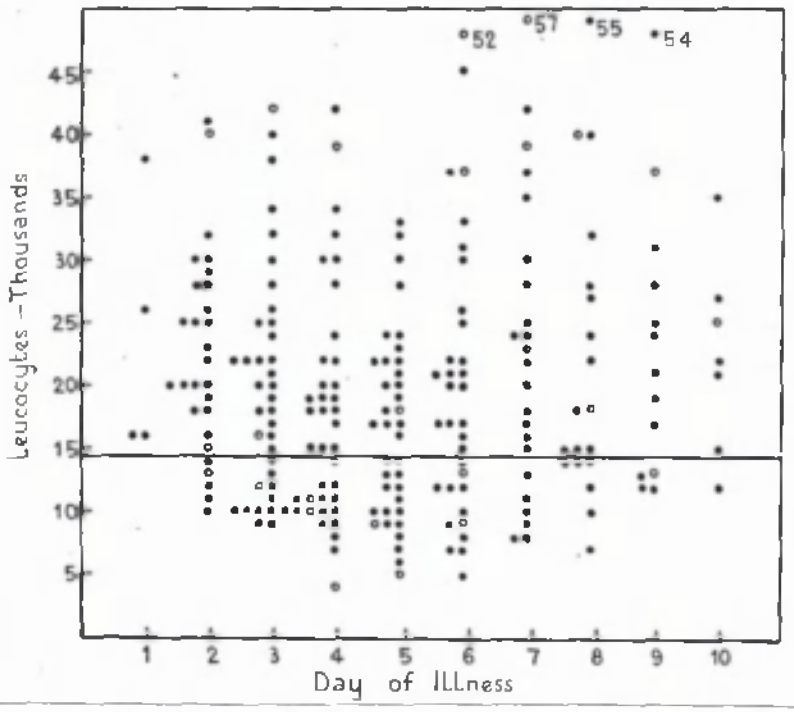
Simpson (1933), corroborating the work of Sabin, Cunningham, Doan and Kindwall (1925), Medlar (1929) and Smith and

McDowell (1929), has shown that the variations from hour to hour in the leucocyte count may be considerable. The administration of Felton's serum raises also the question of the effect of horse protein upon the leucocyte counts, but these considerations are immaterial in the present investigation, which is concerned with the prognostic significance of the leucocyte count in pneumonia rather than with the exact causes of its occurrence.

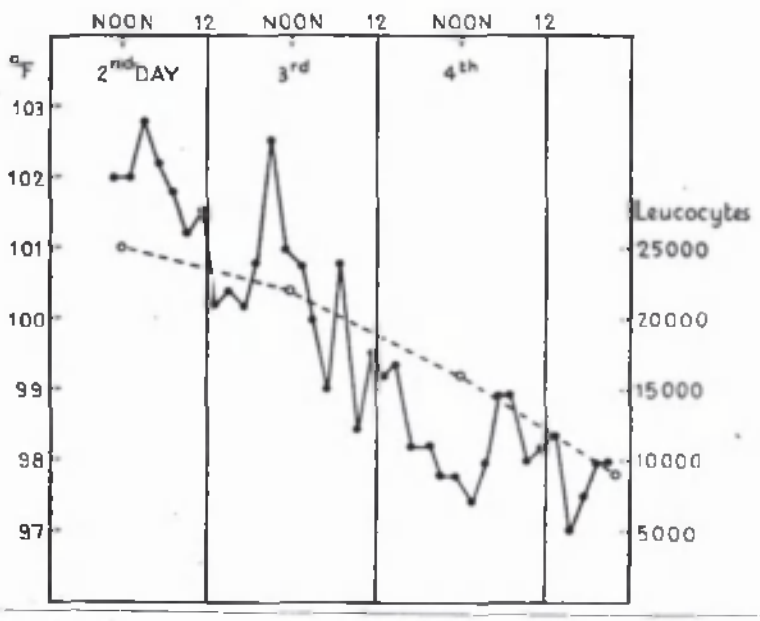
The term 'leucocytosis' has been used to indicate a count of more than 10,000 white cells per c.mm., and leucopenia to indicate a count of under 7,000 cells. In view of the physiological variations in the counts, the term 'adequate' is here used to indicate more than 15,000 cells, and 'inadequate' to indicate a lesser count.

Type I Cases.

Fifty-eight Type I cases were examined of whom four died. Fig. 1 shows the number of cases on each day of illness which had an 'adequate' and an 'inadequate' leucocytosis; e.g. of the thirty-three cases examined on their sixth day of illness, twenty-one had counts exceeding 15,000 per c.mm. and twelve had less than this number. On each day of illness a majority of all cases had more than 15,000 per c.mm. Most of the fifty-four patients who recovered had a normal temperature by the fourth day (39 per cent.) or by the sixth day (a further 26 per



Type I: Leucocyte counts of 58 cases.
● = Leucocyte count made in surviving cases.
o = Leucocyte count made in fatal cases.



R.R.: 37. Type I: Blood culture +.
40·00 units Felton's serum. (Type I).

cent.), so that a large number of the 'inadequate' counts shown on the graph are terminal. Most of those who had a longer illness than this maintained an 'adequate' count till defervescence. Thus of all counts made during the first ten days of illness the great majority exceeded 15,000. High counts were common and leucopenia was rare. The fatal cases had leucocyte curves which tended to the upper and lower extremities of the graph; in this series it happens that the highest and lowest counts both occurred in fatal cases.

In the four cases which were observed from the onset the leucocytosis was high before symptoms were well defined, and on the following days the count gradually diminished, reaching normal figures with recovery. Forty-four cases (76 per cent.) had a curve of this form (Fig. 2), and in all of these the first count was the highest. Included in this group are six patients who had an 'inadequate' leucocytosis throughout; all were sharply ill and one patient died.

Fourteen cases (24 per cent.) had a curve which was the reverse of the usual one, the early counts being followed by higher counts. This group is of special interest.

Admitted on the first day of illness. J.C. was admitted sixteen hours after the onset. A moderate increase of the leucocytosis occurred after the administration of serum. The blood culture was positive. Crisis upon the third day.

Admitted on the second day of illness. Six patients were observed. Three recovered, all of whom had positive blood cultures; two of these were seriously ill. Three died; the blood cultures were positive in two cases; one had a high count from the commencement, but, in spite of youth, a good physique, and a negative blood culture, developed an empyema; the second had low counts on admission which rose on the sixth day, but fell again before death on the eleventh day; in the third case a slight rise after admission was followed by a leucopenia on the fourth day.

Admitted on the third day of illness. Three patients were observed. One had a consolidation of the whole right lung; the blood culture was negative. The second developed pericarditis which may have been the cause of the increased count; the blood culture was negative. The third was seriously ill, but the symptoms rapidly responded to treatment, and the cell count rose; the blood culture was positive.

Admitted on the fourth day of illness. Two patients were observed. One was a healthy woman who aborted on the twenty-second day after admission. The rising leucocyte count probably coincided with the death of the foetus; the blood culture was negative. The second patient had a positive blood culture on admission, and a sterile culture twenty-four hours later.

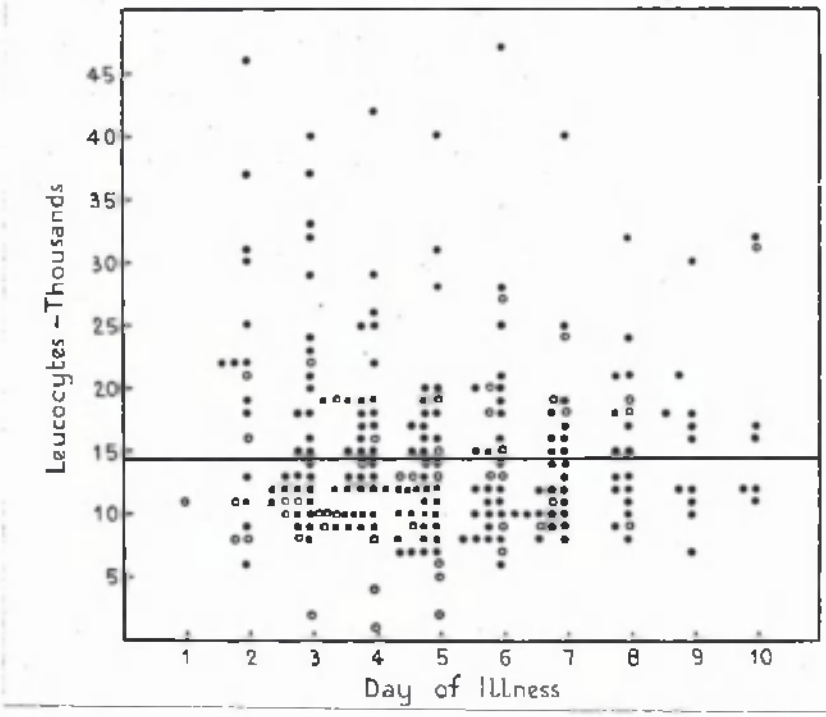
Admitted on the sixth day of illness. Two patients were observed. In both, blood culture was negative. One developed a pulmonary abscess. In the second case resolution was delayed.

All these cases were treated with Felton's serum injected intravenously shortly after admission and after the first leucocyte count. Since, in the majority, the admission count was the highest recorded, it is unlikely that the serum had any specific effect in increasing the leucocytosis.

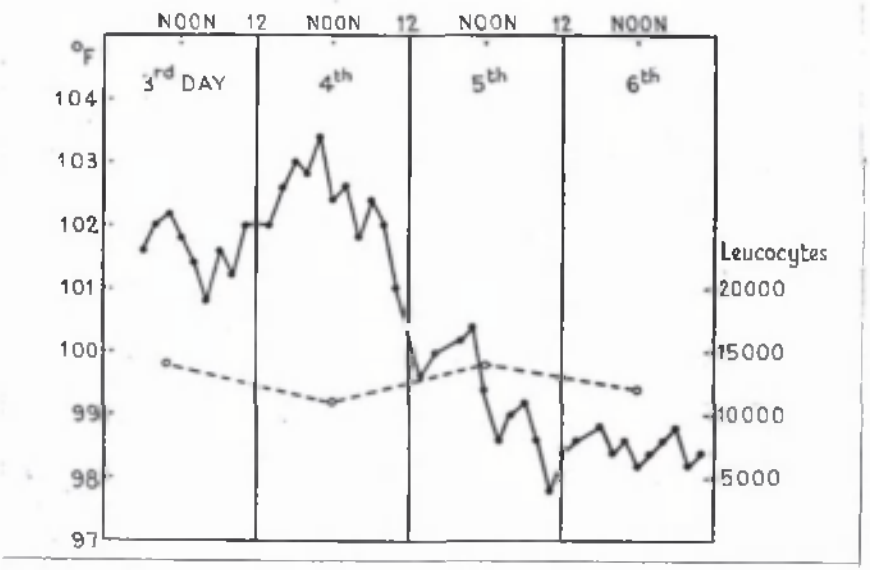
It is thus apparent that while a high leucocyte count in the early stages of the illness is a good prognostic omen, low leucocyte counts occur in many patients who are seriously ill at the outset but ultimately recover, though the mortality in the second group (three of fourteen patients died) is much greater than in the first (one of forty-four patients died).

Type II Cases.

Fifty-one Type II cases were examined; of these ten died. The graph (Fig. 3) shows that the majority of Type II cases have counts of less than 15,000 cells, and that counts of 20,000 cells are relatively few in number. The counts in the fatal cases did not tend to the upper and lower limits of the graph as in Type I cases but were fairly evenly distributed throughout. Very high counts occurred much less frequently, and very low counts much more frequently than in Type I cases.



Type II: Leucocyte counts of 51 cases.
Circles indicate counts made in fatal cases.



B.: 38. Type II: Blood culture +.
40·000 units Felton's Type II serum.

During the first forty-eight hours of the illness the leucocytosis was only moderate in most cases and subsequently tended to remain about 15,000 or below this figure. By the fifth day, at which stage the maximum number of patients were under observation, only one third had an 'adequate' leucocytosis. As in the Type I cases, when the illness continued after the eighth day, the majority had an 'adequate' leucocytosis.

In thirty-five cases (69 per cent.) the first count after admission was the highest recorded (Fig. 4 illustrates a typical case); this includes twenty-two who had counts of less than 15,000 cells throughout the illness, seven of whom died. Two of these fatal cases had a leucopenia and in one the count fell to 300 per c.mm.

The leucocytosis was at first low in sixteen cases (31 per cent.), but later increased. These patients were all acutely ill and three died; two of the latter had counts which rose to 19,000 and 24,000 respectively while the third had a count of 51,000 when death occurred on the fifteenth day. Occasionally the improvement was remarkable, e.g. W.T., aged 27, had a leucocyte count of 9,000 on the fourth day which rose rapidly after the administration of serum reaching 47,000 on the seventh day, when the crisis occurred. Only one case in this group had a complicated illness which might have accounted for the rising count. This was a boy aged 17 who had a severe toxic illness. The count on the fifth day was 8,000 and rose

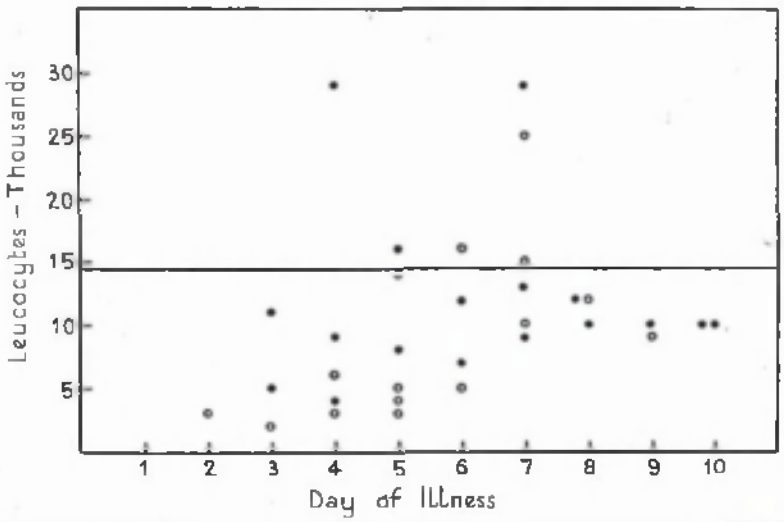
to 25,000 on the eighth day. On the twelfth day when he developed a pneumothorax the count was 15,000 and remained low although he later showed signs of retention abscess. The increasing counts in this group as in the comparable Type I group seemed to indicate response to treatment.

Type III Cases.

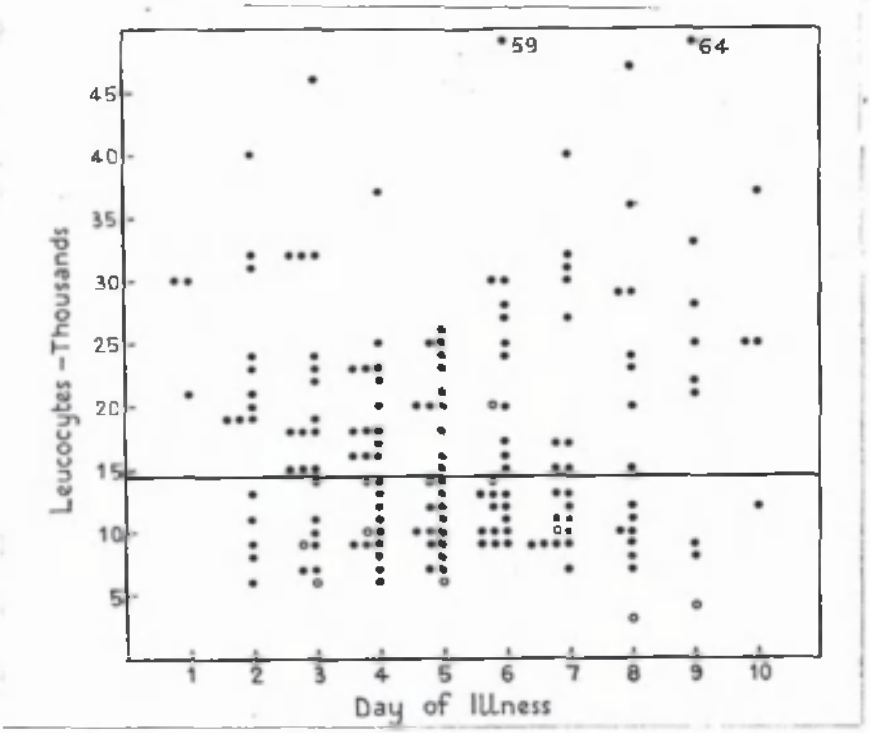
Seven cases were examined; of these five died. The graph (Fig. 5) of the counts made in this small group shows that only a few exceeded 15,000, while the majority were well below this number and leucopenia was relatively frequent. The counts of fatal cases are distributed fairly evenly among these of surviving cases.

One of the five fatal cases was admitted on the second day of illness. The cells numbered 3,000, rose to 16,000 on the seventh day, but fell again before death on the ninth day. Two patients were admitted on the third day of illness. One maintained a feeble leucocytosis until death on the seventh day; the other died on the day of admission, the count being 5,000. One patient, admitted on the sixth day of illness with a count of 6,000 cells, died on the same day. Another admitted on the seventh day with a count of 25,000 cells died on the following day.

One of the patients who recovered had a count of 11,000 on admission on the third day of illness. He was



Type III: Leucocyte counts of 7 cases.



Group "X": Leucocyte counts of 31 cases.

seriously ill, and the count ran below 10,000 cells, but he became convalescent on the eleventh day. The other patient who recovered was admitted on the fourth day of illness with a count of 29,000 cells. The count fell steadily, but he was out of danger on the eighth day. In this case Group 'X' organisms were isolated as well as Type III.

The high mortality of this group of cases is associated with low counts, but a low count may be followed by recovery, and a high count by death. The unusually high counts occasionally observed in fatal Type I and Type II cases were not observed in this series of Type III cases.

Group 'X' Cases.

Thirty-one cases were examined, of whom two died. Fig. 6 shows a fairly even distribution of the counts above and below the '15,000 level'. The counts made in the two fatal cases were mainly below 15,000 and included the lowest counts recorded. The highest counts all occurred in patients who recovered.

In this group a high leucocytosis was observed in the majority of cases during the first two days of illness. By the third day most of the cases fell into one of two groups, some with 'adequate' counts who appeared to be doing well and others with falling or 'inadequate' counts who were reacting less

favourably. On the fifth day a small majority of all the cases examined had less than 15,000 cells but nevertheless terminated favourably about the eighth day. After the eighth day the cases with high counts were generally still fevered. The two fatal cases had severe toxic symptoms; one had a leucopenia on the third day which persisted till death on the fifth day, while the other had a count of 9,000 on the third day reaching 20,000 on the fifth day but falling to 4,000 before death on the ninth day.

The majority of the Group 'X' patients maintained a high leucocytosis during the acute illness and several had a high count for many days thereafter, associated with delayed resolution. Nine cases with less than 15,000 cells throughout the illness yet made good recoveries. Only two patients had leucopenia, one being the fatal case mentioned above, while the other recovered after a severe and protracted illness.

Comment. In the sthenic type of pneumonia which is characteristic of Type I and most Group 'X' cases a leucocytosis rapidly follows the onset and may reach high figures within a few hours. The count is usually maximal by the second day and thereafter falls steadily parallel to but a little later than the fall in temperature. The asthenic illness associated with lower fever and indications of poor response to the infection is most frequent in Type II and occurs also in a small number of

Group 'X' cases. In these the early leucocyte response is usually poor, but the count increases on the third or fourth day after which it falls in company with defervescence as in the sthenic group. In most Type III cases the leucocytosis is either very poor or absent.

The division of Group 'X' cases into two groups, which in their leucocytic responses resemble Type I and Type II respectively, is of interest in view of the work of Winkler and his associates (1934), who found that certain of the Group 'X' strains which they examined had serological affinities with Type I or with Type II; their Type V being related to Type I and their Type VIII to Type II.

The Leucocytosis in Patients with Positive Blood Cultures as related to the Age of the Patient.

In each case blood was taken for culture when the first counts were made, so that to some extent they indicate the leucocyte response in the presence or absence of bacteriaemia. The effect of increasing age in the presence of a positive blood culture is seen in Table I. The young Type I patients had moderately low counts but all recovered. In the decade 30 - 40 the leucocytosis was invariably high but the figures decreased in the higher age groups, becoming 'inadequate' in the fifth decade and associated with a high mortality. It is possible

that in early life the counts are low because high numbers are not required, whereas in later life low figures are due to failure of the leucopoetic mechanism.

In Type II cases low counts were again found at the lower end of the age scale. But while the young Type I cases had, as a rule, an acute but never dangerous illness, the young Type II cases were often seriously ill and had protracted convalescences. The initial counts were 'inadequate' in ten, and five of these died. The three Type III cases with positive cultures died. One had an 'adequate' and two had an 'inadequate' leucocytosis. The only case of Group 'X' infection with bacteriaemia died with a leucocyte count of 9,000.

TABLE I.

The Admission Counts in Cases with Positive Blood Cultures.

	Type I			Type II		
	1,000 per cm.			1,000 per cm.		
Age.	Number of cases.	Average number of cells.	Died.	Number of cases.	Average number of cells.	Died.
10 - 20	3	17	0	1	8	0
20 - 30	3	26	0	6	26	0
30 - 40	11	35	0	1	11	0
40 - 50	2	15	0	3	10	3
50 - 60	4	12	3	4	11	4

The Leucocyte Count as a Prognostic Indication.

A study of the daily variation in the leucocyte count makes it clear that a single count is of little prognostic value unless the duration of the illness, the type of infecting organism, and the age of the patient are also taken into account. An estimation of the relation of leucocytes to mortality in 463 untyped cases at Rockefeller Institute gave the following figures (Avery, Chickering, Cole and Dochez, 1917):

Rockefeller Institute Cases

Leucocytes.	Cases.	Mortality. %
Under 10,000	29	65·5
From 10-20	163	23·7
" 20-30	177	18·0
" 30-40	76	14·0

Although a few daily counts are given it appears that the tabulated figures were collected from single counts done soon after admission. They suggest that the mortality is inversely proportionate to the leucocytosis, but, while this holds true when large numbers are considered together it is too inaccurate to be useful as a guide to prognosis in the individual case.

In this series the figure of 10,000, which is usually taken to be the lower limit of a 'leucocytosis', was found to be too low (Table II).

TABLE II.

Cases with Initial Counts under 10,000 and under 15,000.

	10,000		15,000	
Type.	Cases.	Deaths.	Cases.	Deaths.
I	6	0	12	2
II	16	3	23	7
III	3	3	3	3
'X'	5	1	9	1
Totals	30	7	47	13

Of the total 147 cases thirty failed to exceed 10,000 cells and this number contained 33 per cent. of the total deaths. The forty-seven cases which had counts of 15,000 and under, included 62 per cent. of the total deaths. For this reason it has been found useful to regard a count of 15,000 or more as an 'adequate' leucocytosis during the acute illness.

The remaining two Type I fatal cases had very high counts, 40,000 to 50,000, while of the remaining three fatal Type II cases, one had over 50,000, and two had moderate curves reaching from 15,000 to 20,000. Of the remaining three Type III fatal cases, two reached only 16,000 and the third 25,000. The other fatal Group 'X' case had a curve just reaching 20,000.

These figures agree with those of Naegeli (1923), Meyer (1931) and others who in untyped series found that a fatal issue in lobar pneumonia is usually associated with very low counts, but occasionally with exceptionally high counts. Bullowa (1927), von Wyss (1921) and their associates, on the other hand, found, in an extensive series, no relation between the leucocyte count and the outcome of the illness. Kugel and Rosenthal (1932) suggest that the leucocyte count in pneumonia varies too much to be helpful in prognosis, and are of the opinion that more information is obtained from a study of the relative number of degenerate cells. Middleton and Gibson (1930), from a study of the initial count in 160 cases, state that while on the whole, the absence of leucocytosis is unfavourable and a high total count reassuring, paradoxical results are sufficiently common to discourage dependence on their prognostic significance. This, however, is true only of single counts made without regard to the day of illness or the type of infection. The leucocyte count to be of maximum prognostic value should be made at least once daily during the acute illness. In a recent investigation Davies, Hodgson and Whitby (1935) report on the leucocyte counts in an unspecified number of their Type I and Type II cases. They give it as their opinion that 'a daily leucocyte count is very valuable for estimating general resistance and prognosis' and that 'while initial high counts (20,000 - 30,000) are obtained in all cases that are likely to recover; a normal count

or a leucopenia in the invasive phase of the pneumonic process is an ominous sign'.

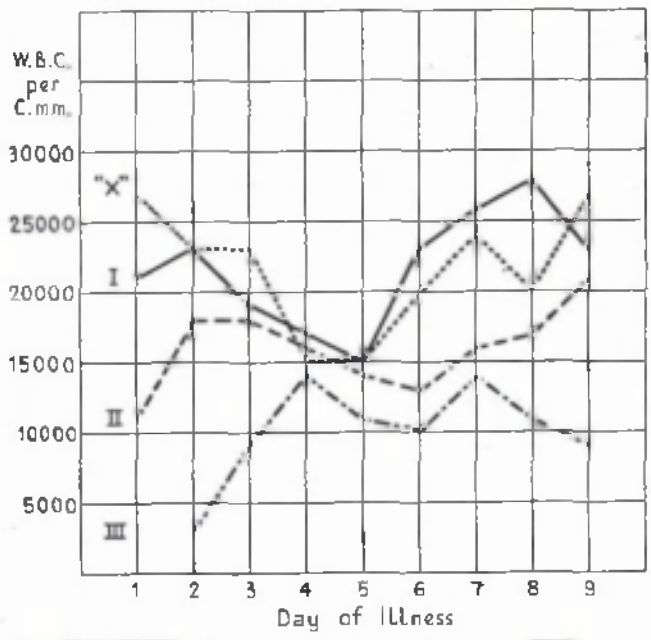
The present series of cases suggests that such a division is too arbitrary to be of value. The day of illness (which varies greatly in relation to the day of admission), the age of the patient, and the type of infection are factors of the utmost importance in the prognostic value of the leucocyte count.

Comment. While it is true that in the first three days of the illness, a leucocytosis above 15,000 generally carries with it a good prognosis, the converse is true to a much lesser extent. For whereas only a small proportion of cases with 'adequate' counts prove fatal, a much larger proportion with 'inadequate' counts terminate favourably. A single count is of little value, a series of counts gives much more information; but all must be considered with reference to the type of infection, day of illness, and age of the patient. In the case of a Type I infection, a leucocytosis of less than 15,000 cells is not of serious significance during the early days of the illness, unless the patient is over 40 years of age; the prognosis becomes more unfavourable with increasing age. If after the third day the disease is still active, as evidenced by rusty sputum and progressive consolidation, an 'inadequate' leucocytosis is now of more serious significance. With Type II pneumonia an 'inadequate' count in the first few days does not carry a serious

prognosis in patients under 30 years of age, although the illness is likely to be severe and protracted, but from the fourth decade onwards an 'inadequate' count is of grave significance. In young patients, when the count in 'inadequate' in the first few days, there still is the chance of a satisfactory response. If by the third or fourth day the count is still 'inadequate' there is much less probability of reaction, and the outlook is unfavourable. The diagnosis of Type III pneumonia carries with it a serious prognosis in the adult groups. Among younger patients the occurrence of an 'adequate' leucocytosis would modify the grave outlook. Most of the Group 'X' cases resemble Type I in having high early counts which indicate a favourable outcome. The occasional cases which have depressed counts on the third and fourth days have a correspondingly bad prognosis varying with the age of the patient.

Value of the Leucocyte Count in identifying the Type.

The curve obtained by averaging the daily counts of each type illustrates to some extent the characteristic features of the leucocyte responses (Fig. 7). In the Type I series the count lies above 20,000 cells during the acute stages of the illness, but falls rapidly coincident with the defervescence of the majority of the cases. After the fifth day, the curve rises sharply, due to the onset of complications, such as abscess and



The average leucocyte count in Type I, Type II, Type III, and Group "X" cases on each day of illness.

empyema, in the few who remain febrile. The Type II curve begins with low figures, rises on the second or third days, and thereafter sinks below 'adequate' figures, although the majority of the cases remained febrile till the seventh and eighth days. The Type III curve begins at a very low level, but from the fourth day onwards is raised by the few who survived. The Group 'X' cases have a high early average count which falls rapidly coincident with the early recovery of the majority. After the sixth day the sharp rise to a high level indicates the onset of complications in some of the remainder. Thus the similarity between the majority of the Group 'X' and Type I cases

is seen not only in the 'adequate' early counts and the rapid fall about the fifth day, but also in the later elevations associated with complications. In a small series of typed cases, Clough (1917) obtained corresponding results; in nineteen Type I cases the average count was 24,000 and in eight Type III cases was 11,000.

To some extent these features will assist in an attempt to differentiate the types. Bearing in mind the influence of age, it is possible to make the generalisation that an 'inadequate' count, or still more a leucopenia, occurring in the first forty-eight hours of a lobar pneumonia, makes a diagnosis of Type II probable. Conversely, a high count during the first forty-eight hours suggests that the infecting organism is a Type I pneumococcus or one of the associated Group 'X' strains.

Conclusions.

1. During the first three days of the illness, a leucocytosis of over 20,000 is characteristic of most cases of Type I lobar pneumonia, while a leucocytosis of less than 20,000 is usually found in Type II pneumonia.

2. The leucocyte curve in most Group 'X' cases resembles that in Type I cases, while that in Type III cases resembles severe

Type II cases with low counts.

3. When the count is below 15,000 the prognosis, irrespective of type, varies with the age of the patient and the duration of the illness.

4. A positive blood culture is associated with a depression of the leucocytosis, but the characteristic features of the curve are not altered in the various types. The depression is maximal in the higher age groups.

5. The average daily counts in the various types occupy separate levels during the early days of the illness. This makes it possible to attempt the differentiation of Type II from Type I and the Group 'X' strains.

6. The leucocyte count is of prognostic value when the type of organism, the age of the patient, and the duration of illness are considered along with it.

THE BLOOD PRESSURE IN TYPED PNEUMONIA.

Failure of the circulation is the cause of death in a large number if not in the majority of cases of acute lobar pneumonia. In a clinical study of 200 fatal cases (Brooks, 1934) cardiac failure was the immediate cause of death in 77 cases and peripheral vasomotor failure in a further 32 cases. Cardiac failure was the terminal event in 75 cases which had septicaemia, and post mortem, 116 in all were found to have an acute or chronic cardiac lesion. The prognosis depends largely on the presence or absence of the signs of cardiac failure, and the adverse effect of an organic lesion is likely to be manifest early in the illness.

In Joules' series (1933) of 59 post-mortem examinations gross lesions such as lung abscess, empyema and peritonitis were found in 25 only. Two had endocarditis while the remainder presumably died of toxaemia inducing cardiac failure. Yet although the heart muscle must suffer from the effects of the pneumococcal toxins from the onset, signs of acute heart failure are not common during the course of the illness. Cardiac enlargement was found only in 3 of 120 cases radiographed during the illness (Davies, Hodgson and Whitby, 1935); all three had systolic blood pressures less than 100 millimetres at the height of their illness. Signs of congestive failure are, on the whole, rare although oedema and hepatic congestion are occasionally seen.

Hypostatic congestion, jaundice and cyanosis being part of the symptom complex of toxic pneumonia, cannot be ascribed specifically to cardiac failure. The electrocardiograph may show right axial deviation, while alterations of the shape of the curves, though common, are slight (Master, Romanoff, Jaffe, 1931). On the other hand, the toxaemia frequently attacks the smaller blood vessels and shortly before death the response to adrenalin may be absent (Perry, 1934). The most convenient method of estimating the tone of the circulation is by observation of the systolic and diastolic blood pressures, and serial records give valuable information as to the progress of the illness.

Cowan (1935) states that the cardiac failure in pneumonia is usually unlike the congestive failure of chronic valvular disease. As a rule, the pneumonic fever causes increasing frequency of the pulse and with it increasing weakness. The amplitude is not at first affected but its force and duration are lessened and it becomes softer and quicker, and perhaps dicrotic. Eventually the volume lessens. He is of opinion that the sequence indicates vasomotor failure. Perry says that at the height of the disease there is markedly impaired efficiency of the contractability of the capillaries, and that part at least of the circulatory failure is due to this. He suggests that treatment should be directed at the peripheral circulation rather than at the heart. MacErlean (1934)

subscribes to the view that the efficiency of the cardiac muscle alone is the main factor in maintaining the blood pressure.

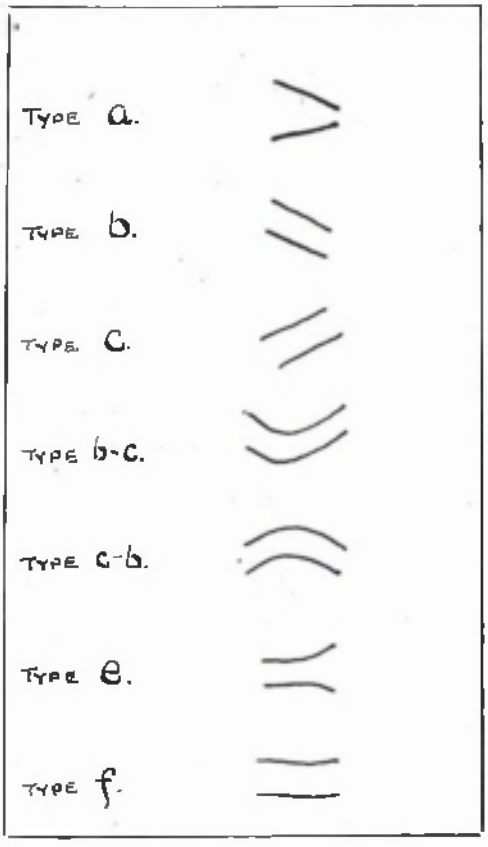
Osler (1909) states that during the first few days there is no change. The extent of involvement seems to have no effect upon the peripheral blood pressure. In toxic cases the pressure may begin to fall early, a drop of 15 to 20 millimetres is perfectly safe but a progressive fall indicates the need for stimulation. A sudden fall is rarely seen just before death. A slow gradual fall means cardio-vascular asthenia, and calls for an increase in stimulation. The crisis has no effect on the blood pressure.

Young and Beaumont (1929) say that the blood pressure usually falls during the course of a pneumonia and quote Gibson to the effect that a sudden rise of pressure suggests the onset of a complication delirium etc., while a sudden fall indicates the inset of cardio-vascular paralysis.

Most of the published observations comment only on the behaviour of the systolic pressure, but since there is evidence that peripheral failure is an important factor in morbidity, the diastolic pressure is likely to give valuable information also.

Method and Scope of Enquiry.

During the present investigation opportunity was offered of investigating the blood pressure sequences in typed



Blood Pressure Curves.

Typical forms.

cases. The first record was made two to three hours after the patients were admitted, by which time the disturbing effects of transportation had worn off. Thereafter a reading was usually made daily until the termination of the acute illness. The graphs in miniature indicate horizontally the day of illness. The figures in the lower right corners are the case numbers. Where the patient died, this figure is enclosed in a ring. Since in a sequence of systolic and diastolic readings we are dealing with two variables, all types of combined curves are to be expected and in fact are found, but an examination of the collected graphs shows at least four types of curve which occur frequently:

Type (a) Many cases show early in the illness a wide divergence of the curves with a tendency to convergence during the following days, maximal about the crisis —

Type I Cases: 144.
Type II " : 26. 116. 195. 135. 172. 176. 23.
Type III " : 170.
Group"X" " : 7. 35. 60. 130. 188. 210. 178.

Type (b) A smaller number have curves which from the onset tend to decline, both curves remaining parallel —

Type I Cases: 96. 121. 175. 179. 198.
Type II " : 106.
Type III " : —
Group"X" " : 87. 113. 133. 143. 167. 182.

Type (c) A third and fairly numerous group have curves which although low in the early stages climb parallel to one another during the succeeding days —

Type I	Cases:	165. 11. 183. 78. 80. 85. 139. 162. 186.
Type II	" :	28. 76. 84. 91. 109. 124. 161. 165.
Type III	" :	118. 155.
Group"X"	" :	130. 63. 77. 88. 148. 172. 180. 188.

Type (d) All combinations of these three fundamental types are seen. A common form combines (b) and (c) in that order. There also occurs a curve in the opposite direction (c) and (b), e.g.—

(b) and (c)	Type I	Cases:	160. 164.
	Type II	" :	192 (combining (c) and (b)).
	Type III	" :	—
	Group"X"	" :	130. 9.
(c) and (b)	Type I	Cases:	119. 145. 175. 179. 198.
	Type II	" :	104. 126.
	Type III	" :	—
	Group"X"	" :	35. 150. 140.

Type (e) A considerable number have curves which diverge a little towards the end of the illness.—

Type I	Cases:	173. 95.
Type II	" :	116. 176. 161.
Type III	" :	118.
Group"X"	" :	190. 196.

Type (f) There remain a number in which there was little change in the systolic or diastolic pressures during the illness —

Type I	Cases:	98. 102. 105. 114.
Type II	" :	6. 8. 12.
Type III	" :	—
Group"X"	" :	—

It seems clear that the varied behaviour of the systolic and diastolic curves can be related to the varying tone of the heart muscle and the peripheral blood vessels respectively. The literature recognises mainly the type where there is a fall of both curves during the illness, that is, a progressive and parallel diminution in the tone of both controlling factors. The cases in this series are too small to indicate relative preponderances of type, but it is evident that this form is not general and probably not even most usual.

A considerable number apparently suffer early shock both peripherally and centrally from which there is a steady and parallel recovery in succeeding days. This type (c) was found in a fair number of serious cases which recovered. In others, the majority of which were Type II cases, there appeared to be considerable peripheral shock at the onset although the heart was less affected, and following this the peripheral tone increased while the cardiac tone as indicated by the systolic pressure began to decline or remained relatively unaffected. This produced converging curves type (a) which thereafter usually declined parallel to one another, e.g. Case 130.

The remainder, and the numbers were small, had curves which were combinations of the principal features of the preceding types, and indicated: (1) parallel improvement after initial shock followed later by depression of both peripheral and

central tonus (type d) or (2) the converse of these circumstances produced this curve inverted. In other cases there was a divergence of the systolic and diastolic pressures towards the end of the illness, indicating mainly a progressive peripheral failure (type e).

Finally a small number had curves which indicated little effect either on the central or peripheral circulation (type f).

The Fatal Cases.

Deaths in this serum-treated series were few in number so that a percentage analysis would be valueless, but an examination of the individual curves may be of interest.

Type I.	Case 181.	Type a curve.
	Case 3.	Single examination 105/70.
Type II.	Case 109.	Type c curve.
	Case 125.	Type b—c curve.
	Case 158.	Divergent-Convergent curve.
Type III.	Case 118.	Irregular type e curve.
	Case 152.	Moribund. Single examination 105/70.
	Case 92.	Moribund. Single examination 105/70.
Group "X".	Case 120.	Type a curve.
	Case 74.	Moribund. Single examination 100/60.

Almost all types of curve appear in this small series so that evidently no type of curve indicates with certainty a favourable prognosis. Two of these cases had convergent curves

although in Montgomery's series (1936) this form suggested a very favourable prognosis. The fatal cases taken in conjunction with the serious cases which recovered, had blood pressure curves which do not lend weight to the prevailing impression that low pressures are of bad prognosis or that fatal cases have low pre-terminal pressures. One case had low curves which fell further towards the end (Type I, Case 181) but a second had low curves which improved before death (Type II, Case 109) and the others had curves which were not markedly depressed. On the other hand, numerous cases which recovered had at some point very depressed curves.

Value of the Diastolic Pressure.

The feature common to most of the curves is the increase in pulse pressure at the onset which is mainly due to the fact that the fall of diastolic pressure is more than the corresponding fall of systolic pressure. This suggests that the toxaemia of pneumonia affects the peripheral blood vessels to a greater degree than the heart.

It is, however, difficult to estimate the value in prognosis of low diastolic and systolic pressures and of a large pulse pressure, for in this series the low diastolic pressures were most commonly found near the onset and there was a tendency for the diastolic pressure to rise as the illness progressed.

Near the crisis while the diastolic pressure continued to rise there was also an upward tendency in the systolic pressure and to a greater degree so that the curves tended to diverge.

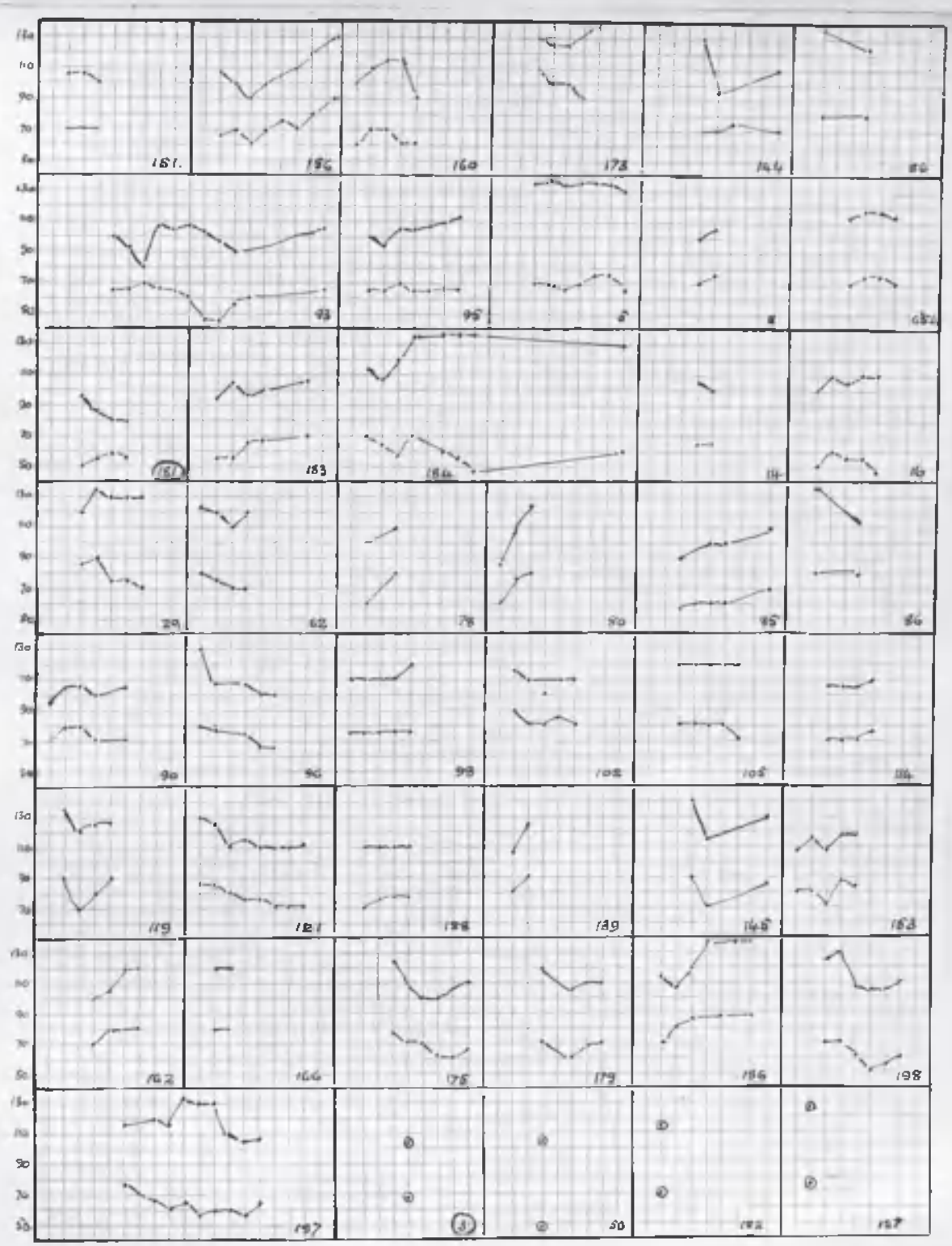
These facts suggest that acute failure of the peripheral or central pressure-maintaining mechanism is not an event becoming more frequent as the illness advances but probably happens suddenly in those cases which terminate fatally (Type I, Case 158). At times, however, extreme failure of the peripheral circulation occurs early in the illness, and seems to determine the fatal issue, e.g. Type II, Case 125; this was an extremely toxic case with severe leucopenia going on to abscess and gangrene: the diastolic pressure at times could not be determined. On the other hand, severe peripheral failure is compatible with recovery (Type II, Case 12). Very low systolic pressures were not frequent and there were few cases where the systolic pressure was maintained below 100. Three of the fatal cases had systolic pressures under 100 throughout the illness (Type II, Cases 109 and 125; Type I, Case 181) but one such case recovered (Type II, Case 53) and this was an isolated reading showing a pressure of 94 mm.

Conclusions.

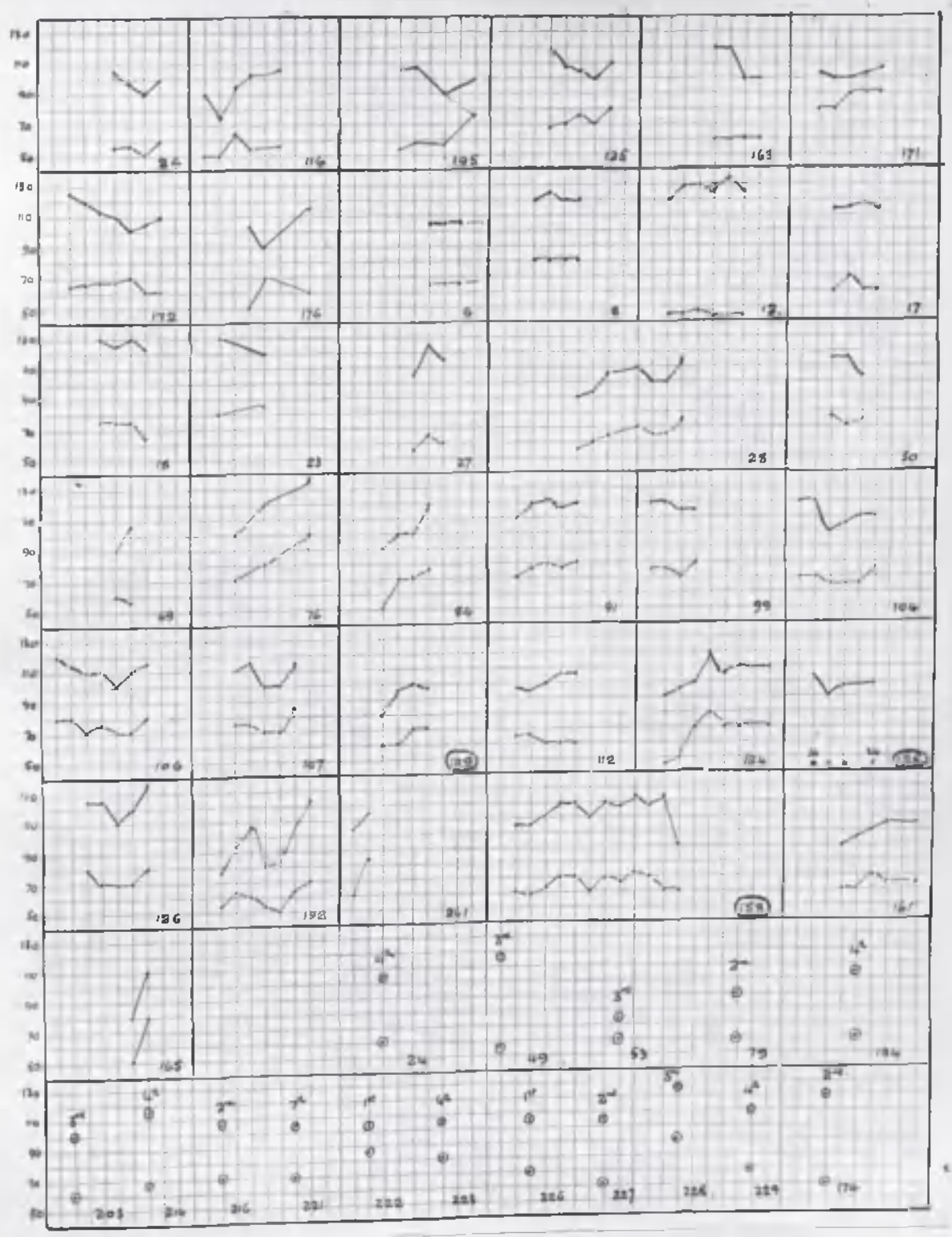
(1) These findings agree fairly well with Montgomery's series. In sthenic cases the initial peripheral shock is evidently compensated for by a rise in systolic pressure. As the illness

progresses the peripheral vessel tonus tends to improve while the increasing weakness of the heart allows the systolic pressure to fall. This combined process is as is to be expected, maximal at the time of the crisis. After the crisis, convalescence brings rest to exhausted cardiac muscle and elevation of the blood pressure to normal levels if recovery is adequate. In this series although divergence of the curves was noted in a considerable number after the crisis, it was due more to the recovering systolic pressure than to a secondary diastolic fall. But while a clearly defined converging-diverging curve occurred in more than half of Montgomery's series, in this series there was no large number conforming completely to this pattern.

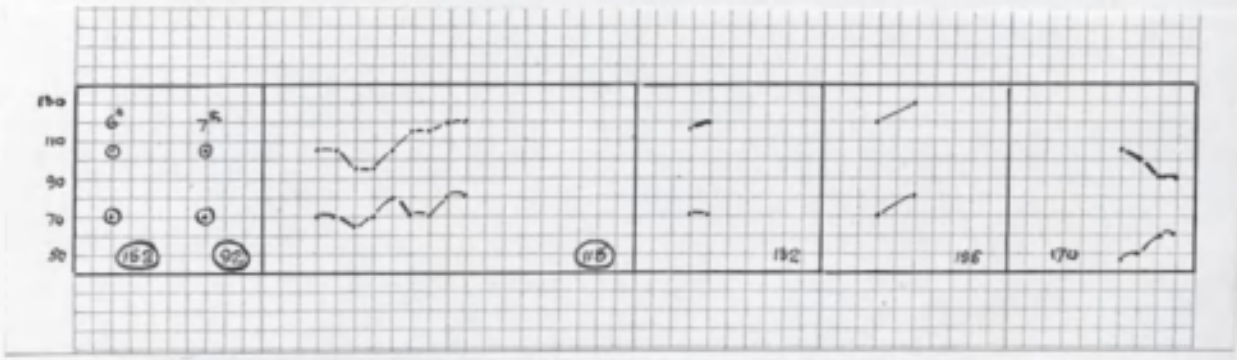
(2) No characteristic curves were identified as being specially associated with one or other type of infection. The form changes according to the severity of the infection, and its incidence on the heart and the peripheral arterial tonus.



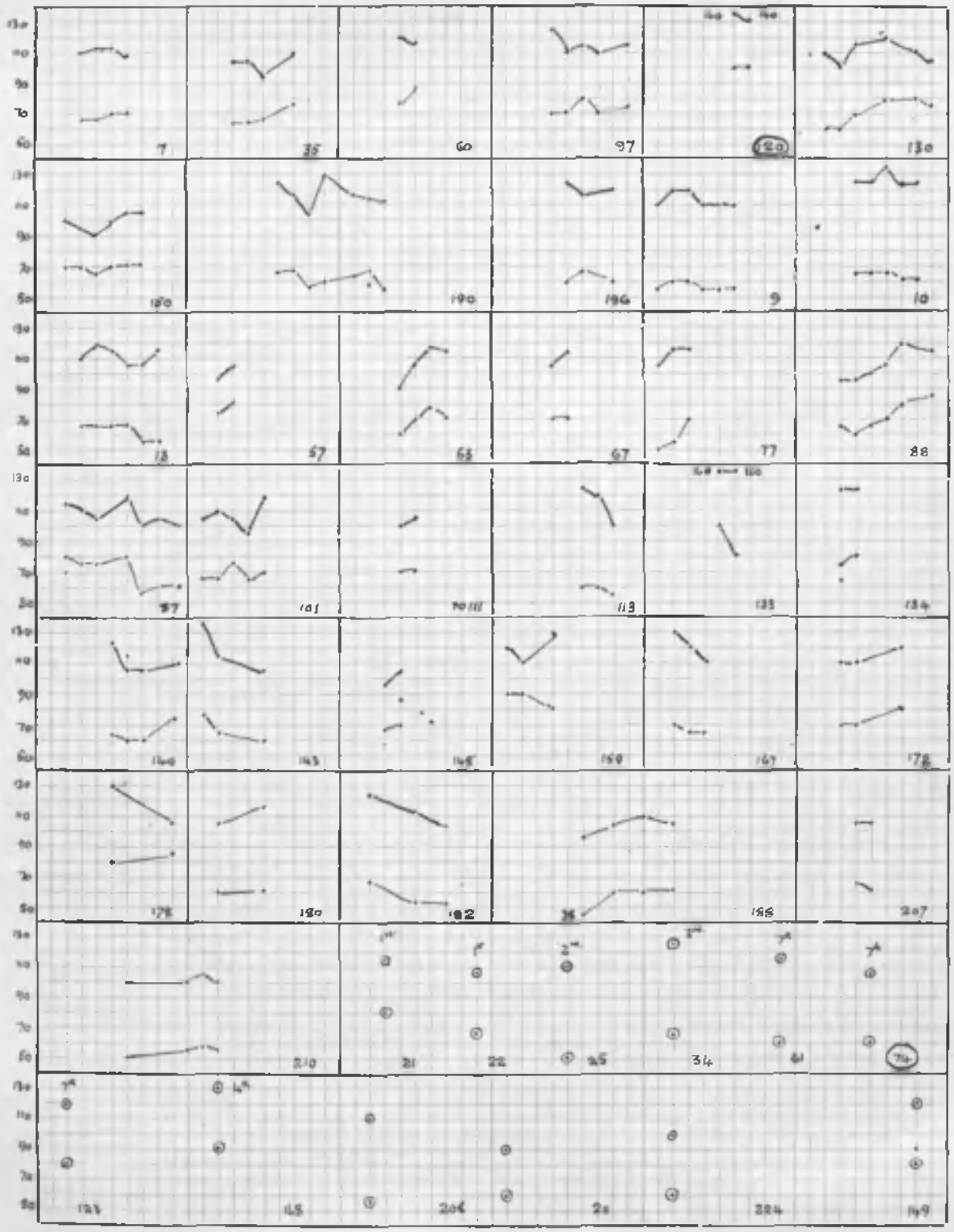
I. Blood Pressure Charts : Type I Cases.



II. Blood Pressure Charts : Type II Cases.



III. Blood Pressure Charts : Type III Cases.



IV. Blood Pressure Charts : Group "X" Cases.

GENERAL COMMENT AND CONCLUSIONS.

Is clinical differentiation of Type possible?

After some years' experience of the differentiation of the pneumococcal pneumonias by bacteriological typing, the senior members of the Royal Infirmary group controlling the investigation had the general impression that the clinical signs and symptoms alone would not form a substantial basis for the diagnosis of Type. In this respect pneumonia would not differ from many other infectious diseases.

Typhoid fever is regarded as a clinical entity separate from paratyphoid fever, yet the clinical picture of the latter is only distinguishable in that in the majority the illness runs a milder course, although in exceptional cases all the major symptoms of typhoid fever occur. While severe cases of diphtheria with cardiac failure and mucous membrane haemorrhages are clinically quite distinct from the average case of most recent epidemics and are usually associated with the long virulent bacillus, yet one may meet with violent symptoms in infection with the mild type of organism. Similarly, the clinical types of cerebro-spinal fever are variable in every epidemic and offer no basis for correlation with Gordon's four serological types. A suspicious throat is an indication for diphtheritic antiserum and a doubt as to agglutination titre does not invalidate the immediate use of antityphoid serum.

Further, the finding of a meningococcus indicates serum and though in the meantime it may require to be polyvalent serum, nevertheless its use is indicated immediately the diagnosis has been made. But in pneumonia the separation into Types has a greater significance for therapy. It is of some value to give a polyvalent pneumococcic antiserum; better than this, a serum containing antisubstances to Type I and Type II, as far as the recent epidemics in Glasgow indicate, has about a one in three chance of being partially specific. But the usefulness of the serum is so enhanced, if, the Type being known, the proper antiserum is used, that to use it blindly is both financially wasteful and deprives the patient of maximum benefit.

Most clinicians with experience of the method are agreed that Type I antiserum is a valuable remedy in Type I pneumonia. A less complete experience, which we hope to amplify, suggests that Type II antiserum can be equally successful if administered very early in the illness. These two, apart from the therapeutic possibilities inherent in the bacteriological diagnosis of the separate strains of Group "X", render it expedient that the clinician should make a diagnosis of Type secondary to a diagnosis of lobar pneumonia, and it is not too much to say that the diagnosis 'lobar pneumonia' is nowadays as unsatisfactory as the diagnosis 'sore throat' or 'P.U.O.' More than in any other infectious state the diagnosis 'lobar pneumonia' while clinically precise is bacteriologically

indefinite, with the added onus that to be bacteriologically indefinite is to be, to an unusual degree, therapeutically unsound.

In the preceding studies the object which linked all the sections was to see if the clinical picture in each of the two main types, especially, is sufficiently distinctive to make the diagnosis wholly or partly independent of the bacteriological findings, and the following summary indicates to what extent this question was answered.

Studies Associated with the Onset.

(1) Previous Respiratory Illnesses.

The conclusions indicated that in each Type a second attack of pneumonia tended to affect the part of lung previously affected and there is some evidence that a second attack is likely to be caused by a pneumococcus different in type from that which first caused the attack.

This merely corroborates for pneumonia of each Type what has long been recognised for pneumonia in general and suggests that there may be some immunity to a given Type. But the data offers no help towards differentiation of Type.

(2) Upper Respiratory Infections preceding the Onset.

In this series, acute respiratory infections preceding the onset of lobar pneumonia were uncommon and contrary to

widely accepted view, this was notably true of the common cold, although it seems clear that during some epidemics of lobar pneumonia acute upper respiratory infections occur, due to the same Type of pneumococcus.

The absence of preceding upper respiratory infections was in this series common to all Types.

(3) Faucial Congestion.

A varying but usually mild degree of faucial congestion was found in all Types but was never severe and since a considerable majority of the cases were Type I and Type II, it seems reasonable to assume that in these two at least there is no tendency for more than a local irritation, due probably to cough and to the evacuation of inflammatory products. On the other hand, there is evidence from other workers that Type III and probably some associated strains in Group "X" have more tendency to cause acute membranous pharyngitis with septic non-pulmonary complications. In the presence of such acute conditions, therefore, Types I or II would be unlikely. In this particular case there may be a slender basis for differentiation.

(4) The Influence of Exposure on Susceptibility.

Remarkably few of the patients gave a history of 'chilling' prior to the onset of their pneumonia, and the only

comment bearing on Type that could be made is that in this series a large number of the patients earned their living in occupations which exposed them to the weather, and that this was notably so in the Type II cases. This has no statistical value, however, in face of the fact that a majority of the cases in all Types led sheltered lives and had not been exposed to chill. The interest of these findings is therefore quite general and seems to emphasise the importance of an individual susceptibility to infection not related in any close way to the hazard of sudden chilling. Further, the cases lend no support to the current belief that individuals engaging in strenuous work out of doors are specially susceptible.

Symptoms Associated with the Onset.

The foregoing sections of the investigation which deal with events prior to the actual onset, while they allow of comment applicable in general to the lobar pneumonias, offer little help as to the Type of infection which is to be expected. The question was then asked; do the symptoms which first suggest a diagnosis of lobar pneumonia group themselves in such a way that the different Types are recognisable? The data indicate that with small variations the great majority in all Types have an onset ushered in by rigor followed by pain in the chest, or *vice versa*, and emphasise the general principle that these

symptoms are so constant as to justify a tentative diagnosis of lobar pneumonia when other signs and symptoms are in abeyance. It was noted that a preliminary period of malaise was a more constant occurrence in the Type II cases than in those due to other Types.

Symptoms and Signs during the Course of the Illness.

Since in the matter of Type differentiation the early symptoms are of little help, an examination was made of the signs and symptoms which tend to develop during the course of the illness to see if their early recognition would be of value.

In lobar pneumonia a fatal issue occurs by one of three processes or a combination of them; they are coma, cardiac failure or toxaemia.

(1) Coma.

Coma is hardly ever an early occurrence in adults and is usually terminal in cases which have been toxic throughout. Although it indicates death due to cerebral disturbance and is usually preceded by a preterminal delirium, delirium may occur during the first few days in sthenic cases, especially young persons, who later make a perfect recovery. It is therefore of little help even in prognosis, except when considered with the rest of the clinical picture; the number in this series who became delirious was too small to justify an attempt at Type differentiation.

(2) Cardiac Failure.

This has been shown by many workers to be a frequent cause of death in lobar pneumonia, and it seemed likely that many cases would show signs of cardiac affection early in the illness. Disturbance of the cardiac rhythm and signs of endocardial or myocardial damage, as shown by the development of murmurs or increase in the cardiac area were very rare, but serial examination of the systolic and diastolic blood pressures showed that although the heart and the peripheral blood vessels reacted to the stimulus of the onset and the subsequent toxaemia in such a way that various types of curve were recognisable, none was predominant in the fatal cases and all forms were found in Types I, II, III and Group "X". It was, however, frequently found that the diastolic pressure was notably low early in the illness in the majority of the Type II cases examined as compared with the Type I cases.

(3) Toxaemia.

Studies of mortality and morbidity according to Type have shown that Types II and III are more serious than Type I and the majority of the Group "X" cases. Also, clinical observation has shown, as was to be expected, that, in the later stages at least, signs of toxaemia are more severe in the Types showing the higher mortality.

Since the pneumococcal toxin affects to some extent all the body tissues, a detailed examination might show selective effects relative to the Type of infection.

The most accessible tissues for this investigation are the liver, the kidneys and the blood. An elaborate study of the chemistry of the urine was undertaken by the biochemist of the team. The results were of general interest but there were no features characteristic of any one Type.

Jaundice.

Clinical jaundice is not an accurate measure of liver damage although it is seldom absent long if the damage is severe. But slight increase in the serum bilirubin is a fairly accurate indication of liver cell disturbance. Using Meulengracht's Icterus Index method, subclinical jaundice was found to be common in all the cases irrespective of Type and was not specially severe in any one Type nor in the fatal cases.

The Blood.

Much the most striking effects of the toxaemia were found on examining the blood. It was possible to show that the more toxic Types II and III affected the blood and especially the white cells much earlier in the illness and more intensely than did Type I and the Group "X" cases. This is specially true of the leucocyte counts which behaved in so constant a fashion that it was possible to attempt a differentiation of Type I and the Group "X" strains from Type II in the early days of the illness, since the leucocyte counts tend to occupy different levels.

Further, indications of toxic damage to the white

cells were found to occur early in those cases which had low total counts, i.e. mainly the Type II and Type III cases.

Summary and Conclusions.

(1) There is a tendency for Type II cases to have a premonitory period of malaise; this is less common in Type I cases.

(2) Acute pneumococcal pharyngitis, while occurring in some Type III and Group "X" cases, is uncommon in Type I and Type II.

(3) A very low diastolic pressure in the early days of the illness is more common in Type II than Type I.

(4) A leucocytosis of less than 20,000 during the first four days of the illness is unusual in Type I cases, while Type II and III cases usually have counts below 15,000 during the same period. Toxic changes in the leucocytes appear early in Type II and Type III cases in association with the low white cell counts.

(5) The diastolic blood pressure is notably low in the majority of the Type II cases during the first few days as compared with Type I cases.

With the exception of the leucocyte count, which gives remarkably constant indications, these findings offer only a

slender basis for differentiation. Further study of cases later than those considered here and making a total of more than three hundred, does nothing to alter this impression. For the rapid and accurate use of serum, therefore, we are still dependent on bacteriological differentiation. This would be a serious matter if it had to be left to those having special skill in bacteriological methods. But the bacteriologist has put into the hands of the clinician a method of Typing so rapid, simple and accurate that it can take its place with the blood count and the sedimentation rate as a routine method, requiring only a little practice and experience.

The problem of pneumonia presents itself in a more epidemic form in America than in this country, and it is associated with a higher mortality. It has led to a nation-wide interest in the use of serum and to the establishing of diagnostic centres where the sputum can be typed and suitable antiserum obtained.

In Great Britain the use of Felton's serum still makes slow progress. This is in part due to its high cost and also to the need for typing. In part, however, it is due to the fact that by the time many patients come under observation they are in the 4th. or 5th. days of their illness and antiserum in these circumstances is of little value. The first need, therefore, is to teach not Lobar Pneumonia but Lobar

Pneumonia Type I, Lobar Pneumonia Type II, etc. The higher degree of clinical accuracy which this implies will make for earlier diagnosis and this will go far to justify the use of these expensive antisera.

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SUMMARIES OF CASE HISTORIES.

APPENDIX A to thesis "Observations on the Clinical Differentiation of Typed Lobar Pneumonia".

By John Fleming, M.B., Ch.B., F.R.F.P.S.G.

I N D E X.

TYPE I.

Case No. 5. Male, aet. 57, admitted on 4th. day. A severe case, R.2, 3 involved, temperature did not run high, toxaemia ++. He seemed to be helped by the serum. The pulse records are inaccurate owing to frequent extra systoles which were often, for long periods, in couples. There were, however, no suggestions of cardiac failure at any time, apart from this.

Case No. 11. Male, aet. 13, admitted on 5th. day. An acute case in a boy. The temperature came down by crisis on the day of admission and he had a rapid convalescence. One dose of serum was given but no conclusions could be drawn as to its effect. Serum reaction, urticaria occurred on the 9th. day after serum.

Case No. 14. Male, aet. 26, admitted on 5th. day. An acute attack of considerable severity in a young adult. He was toxaemic and cyanosed on admission but after 2 doses at short intervals these symptoms entirely disappeared and on the following day he had a crisis. Serum effect could not be judged.

TYPE I.

Case No. 16. Female, aet. 25, admitted on 3rd. day. A moderately acute attack complicated at the beginning by very congested fauces and an incipient double otitis media. She had full doses of serum for 2 days and on the 6th. day of illness the temperature gently subsided by lysis. Otitis media.

Case No. 29. Male, aet. 38, admitted on 2nd. day. A severe pneumonia involving the L.1 lobe some days after L.2. Cyanosis and dyspnoea were acute. The temperature was never high. 14 days after the onset he developed a thrombosis of the R. short saphenous vein. Thrombosis. Tachycardia.

Case No. 31. Female, aet. 44, admitted on 2nd. day. A severe illness accompanied by marked cyanosis. The curves moderated 2 days after admission but the pneumonic process seemed to continue for 3 days more before being arrested. The serum was of undoubted help in this case.

Case No. 37. Female, aet. 26, admitted on 4th. day. A typical acute attack in a healthy young adult. The illness progressed normally except for the fact that the pulse rate remained rather unsteady and rapid for 2 weeks after the temperature fell. 22 days after the crisis she aborted a 5 months' foetus. Thereafter she was more composed and the pulse came down to normal.

TYPE I.

Case No. 40. Male, aet. 46, admitted on 3rd. day. A very severe 'patchy' pneumonia involving both lungs. He was extremely cyanosed and dyspnoeic on admission and was in a state of low delirium which suggested an alcoholic basis. After 6 doses over 48 hours all the curves subsided and the lungs began to clear. Slight 'wandering' persisted for 72 hours after the curves fell. The effect of the serum was dramatic.

Case No. 45. Male, aet. 17, admitted on 2nd. day. A moderate attack in a healthy youth involving the R. upper and apex of R. lower lobes. He responded quickly to serum and convalescence was normal. After the first 2 doses of serum there were acute immediate serum reactions.

Case No. 50. Male, aet. 22, admitted on 4th. day. A moderate attack involving mainly the R. upper lobe. Toxic symptoms were not conspicuous but during the more acute illness he exhibited a respiratory rhythm of the Cheyne-Stokes type.

TYPE I.

Case No. 54. Female, aet. 52, admitted on 4th. day. A fairly severe illness in an elderly woman. There was a small lesion at the apex of the R.3 lobe. Cyanosis and dyspnoea were mild. An elderly woman with chronic bronchitis and emphysema.

Case No. 59. Female, aet. 37, admitted on 2nd. day. A severe attack involving two lobes of the R. lung. All the symptoms were eased after the 3rd. dose of serum and the curves subsided. Resolution was slow but uneventful. Seen as out-patient on 10/11/30, chest normal. Course of vaccine given.

Case No. 62. Male, aet. 26, admitted on 2nd. day. On admission he was dyspnoeic and 'dusky' with cyanosis. There was consolidation of the upper half of R.3. Immediately after admission the temperature settled by lysis. The urine was acid till the 25th. Full doses of diaphoretic were then given and 48 hours later the urinary reaction began to change. The acute stages of the illness were accompanied by a very acute nephritis, probably an exacerbation of a mild chronic nephritis.

TYPE I.

Case No. 64. Male, aet. 38, admitted on 4th. day. A pneumonia of average severity in a healthy adult. On admission he was very dyspnoeic and cyanosed and the pulse was of poor quality. 12 hours later the curves were normal and cyanosis minimal. Only the L.2 was solid but bronchitis was ++ elsewhere in the chest.

Case No. 68. Male, aet. 18, admitted on 3rd. day. A typical illness involving the left lower lobe. The response to serum was apparently immediate and by the following evening the curves were normal. Convalescence was uneventful.

Case No. 78. Male, aet. 31, admitted on 2nd. day. This is our first serum case observed from the beginning. When seen in the casualty ward he was quite well except for R.2 pain and friction, no consolidation. Curves rose sharply and he developed cough and bloody spit. Consolidation did not develop completely.

TYPE I.

Case No. 80. Male, aet. 30, admitted on 1st. day, 16 hours after onset. In this case serum was instituted early with excellent results. The illness was a typically severe one, involving the lower half of R.3 but with very little bronchitis. 40,000 units brought down all the curves and the third dose was not given. In the evening, however, 48 hours after the onset the curves rose again. The whole of R.3 now was involved. Three further doses completed the lysis of the curves and 72 hours after the onset he was very well. This case convinced Dr. A.W.H. Resolution was very rapid. The leucocyte response was observed here.

Fig.: Chart, Case 80.

Case No. 81. Female, aet. 24, admitted on 3rd. day. A typical acute illness in a healthy girl. There was a previous attack on the same side 8 years before. R.3 was very solid and cyanosis and dyspnoea were troublesome. The temperature fell by crisis on the 4th. day. She exhibited continued leucocytosis but developed an acute tonsillitis 6 days after the crisis.

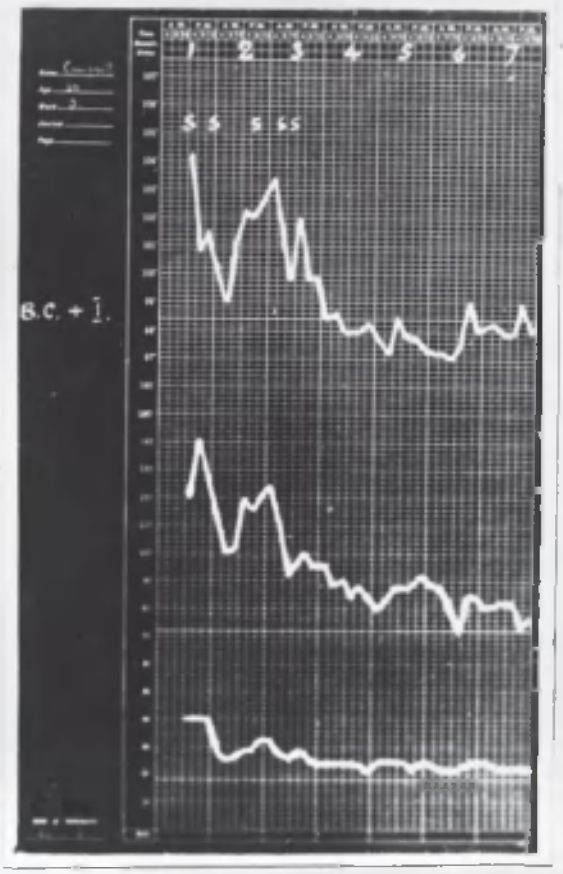

Fig. Chart, Case 80.

Showing the rapid response of a Type I case who had Type I antiserum sixteen hours after the onset (100,000 units).

TYPE I.

Case No. 85. Male, aet. 32. Serum on 2nd. day. This man was admitted with swelling of the legs accompanied by pain in the joints. A week (2/1/31) after admission the temperature began to swing for no obvious reason; there was no response to salicylates. 4 days later (6/1/31) the other curves rose and pneumonia appeared. All the curves subsided 48 hours after serum commenced. 4 days later (12/1/31) the temperature again began to swing. The R.2 and R.3 lobes were slow to resolve. 2 months later (17/3/31) a large quantity of tough retained secretion was got rid of, after which convalescence proceeded normally. An adequate response to serum but slow resolution. Abscess of lung.

Case No. 86. Male, aet. 38, admitted on 2nd. day. This was a very interesting case. A 40-hour pneumonia in a healthy man whose blood culture was still positive and in whom was found only a moderate leucocytosis. 20,000 units caused almost immediate resolution of symptoms accompanied by great improvement in the general appearance and a large leucocytosis. Serum was discontinued but the curves tended to rise a few hours later. 2 further doses completed the subsidence.

TYPE I.

Case No. 90. Female, aet. 19, after 36 hours. This case was watched from the onset. Serum was administered within 48 hours with spectacular results. Convalescence was uneventful although slow resolution was found to be due to slight serous effusion. Serous pleurisy.

Case No. 93. Female, aet. 45, admitted on 5th. day. The serum seemed to help considerably here. Cyanosis and toxaemia were ++ on admission and she was almost moribund. The serum terminated the pyrexia and left her to fight a bronchitis, which she managed to do with difficulty. Repeated atropine at one point seemed to avert a crisis, and continuous alcohol was very much indicated. Chronic otitis media. 'Red Biddy' enthusiast.

Case No. 95. Male, aet. 20, admitted on 4th. day. There was a well defined L.2 consolidation. Serum was not administered at once as he seemed well enough to await typing. In the interval all the curves subsided and there was no secondary rise. He made an uninterrupted recovery. No serum.

TYPE I.

Case No. 96. Male, aet. ? admitted on 1st. day. On admission there were signs of patchy dulness at both bases with a little tinged spit. Everything subsided after admission. Clinically not a pneumonia. No serum.

Case No. 98. Male, aet. 36, watched from onset. On admission he was fevered with slight cough and R.-sided pain. Signs of consolidation became evident 24 hours later and the symptoms were those of acute pneumonia. Following exhibition of serum there was complete disappearance of symptoms in 24 hours with a feeling of well being.
N.B. In this case the B.C. was negative although his symptoms were watched from the onset.

Case No. 100. Male, aet. 6, watched from commencement. A typical lobar pneumonia in a child. Onset convulsions, sickness and signs suggesting meningitis. Illness ran a normal course and settled by crisis. No serum.

Case No. 102. Male, aet. 37, admitted on 2nd. day. A sharp attack in a small wiry man. There was consolidation at the R. and R.2 lobes but never fully developed and therefore was rapidly dispersed. A blood culture + on admission was sterile 24 hours later after 2 doses of B.W. Type I. He made an uninterrupted recovery.

TYPE I.

Case No. 103. Male, aet. 6, admitted on 2nd. day. He developed a consolidation on the 4th. day which had resolved by the 8th. day, by which time he was quite well.

Case No. 105. Male, aet. 37. B.W. serum. Admitted on previous day, indefinite symptoms for 4 days. The signs on admission were equivocal, the most obvious thing being a profuse bronchitis. Next day the apex of R.3 and R.2 were clinically pneumonic and the X-ray showed that R.1 was also involved although throughout the illness three observers failed to detect clinical signs of consolidation. The response to serum was rapid and in 24 hours he was quite convalescent. Serum 12 noon: 20 minutes later, giant urticaria. Began to disappear in an hour; quiteaway by 3 p.m.

Case No. 108. Male, aet. 24, admitted on 2nd. day. A fairly acute case with considerable dyspnoea and cyanosis. The pneumonia was well established and involved the R.3 lobe. Following 30,000 units of Type I antibody everything subsided. On the 12th. day after serum he developed a temperature and complained of stiffness in all the joints, probably a delayed serum reaction. Chronic otitis media. Serum reaction. 15/5/31. X-ray, a fairly dense shadow over the whole R.3 lobe. 18/5/31. Clear R.3 lobe except in its lower half where there was slight haziness.

TYPE I.

Case No. 110. Male, aet. 12, admitted on 1st. day. An ordinary acute pneumonia on a healthy body. Invasion was rapid and for 6 days the illness ran its usual course, falling by crisis. No serum.

Case No. 114. Female, aet. 38, admitted on 4th. day. Defervescence occurred 2 days after admission but the illness was considerably disturbed by a 3 months' abortion with retained placenta. An extensive pneumonia of both lower lobes. The temperature rose again at the time of the abortion and there was interference with resolution for several weeks afterwards. Ultimately she made a good recovery.

Case No. 119. Male, aet. 24, admitted on 2nd. day. A typical attack in a healthy boy. The response to serum was rapid and complete. X-ray 19/9/31 — resolving pneumonia R. lower lobe.

TYPE I.

Case No. 121. Male, aet. 33, admitted on 1st. (?) day. On admission he complained of malaise and pain in the knees of over 2 days' duration. The signs of pneumonia were, however, very indefinite and P.T.R. were only slightly elevated. During the night all the curves rose and pneumonia of the R.2 lobe became well defined, later extending to the R.1 lobe. At first the spit was reported as Group "X" but later was found to be Type I, and the blood culture on admission was positive for Type I. On account of the first report he had no serum and the illness ran a typical undisturbed course ending by crisis on the 8th. day.

20/11/31. 2 months later, sputum contained pneumococci, Group "X", and streptococci.

22/9/31. X-ray — Consolid. R.2 commencing R.1.

24/9/31. X-ray — Consolid. R.1 and R.2.

Fig.: Chart, Case 121.

Case No. 122. Female, aet. 60, admitted on 2nd. day. The signs at the R. base were indefinite but in conjunction with a rusty spit made the diagnosis. Convalescence was uneventful. X-ray, old bronchitis.

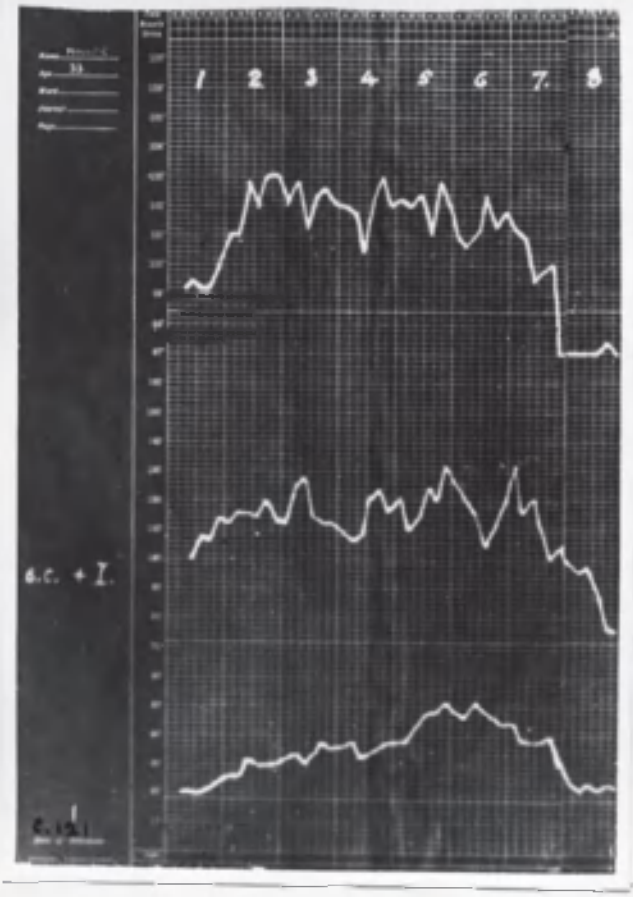

Fig. Chart, Case 121.

Showing the undisturbed course of a Type I case which had no serum.

TYPE I.

Case No. 127. Male, aet. 10, admitted on 2nd. day. This was a rather curious case. He was very toxic on admission although the temperature was low and he had a high leucocytosis. The consolidation suggested more than a 2-day illness but the history of onset was fairly definite. Convalescence was uneventful.

Case No. 128. Male, aet. 21, admitted on 2nd. day. A typical illness in a healthy adult. The response to serum was immediate and satisfactory.
14/10/31. X-ray — 'Consolid. R.3 lobe.' Upper ½ R.3.

Case No. 136. Female, aet. 37, admitted on 2nd. day. A typical acute attack. Serum was given too slowly so that the result was not so dramatic as usual.

Case No. 137. Male. Treatment began on 4th. day. An excessively severe Type I illness. Patient moribund when treatment commenced. Toxaemia was profound. Large doses of serum modified the course of events but convalescence was very rocky.

TYPE I.

Case No. 139. Male, aet. 42, admitted on 2nd. day. A mild attack cut short on the 3rd. day. Convalescence was slow and resolution protracted.

8/3/32. 3 months after onset only streptococci were recovered from the spit.

Case No. 144. Male, aet. 35, admitted on 3rd. day. An acute Type I illness running a normal course then complicated by pleuro-pericarditis which prolonged his semiconvalescence. Pleuro-pericarditis. Retention abscess. On 1/3/32, i.e. a month after the onset, only streptococci could be recovered from the spit.

X-rays:-

29/1/32. Large opacity to right of mediastinum.

1/2/32. Large abscess to right of mediastinum.

2/2/32. " " " " " " bigger. A lateral view showing the ? fluid, pear-shaped.

3/2/32. Thick-walled abscess about ¼ empty.

8/2/32. Abscess 1/3 empty: upper part of wall resolving.

16/2/32. Vertically the cavity seems to have filled, but has shrunk laterally.

26/2/32. Abscess has disappeared: slight indication of its outer wall. Satisfactory resolution.

TYPE I.

Case No. 145. Female, aet. 54, admitted on 5th. day. She was approaching the crisis on admission but was very cyanosed and acutely ill. One dose of serum caused the illness to subside. Resolution was rapid. Probably nothing can be claimed for the serum here, but the termination of illness on the 5th. day is not the rule and after serum the expected result was obtained.

Case No. 146. Male, aet. 29, very indefinite (3rd. day). He resembled a commencing pneumonia on admission. The signs were mainly of pleurisy at first. The X-ray showed nothing at the right base and dulness at right apex although clinically the signs were the reverse of that.

Fig.: Chart, Case 146.

Case No. 151. Female, aet. 27. An acute illness responding rapidly to serum. Convalescence was rapid.

N.B. Very large leucocytosis.

Fig.: Chart, Case 151.

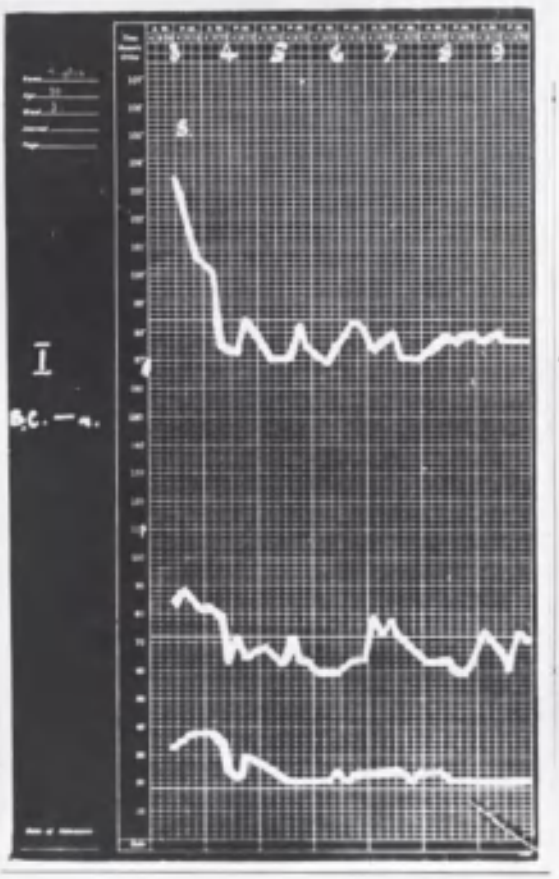

Fig. Chart, Case 146.

Showing the response of a Type I case to 20,000 units of Type I antiserum.

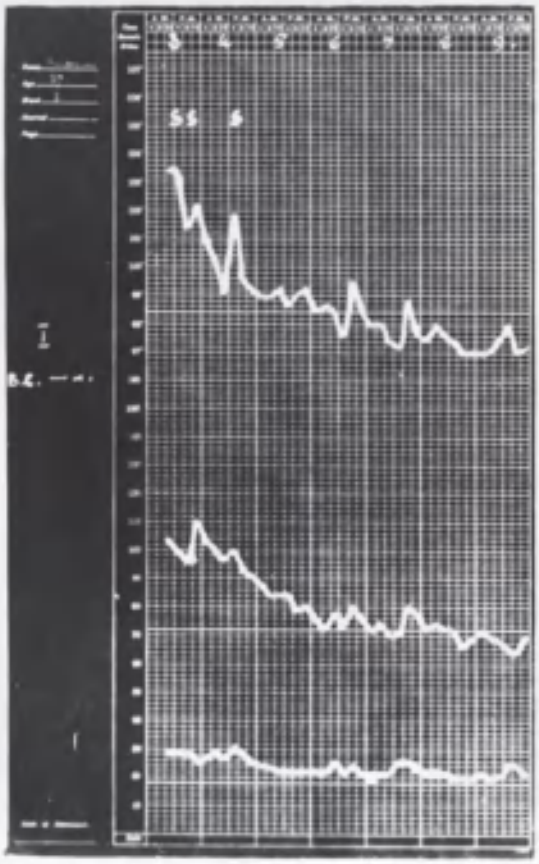

Fig. Chart, Case 151.

A case similar to 146 but in a female patient. There was a rapid response to 60,000 units of Type I antiserum.

TYPE I.

Case No. 153. Male, aet. 33, admitted 2nd. day (30 hours). A very acute illness. Serum was given early, but although it modified the course of the illness, insufficient was given to abort the crisis. 10 days after his admission the curves became unsteady and he complained of pains in the fingers. Serum reaction.

Herpes.

22/2/32. Type I spit, positive blood, and virulent illness.

26/4/32. 'Mouse well after 4 days.' Swabs from throat ? carrier.

1/4/32. Brother, Robert Watt, also convalescent pneumonia, tested as carried:— 'Mouse alive after 7 days'; this was on a swab (spit is better if obtainable).

TYPE I.

Case No. 156. Female, aet. 38, admitted on 2nd. day. A fairly severe illness on admission which reached its height on the following day. The serum had little effect on the curves and the dosage appeared to be inadequate. The illness defervesced completely on the 6th. day. The pulse remained up *circa* 110*. On 11th. day temperature began to swing and there were signs of effusion; a little serous sterile fluid removed. Thereafter the X-ray appearances were of a large pleural effusion but repeated tapping failed to find fluid so that the X-ray appearances were probably due to thickened fibrinous pleurisy with non-resolution. The curves continued to swing a little until dismissal. ? Pleural effusion.

*N.B. Is this not the most frequent clinical link joining primary illness and complication?

X-rays:-

31/3/32. Pleural effusion L. side.

12/4/32. Extensive pleural effusion with displacement of heart.

21/4/32. Complete opacity left side of chest with displaced heart.

22/4/32. Pleural effusion L. side.

11/5/32. For comparison.

25/5/32. Extensive effusion L. side.

TYPE I.

Case No. 157. Male, aet. 65, admitted 24 hours. A typical illness involving the whole right lung. He was never less than 'critically' ill. Two weeks after the onset he developed acute pain in the R. axilla with dyspnoea and cyanosis, leucocytosis was still 26,000 and the pulmonary signs suggested pneumo-thorax. This settled but at the end of another week pain suddenly appeared at the left side. For 24 hours there was nothing abnormal then very coarse friction appeared all over the left lower lobe from the posterior axillary line forward.

Case No. 160. Male, aet. 58, admitted 28 hours. Died. A schoolmaster prematurely aged, poor physique and grey. Wakened 2.30 a.m. with right-sided severe pain and bloody spit. The illness began in the R. upper lobe and spread downwards. A non-reactive case from the onset with low leucocytes. Depressed B.P. and moderate curves. Cyanosis and toxaemia were mild and he died a cardiac death.

The leucocytes on 3rd. day were under 5,000 and were all 'to the left'. Leucopenia.
The post-mortem suggested that the illness was of longer duration than would appear from the clinical history.
28/4/32. (3rd. day) Leucocytes 4·375: Lymphocytes 50%; Polymorphs 50% (all seen were bi-lobed).
An attempt to type from the spit suggested that it was neither I nor II. This delayed full doses of serum a little.
P.M. Consolidated R. lung, R.1 advanced grey hepatisation; R.2, 3 red hepatisation with overlying thick fibrinous pleurisy. Perisplenitis. Heart, kidneys and liver were normal for his age.

TYPE I.

Case No. 163. Male, aet. 24, admitted on 4th. day. An acute L.2 pneumonia. The fever ran a remitted course finishing on the 7th. day by crisis. One dose of serum modified the curves but was insufficient to abort the illness.

First case typed direct.

Case No. 164. Female, aet. 44, admitted on 3rd. day. A very severe attack. All the curves were high. Following 2 doses there was complete subsidence of the curves but the spit remained rusty for 4 days. Thereafter, was the local condition burning itself out although the serum neutralised the circulating toxin? The leucocytes were 9,000 on admission. Direct typing and mouse inoculation failed to identify the organism.

30th. Mouse inoculated; fluid withdrawn 1st., no organisms; mouse alive.
2nd. " " mouse died 3rd., Type I.
3rd. " " " " 4th., Type I.

Fig.: Chart, Case 164.

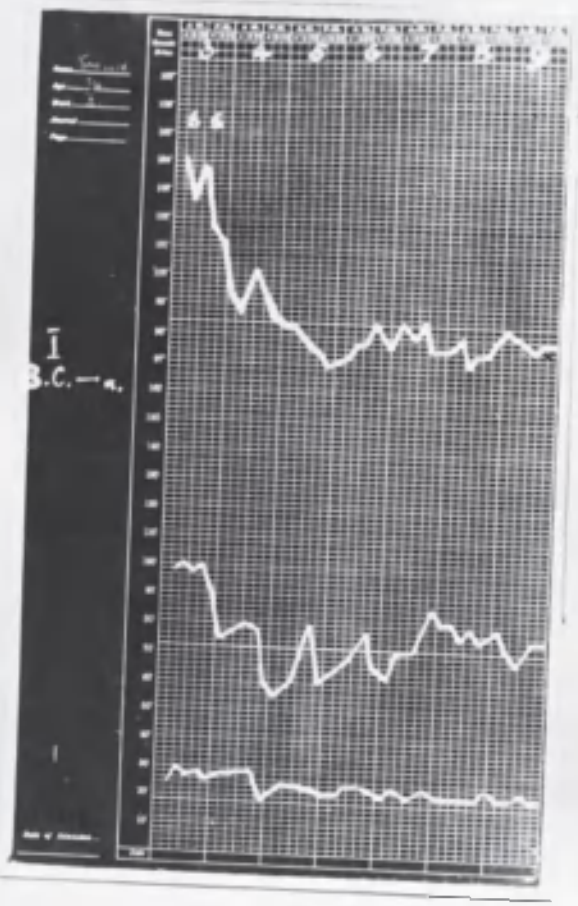

Fig. Chart. Case 164.

Showing a rapid response to 40,000 units of Type I antiserum.

TYPE I.

Case No. 166. Male, aet. 39, admitted on 2nd. day. A fairly acute attack in a poor subject. The lower R. lobe and upper R. were involved. Convalescence was uneventful.

Case No. 169. Male, aet. 27, admitted on 2nd. day. A very sharp left lower attack which responded quickly to serum.
N.B. The consolidation increased for a day although the curves subsided.

Case No. 173A. Male, aet. 59. Admitted on 2nd. day. A very acute illness in an elderly patient. There was response to small dose of serum. One month later he had a slight thrombosis of the left leg.
N.B. Low leucocytes and a positive blood culture. Slight thrombosis L. calf.

Case No. 175. Male, aet. 17, admitted on 5th. day. A very acute case admitted late and serum therefore of little benefit. The illness lasted 7 days and finished by lysis.

TYPE I.

Case No. 179. Male, aet. 30, admitted on 2nd. day.
Clinically a type I case admitted on 2nd. day. The organisms were very scanty and the spit was reported ? II direct
IV indirect.
One dose was given and discontinued in view of the Bact. report. The illness ran a normal 6 day course to crisis. It was definitely reported I on the 5th. day.

Case No. 181. Male, aet. 57, admitted on 4th. day. Died.
A very scanty Type I illness in an elderly patient. There was no reaction, failing temperature, leucocytes, etc. Toxaemia (delirium was ++). Cyanosis ++.
Failing circulation 88/50. Leucocytes very low.
Towards the end the spit was golden in colour and loaded with pneumococci in almost pure culture.

Case No. 182. Male, aet. 19, admitted on 2nd. day. A severe illness in a healthy lad. Reaction was good and leucocytes high. The spit, however, although containing numerous organisms was Group "X" two direct, three indirect on successive days. The illness ran an acute 10-day course finishing by crisis; on the 10th. day the blood culture taken on admission (2nd. day) showed a growth of Type I organisms.

TYPE I.

Case No. 183. Female, aet. 31, admitted on 2nd. day. A very severe Type I case in a frail woman. Low B.P., very dyspnoeic but high leucocytes. The oxygen chamber was of considerable benefit. She was more restful and there was less need for nursing disturbance.

Case No. 184. Male, aet. 35, admitted on 2nd. day. A very severe toxic illness. Wild delirium, severe cyanosis but adequate heart and strong man. Serum was peculiarly ineffective. He was nursed in the oxygen chamber. Spit after 3rd. day was loaded with organisms.

Case No. 185. Female, aet. 25, admitted on 2nd. day. A very acute pneumonia in a young girl. The serum terminated the illness 48 hours after the onset.

N.B. A large labial herpes appeared on day of admission and progressed for 2 further days after the curves subsided.

Serum reaction. Asthmatic.

TYPE I.

Case No. 187. Male, aet. 33, admitted ? 5 days. A severe spreading pneumonia in a poor subject. He had a crisis on the 11th. day. 50 days after crisis he evacuated evidently a retention abscess. Alcoholic. ? Lung abscess.

X-rays:-

14/1/33. Pneumonia. No definite evidence of fluid.

20/1/33. Appearance consistent with unresolved pneumonia.

17/2/33. Unresolved pneumonia.

16/3/33. No evidence of abscess. Small unresolved pneumonia patch left middle lobe.

Case No. 193. Male, aet. 42, admitted on 2nd. day. An abortive pneumonia of short duration.

TYPE I.

Case No. 197. Male, aet. 44, admitted on ? 5th. day. There was some doubt as to the duration of this case. Shivering began 6 days before admission with sickness and vomiting. He did not have pain in the side till 2 days before admission accompanied by rusty spit. The pneumonia started in R.3 and extended upwards. R.3 was clearing 5 days after admission when R.1 and 2 were still actively involved. The whole illness probably lasted 12 days. (Creeping pneumonia.) The temperature was moderate throughout: the pulse had bouts of rapidity. Spit was rusty throughout and loaded with Type I pneumococci till the 10th. day when they entirely disappeared and the spit was loaded with heterogeneous organisms (strep. IV, pneum. etc.). In view of the lateness of his admission he was given no serum: cf. Millar 121. Large leucocytosis. Herpes.

Case No. 198. Male, aet. 16, admitted on 5th. day. The illness was 'missed' outside because pain was mainly abdominal. No serum. Ran an 8-day illness terminating by crisis. Direct typing showed no 'ballooning' but subsequent investigation isolated a Type I. The leucocytes were adequate.
X-ray on 19/7/33 — Small area partial consolid. R. costo-pleural angle. Abdominal pain.

TYPE I.

Case No. 204. Male, aet. 56, admitted on 2nd. day. Died. A severe L.2 pneumonia in a man old for his years. There was no temperature reaction but in the later days a huge leucocyte reaction. The infection advanced to involve the whole left lung and toxaemia became severe.

Case No. 205. Male, aet. 25, admitted on 2nd. day. Died. A severe right-sided pneumonia involving all 3 lobes in a slim young adult. An 8-9 day illness distinguished by low temperature, but high pulse, respirations and leucocytes. Effusion was detected on the 4th. day. On the 19th. day pus was obtained (Group "X"). This was complete failure of typing for the empyema pus was later confirmed to be Type I. Empyema.

Case No. 212. Female, aet. 18, admitted on 3rd. day. A typical acute case with complete R. lung involvement. The curves subsided after serum and convalescence was rapid. Small serous effusion.

TYPE I.

Case No. 215. Female, aet. 49, admitted on 6th. day. A very severe case admitted late. No serum. She ran a toxic depressed course but with good leucocytosis throughout and reached convalescence on the 10th. day.

TYPE II.

Case No. 4. Male, aet. 13, admitted on the 5th. day. Acutely ill and delirious. Improvement was steady. On the 11th. day pus was found in R. pleura and he was transferred to Mr. Taylor's wards. He made a good recovery. He had one dose of serum.

Case No. 6. Male, aet. 23, admitted on 6th. day. There was considerable delirium and incontinence. He had a Biblical crisis on 21st. and was afebrile on 23. Serum seemed to be helpful.

Case No. 8. Male, aet. 16, admitted on 3rd. day. The effects of the serum could not be judged as he made a rapid recovery and was well on the 6th. day. Although, as judged by the heavy bacterial infection in the sputum, this was a serious case, he had a good reaction and there were no toxic symptoms.

Case No. 12. Male, aet. 42, admitted on 3rd. day. An acute attack in a poor subject. There was a positive Wassermann reaction and a severe aortic regurgitation. Although his condition gave reason for much anxiety in the first few days the illness quietly subsided. The serum seemed to help considerably. Syphilis - aortic.

TYPE II.

Case No. 17. Female, aet. 24, admitted on 4th. day. A severe pneumonia in a slight young woman. Toxaemia was well marked on admission but moderated after the exhibition of serum and the illness thereafter ran a modified course. Serum was a definite help.

Case No. 18. Female, aet. 39, admitted on 5th. day. The illness resembled more a widespread bronchitis with patchy consolidation than a primary pneumonia. Toxaemia was present for some days after admission but neither sleepiness nor delirium were conspicuous. She was an excellent patient.

Case No. 19. Male, aet. 57. Died. Admitted on 3rd. day. A serious case in which cardiac symptoms predominated. A period of fibrillation was followed by a terminal flutter. Toxaemia became marked 3 days before death. Alcoholic. Serum seemed to help.

TYPE II.

(Group IV Sputum)

Case No. 23. Male, aet. 44, admitted on 2nd. day. Died. A severe case in an alcoholic and a 3rd. attack. Toxic symptoms were marked throughout but increased with each day of illness. Wild delirium distinguished the last 3 days. The bacteriological findings were confusing. Alcoholic. Serum had no effect, but was not given continuously in view of the sputum bacteriological findings.

Fig.: Chart, Case No. 23.

Case No. 24. Female, aet. 24, admitted on 4th. day. She was fairly toxic on admission but responded readily. The pneumonia finally restricted itself to the right lower lobe. After 2 days' treatment the illness ran a modified course. Serum effect could not be judged.

Case No. 26. Male, aet. 23, admitted on 5th. day. A typical acute attack which ran a modified course. 10 days after the first dose of serum the curves rose and remained unsteady over a period of 14 days. Syphilitic. Serum was helpful. Serum reaction.

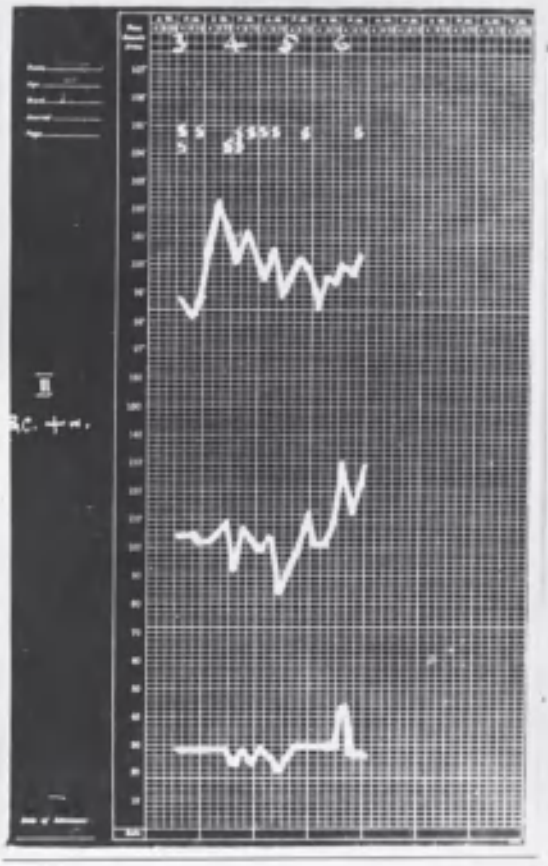

Fig. Chart, Case 23.

A fatal case of Type II pneumonia admitted late on the third day. There was no response to 220,000 units of Type II antiserum.

TYPE II.

Case No. 27. Female, aet. 23, admitted on 5th. day. On admission she was very toxic and the physical signs were indefinite. Patchy consolidation seemed to creep about but was mainly localised in the upper R. lobe. Toxaemia was controlled after 2 days and the fever fell by crisis. On the 12th. day of illness there was serum reaction associated with pyrexia and arthritis. Serum was helpful.

Case No. 28. Male, aet. 64, admitted on 6th. day. A low pneumonia mainly of the R.3 lobe. The curves were never high but he was very debilitated throughout, to a greater extent than the physical signs warranted. Sputum latterly was very copious and purulent and the signs suggested cavity. Syphilitic.

Case No. 30. Male, aet. 20, admitted on 3rd. day. A typical acute case involving mainly the R. lower lobe. Incipient otitis media. His main complaint was of pain in the right ear. The M.T. was much reddened but did not rupture. The pneumonia was poorly developed and rapidly resolved.

TYPE II.

Case No. 32. Female, aet. 42, admitted on 5th. day. A severe illness distinguished by much toxaemia. Definite consolidation only of R.3 but patchy elsewhere. Insomnia was troublesome. The curves came down by lysis but one day after reaching normal they rose again, the temperature reaching 107°F. after which they subsided. During this episode blood and albumin appeared in the urine and pneumococcus was found in pure culture in the urine. Persistently acid urine associated with acute nephritis.

Case No. 38. Female, aet. 14, admitted on 2nd. day. The illness was undistinguished except for a pseudocrisis at the 4th. day. The pulse tended to be a little rapid but otherwise her convalescence was normal. A 'nervous' child.

Case No. 39. Male, aet. 22, admitted on 4th. day. An acute attack in a healthy young adult involving only the R. upper lobe. The illness ran a normal course but he was rather restless for several days after the curves fell. Serum seemed of definite help.

TYPE II.

Case No. 41. Male, aet. 33, admitted on 2nd. day. A mild case with consolidation of one lobe. Temperature descended by lysis after commencement of treatment. This was said to be a second attack. The effect of the serum could not be judged.

Case No. 42. Male, aet. 26, admitted on 4th. day. An acute attack involving the whole left lung. On admission he was acutely ill but immediate improvement followed the administration of serum. Convalescence was uninterrupted. This was a second attack, but no information could be obtained of the first which happened while he was at school.

Case No. 44. Male, aet. 14, admitted on 2nd. day. He was extremely toxic on admission and seemed moribund. After administration of serum he improved remarkably and in 24 hours was well. The lung signs had not time to develop fully but were mainly confined to the bases. This was a "fifth" attack. There was a rather severe serum reaction.

TYPE II.

Case No. 46. Male, aet. 17, admitted on 3rd. day. A moderate attack in a well nourished young man. The L.2 lobe was solid on the 3rd. day of illness but the curves came down on the following day after serum and thereafter progress was uninterrupted. Toxaemia was mild. Serum seemed helpful.

Case No. 47. Male, aet. 23, admitted on 3rd. day. A very severe Type II pneumonia. Resolution failed to occur and after some weeks T.B. were found in the spit. The temperature fell on 25th. June to 100°F. About the beginning of July 1930 the temperature again rose and he maintained an irregular pyrexia which did not subside. The interpretation of the case probably is that 'a tubercular boy contracted an acute pneumonia from which he recovered but the illness awakened the tubercular process which subsequently progressed unsatisfactorily'. Unresolved T.B.

Case No. 49. Male, aet. 38, admitted on 2nd. day. On admission the signs were poorly developed but on the 3rd. day the R. lower lobe was completely consolidated. The illness was fairly mild and resolution was normal. The serum appeared to be of definite help.

TYPE II.

Case No. 51. Male, aet. 46, admitted on 4th. day. A mild case which responded at once to serum. Resolution, however, was notably slow but the chest cleared very well. He was rather debilitated previously and apparently had poor recuperative powers.

Case No. 52. Female, aet. 29, admitted on 2nd. day. A mild attack affecting mainly the R. lower lobe but with bronchitis throughout the chest. Resolution and convalescence were normal. On the 2nd. day after serum a macular rash appeared. On the 10th. day she had an urticarial eruption on trunk and limbs. Serum reaction.

Case No. 53. Female, aet. 29, admitted on 2nd. day. A moderately severe attack involving the L. lower lobe mainly. She was slightly cyanosed and dyspnoeic on admission but responded quickly. The heart showed a marked irregularity due to extrasystoles which were most numerous at the height of the illness but later subsided. Serum reaction, a macular rash on trunk 24 hours after serum. Extrasystoles.

TYPE II.

Case No. 56. Male, aet. 37, admitted on 2nd. day. A typical pneumonia of the left lower lobe distinguished at its onset by unusually severe pleuritic pain. No crisis occurred and later pus was found in the L. pleural cavity. Haematuria occurred. Empyema.

Case No. 58. Female, aet. 38, admitted on 2nd. day. A severe L.2 lobe attack complicated by much bronchitis elsewhere in the chest. The response to serum was very satisfactory. The bacteriological findings were anomalous. Spit was Group IV. 11/3/31. First day. Seen in casualty where she was admitted for L. mastitis (streptococcic). There was no loss of percussion resonance over either lung but a good deal of bronchitic râle was found in the chest and especially at the L. base. Bacteriological examination — spit Type IV, previously Type II. A vaccine administered.

Case No. 69. Male, aet. 59, admitted on 5th. day. Died. Admitted moribund with failing heart and very low blood pressure. The serum w as apparently of no benefit and he required constant stimulation during his admission period. This was a 4th. attack. Cardiac failure.

TYPE II.

Case No. 76. Male, aet. 27, admitted on 4th. day. Possibly our worst case with recovery. Began as a very severe R. sided infection spreading on the 6th. day to involve most of the left side. Cyanosis was very severe and owing to delirium was difficult to control. At the height of the illness distension was a problem but he responded to mild enemata with pituitrin. It was notable that a very large leucocytosis developed after the serum was given.

Case No. 79. Male, aet. 41, admitted ? 3rd. (5-7) day. Died. He was admitted moribund in delirium and prostration. An intense degree of cyanosis was present and the heart sounds were hardly perceptible. There was no response whatever and he died 6 hours later. According to the P.M. evidence this was a pneumonia of at least 7 days, the R.l. lobe being in a state of incipient softening. Pneum. identified from spleen — P.M.

Case No. 83. Female, aet. 52, admitted on 4th. day. A severe illness involving both lungs. Prostration was severe but she gradually pulled round. Convalescence was very slow. The serum was probably of benefit. It was noteworthy that although toxicity seemed severe there was no delirium.

TYPE II.

Case No. 84. Male, aet. 30, admitted on 2nd. day. A very serious case. The whole L.2 was solid, the temperature was low, and there was a minimal leucocytosis. Serum was pushed and after 48 hours the blood pressure rose. A leucocytosis developed and the temperature rose. The spit remained very rusty till the 7th. day of illness when it became mucopurulent and the curves subsided. The leucocytosis persisted during the following week. Serum reaction. The serum appeared to be the deciding factor here.

Case No. 91. Female, aet. 44, admitted on 3rd. day. Died. A severe illness in a very stout woman. Both lungs were involved and bronchitis was severe. Dyspnoea was +++ throughout although cyanosis was kept under control. The serum seemed of little benefit although after its commencement there was a gradual lysis of the temperature. The other curves remained high. During the last 3 days the pneumonia was stationary or a little improved but the heart failed. This case suggests that adequate serum was given but not rapidly enough. It should have been pushed much more in the first 24 hours.

TYPE II.

Case No. 99. Male, aet. 36, admitted on ?2nd. day. Died. A very serious invasion from the onset. The lung signs were not very evident on admission, but advanced with great rapidity in the following 48 hours. The serum seemed to affect the temperature and pulse curves at once but the dyspnoea became worse. There was no leucocytosis and the count declined every day. Due to absence on holiday the serum was given slowly over several days. Chronic bronchitis. ? Alcohol. P.M. - Purulent softening of R.1 and 2. Pneumonia at least 6 days old?

Case No. 104. Male, aet. 56, admitted on 2nd. day. A fairly severe pneumonia in a well preserved man of 56. Owing to the large leucocytosis a I serum was given. There was no effect on the curves and the illness had an irregular finishing by mild crisis. The serum had no effect.

TYPE II.

Case No. 106. Female, aet. 19, admitted on 3rd. day.

A very acute illness in a delicate young girl. After serum intravenously there was no response and during the next 2 days she was very ill. Although there was much lung involved there was little or no bronchitis and spit was absent almost throughout. Asphyxia was the most distressing feature but toxaemia never became very severe. There was a slow lysis of the fever with a fairly rapid termination on the 7th. day. The serum may have reduced the toxaemia but did not shorten the duration.

11/5/31. Differential count.

Poly. 14·1%
Band forms 72·1%
Mono. 5·2%
Lymph. 8·0%
Leuc. 0·6%
Considerable megalocytes.

TYPE II.

Case No. 107. Male, aet. 43, admitted on 2nd. day. Died. A very severe pneumonia in a poor subject. From the onset he had all the signs of failure of reaction. The serum seemed to be of little benefit although there was a slightly improved leucocyte count and delirium did not appear till the termination Leucopenia. This man in 48 hours had 70 c.c. of serum, i.e. 700,000 units of Type II, yet 2 hours after his last dose there was no appreciable II antibody in the blood. This is in agreement with Park's contention that in the later stages of a II pneumonia so much s.s.s. is present that impracticable doses of serum would be necessary to neutralise it.

12/5/31. Differential count —

Neutrophil band forms 64·8%
Poly. 5·4%
Lymph. 27·0%

13/5/31. Band forms 40·5%
Poly. 3·6%
Lymph. 36·1%
Mono. 4·0%
Eosin. 2·8%

TYPE II.

Case No. 109. Male, aet. 44, admitted on 3rd. day. Died. A very severe pneumonia in a poor subject. On admission he presented all the non-reactive features of a bad II case, few leucocytes, low temp., low B.P. After 20,000 units of II antibody given at once the temperature rose a little and he seemed better, but this was only transient. He died on the 6th. day.

N.B. The blood culture in spite of large doses of serum was positive on 3 successive days. There was no delirium. ? Is this batch of serum especially lacking in potency against II?

Differential counts:-

26/5/31.	Band.	77·0%
	Poly.	8·8%
	Lymph.	8·8%
	Mono.	4·0%
27/5/31.	Band.	60·0%
	Poly.	12·5%
	Lymph.	22·5%
	Mono.	5·0%
25/5/31.	Band.	70·5%
	Poly.	11·5%
	Lymph.	14·0%
	Mono.	4·0%

28/5/31. X-ray — Pneumonia of R. middle and lower zones.

TYPE II.

Case No. 112. Male, aet. 59, admitted on 4th. day. A 'typical' II case. Admitted with all the signs of non-reaction to a severe illness. Serum was not given as, owing to the advanced stage of the illness, it was unlikely to be of benefit. There was an advanced pneumonia of the whole R. lung. Low temp. and blood pressure, relative leucopenia, copious brown semifluid spit. There was no delirium. (Delirium is uncommon in these non-reacting cases till the terminal few hours.)

X-ray:- 3/6/31. Consolidation R.1.2.3.

2/6/31. Arterial puncture for PH determination.

Case No. 116. Male, aet. 28, admitted 25 hours after onset. A second attack (caught very early) in a weakly man. (There was a dramatic response to adequate early dosage.) The onset of illness was mistaken for gastric influenza, severe vomiting. 25 hours after, he was blue with cyanosis and looked moribund. Serum was given freely. Next morning the curves had settled and by the following day he was convalescent.

X-ray:- 16/7/31. Consolid. middle zone R. lung.

Fig.: Chart, Case No. 116.

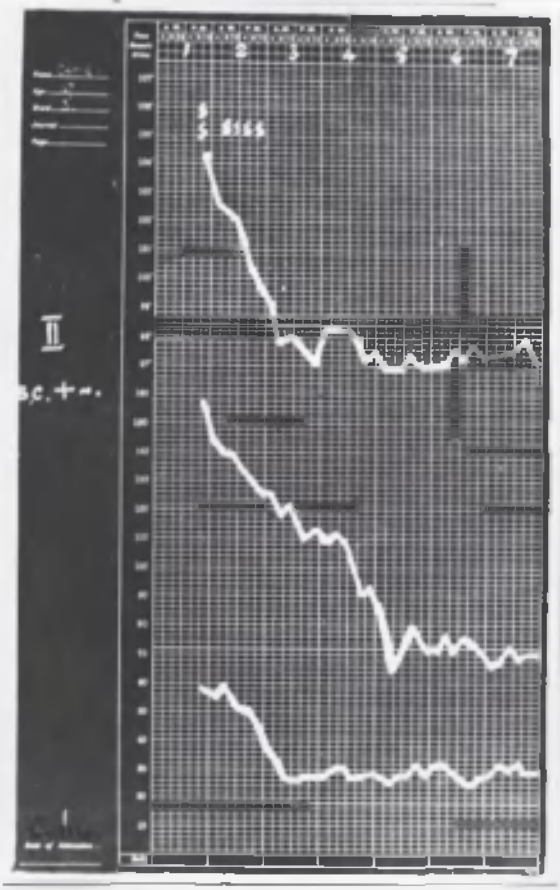

Fig. Chart, Case 116.

A very favourable result in an early Type II case who had 120,000 units of Type II antiserum.

TYPE II.

Case No. 124. Male, aet. 28, admitted on 3rd. day. A very severe double pneumonia in an old chronic bronchitic, probably bronchiectasis. Cyanosis was severe but was quite relieved by oxygen. He made a very good fight, although stimulation was necessary from the beginning. Bronchiectasis. Clubbed fingers.

X-ray:- 7/10/31. Resolving pneumonia R.3.
Consolidation L.1 and L.2.

Case No. 125. Male, aet. 14, admitted on 3rd. day. Died. A thin boy of average physique. When admitted, there was a consolidation of R.3 and the spit was reported Group "X". No serum was given until 2 days later by which time the culture was reported Type II. Things seemed to be settling; falling leucocytosis, etc. On the 6th. day he took a rigor and the temp. began to rise again and he went steadily downhill, dying on the 9th. day. The onset of empyema was not heralded by rising leucocytosis, 7th. day 7,600. P.M. R. pleural cavity 10 oz. sero-purulent fluid with acute recent pleurisy of R.3. Old patch of organised purulent pleurisy at the pleuro-pericardial junction. Upper lobes R.1,2 few small decomposed gangrenous patches.
R.3: airless, old pneumonia recent unresolved. Empyema.
X-ray:- 31/7/31. Some mottling of lung, chiefly at R. base.

TYPE II.

Case No. 126. Male, aet. 22, admitted on 3rd. day. A sharp attack involving most R. lung. Although rather late for effective serum the severity of the course of illness was mitigated and he was convalescent by the 4th. day. Serum reaction. Joint pains were complained of on the 10th. day.
X-ray:- 18/10/31. Consolidation R.1, 3. R.3 clearing — R.1 still very dense.

Case No. 129. Male, aet. 15, admitted on 1st. day. A very sharp attack cut short on the 2nd. day. ('A most dramatic case.' A.W.H.) He had a well marked reactive rise on the 3rd. day after serum but this settled in 24 hours. Reactive rise.
9/12/31. 4 weeks after pneumococcus Group "X" (type 8).
X-ray:- 5/11/31. Consolidation upper ½ L.2.
Old healed T.B. right upper zone.

Case No. 131. Male, aet. 27, admitted on 7th. day. A L.2 pneumonia which apparently ran an ordinary course and ended on the 6th.? 7th. day. Convalescence was ordinary. No serum.

TYPE II.

Case No. 135. Male, aet. 17, admitted on 5th. day. A severe illness in a young boy. Leucocytes on admission very scanty. This with a severe toxic illness in a young man suggested clinically Type II. Convalescence was stormy and on 12/12/31 he developed a pneumothorax; there was no evidence of T.B. Pneumothorax. Abscess of lung.

X-ray:-

9/12/31. Consolid. R.3, L.2.

12/12/31. " " Pneumothorax R.1.

16/12/31. Resolving pneumothorax R.1.

16/1/32. Pneumothorax whole R. lung: poor resolution.

28/1/32. Complete pneumothorax: adhesions broken down.

11/2/32. Pneumothorax commencing expansion of lung.

22/2/32. Commencing re-expansion with satisfactory resolution. A lateral view shows well considerable adhesions.

Case No. 139. Male, aet. 20, admitted on 4th. day. A healthy young man. The illness was probably nearing its end when he was admitted, but after serum all the curves declined. Acute nephritis.

20/1/32. Mouse inoculation:- 4 weeks after; not dead after 5 days.

TYPE II.

Case No. 141. Male, aet. 35, admitted on 2nd. day. Serum reaction. He ran an average course with adequate reaction. The illness terminated by crisis on the 8th. day. He complained of some joint discomfort in knees and elbows on the following day.

Case No. 158. Female, aet. 41, admitted on 2nd. day. Died. This woman was very ill on admission, very cyanosed and dyspnoeic. Pneumococci were abundant and no difficulty was found in typing it directly. Serum in large doses seemed at first to modify the illness but on the whole was ineffective. The leucocytes were 22,000 on admission and towards the end became very high. The whole left lung was involved finally. Very high leucocytosis.

Differential count. 4/7/32 (terminal day with leucocytosis of 51,000)

Poly.	52·0%
Transit. Poly.	39·7%
Mono.	0·3%
Lymph.	6·6%
Myelo.	0·6%
Eosin.	0·6%

TYPE II.

Case No. 161. Male, aet. 49, admitted on 4th. day. He looked exhausted on admission and had probably weathered the worst of his illness. Blood pressure and leucocytes were low, the count improved towards the end of the illness. The blood pressure was low during convalescence. On admission there was slight yellowing of the conjunctivae; this cleared in 2 days.

Case No. 163. Male, aet. 58, admitted on 5th. day. Died. Looked hopeless from the start. An alcoholic under-nourished scraggy man. On admission, consolidation involved the whole L.2 and was commencing in R.3. 6 doses of serum seemed to give slight improvement during the first 2 days. Alcohol.
Low leucocytes.
Bacteriologically interesting.
Direct typing on admission was unsatisfactory but the day after was a definite II.
Mouse inoculation gave pneumococci Group "X" and coliforms and the blood was indefinite.
P.M. A pure culture of Type II was recovered from the spleen.

TYPE II.

Case No. 165. Male, aet. 19, admitted on 6th. day. Admitted delirious and very toxic. A dose of serum was given in view of the diagnosis but too late to be of any use. The delirium was probably post-critical. Convalescence was uneventful.

Case No. 171. Female, aet. 21, admitted 36 hours after onset. A severe Type II illness adequately dealt with from the first. Curves normal 48 hours after onset. Convalescence uneventful except for mild arthritic pains 10 days after serum. Serum reaction.

Fig.: Chart, Case No. 171.

Case No. 172. Male, aet. 24, admitted on 3rd. day. Consolidation of R. lower lobe. The temperature remained unsteady beyond 7th. day but the illness seemed to be modified by the serum.

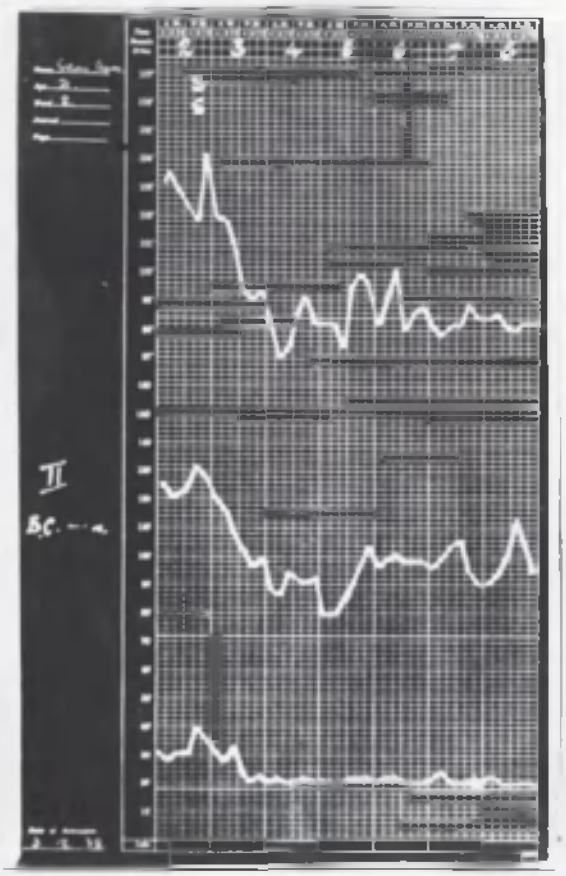

Fig. Chart, Case 171.

Showing the rapid response of a Type II case admitted early in the second day to 40,000 units of Type II antiserum.

TYPE II.

Case No. 173. Male, aet. 40, admitted on ? 3rd. day. Died. A well nourished man, mildly delirious and excited. Cyanosis + mild dyspnoea. Felt seedy for several days and very uncomfortable while driving home from Forfar to Paisley. Consolidation of L.2 lobe with considerable bronchitis. Spit rusty from 3rd. day. Pneumococci abundant. 3 doses of serum after 72 hours. Toxaemia ++. cf. Case No. 137.

Case No. 174. Male, aet. 21, admitted on 2nd. day. An acute R.3 attack which was modified by serum.
N.B. Low leucocytes.

Case No. 176. Male, aet. 17, admitted on 4th. day. An acute toxic illness running a 6-day course. Labial herpes.

Case No. 177. Female, aet. 36, admitted on ? 3rd. or 6th. day. A moderate attack of indefinite duration. Serum was withheld as she was beyond benefit of it.

TYPE II.

Case No. 192. Male, aet. 37, admitted on 2nd. day. Died. On admission there was massive consolidation of R.3 but he was not very ill. He was not typed till the 3rd. day. From 2nd. to 6th. day he had 5 doses of combined I and II and 2 doses of II only, i.e. 40,000 units II. Although the lung condition did not spread further he became gradually more toxic and heart failure terminated the illness. Serum was singularly ineffective. After an early improvement there was no appreciable effect. Would the serum have been more effective if all given in first 2 days?

Case No. 194. Male, aet. 55, admitted on 4th. day. A subacute insiduous pneumonia in a weatherbeaten man who looked 10 years more than his age. He struggled to recovery but was dismissed with considerable dulness at both bases.

Case No. 195. Male, aet. 29, admitted on 4th. day. A very severe pneumonia. Day of onset doubtful, 4th. according to symptoms, 2nd. according to physical signs which were not definite till 2 days after admission. Sputum was in fair quantity, bloody on admission and darkly bloody during the next two days, with plentiful II organisms. Serum was given in large quantity during 24 hours and seemed to arrest the downward course.

TYPE II.

Case No. 199. Male, aet. 21, admitted on 3rd. day. A very severe pneumonia in a healthy young adult. He had a copious II infection which however, although organisms were ++ in spit, was difficult to type in artificial light.

N.B. Direct typing by artificial light is more difficult; better to let the spit lie for 30 mins. before examining. He had 60,000 units Conc. II in 18 hours and had a crisis rapidly with amelioration of symptoms although the consolidation remained massive with friction for several days afterwards.

Case No. 200. Male, aet. 14, admitted on 7th. day. He was still sharply ill on admission but after 3 days had a crisis and made a good recovery. There was only patchy consolidation but copious organisms were present in the sputum and he was semi-comatose and delirious.

TYPE II.

Case No. 201. Male, aet. 29, admitted 30 hours. A very severe illness starting in L.1 then L.2. 60,000 units of II in 18 hours with great amelioration of symptoms and immediate depression of the curves. The consolidation on the second day of admission was denser although the general condition was much better.

28th. 2nd. day numerous pneumococci only a few ballooning with Type II antiserum.

29th. Pneumococci + + the ballooning with Rabbit II antiserum was only fair but with horse antiserum the capsules were large.

30th. Horse serum Pn. + + + and very large, few unballooned; with rabbit serum the effect was less, many unballooned. The horse antiserum in this case was more potent.

Oct. 1. Very scanty II with both rabbit and horse antiserum.

Oct. 2. Pn. absent scanty "X".

TYPE II.

Case No. 202. Male, aet. 21, admitted on 2nd. day. A healthy young lad whose illness began like an acute abdomen. He had no serum for 3 days after the onset. Small consolid. L.2. On the 4th. day II was diagnosed from a small rusty spit. The curves began to fall and no serum was given but subsequently the pneumonia spread to R.3. Absence of spit for 3 days.

Case No. 203. Male, aet. 26, admitted on 4th. day. A severe infection but adequately controlled by 5 doses of serum. Resolution was slow. Consolidation was well advanced on admission. He was restless but not delirious and gave no cause for alarm after the serum. There was probably some serous effusion.

Case No. 206. Male, aet. 21, admitted on 2nd. day. A severe illness in a young healthy adult. The whole L.2 lobe had massive consolidation. Serous effusion was evident on the 4th. day. Resolution had commenced before the curves subsided. Recurrent case. He had Type I pneumonia with empyema, Belvidere 2½ years before. Serous effusion.

TYPE II.

Case No. 213. Male, aet. 13, admitted on 3rd. day. A fairly severe lobar pneumonia in a mentally deficient child. He made a rapid recovery. The sputum contained copious organisms which persisted well into convalescence.

Case No. 214. Male, aet. 34, admitted 4th. or 5th. day. Died. A mental patient admitted moribund who died 24 hours later. No serum.

Case No. 216. Male, aet. 39, admitted on 2nd. day. Died. Failure of direct typing meant no serum till the 3rd. day. Thereafter 80,000 units II in 48 hours but went steadily downhill. The whole right lung was involved, a consolidation going on rapidly to septic softening. The Blood Culture was still positive after serum.

Case No. 219. Male, aet. 18, admitted on 3rd. day. A fairly acute attack in a wiry lad deformed with rickets. Recovery was satisfactory.

TYPE II.

Case No. 221. Male, aet. 55, admitted about 7th. day. A fairly diffuse pneumonia near to termination. Recovery was normal.

Case No. 222. Male, aet. 21, admitted on 1st. day. A patient very ill from the onset. 140,000 units given in 24 hours, with complete remission. Convalescence normal after a reactive rise of the curves. B.C. repeated after serum was still negative. N.B. Increased leucocytosis.

Case No. 223. Male, aet. 34, admitted on 4th. day. A very severe attack. Onset was indefinite so he was given 100,000 units with excellent result. The serum probably only aided a good intrinsic reaction but the large dosage given rapidly seemed to abort the course.

Case No. 225. Male, aet. 13, admitted on 3rd. day. An acute illness in a healthy boy running a rapid course like a Type I illness. Organisms were copious in the sputum.

TYPE II.

Case No. 226. Male, aet. 29, admitted on 2nd. day. Acute onset in healthy man. Serum reaction. Slight fever; pains — arms, shoulders.

Case No. 227. Male, aet. 19, admitted 36 hours. A very acute onset in a healthy lad. He was sent in as an appendix. Consolidation of L.2 was barely evident on admission at 36 hours. Next morning the signs were well developed but with 40,000 II units the curves all subsided. For 7 days there was little change then resolution proceeded rapidly. The sputum on the day of admission was chocolate brown and non-aerated and was loaded with II pneumococci.

Case No. 228. Male, aet. 22, admitted on 3rd. day. On admission he was 'sharply ill and delirious'. A large consolidation involved R.1 and later R.3. For 3 days he was critically ill with low leucocytes but after this the consolidation at R.3 became very massive, the leucocytes rose and he began to improve. On the 29th. day of illness he developed a thrombosis of the posterior tibial vein (L.). Thrombosis of leg.

TYPE II.

Case No. 229. Male, aet. 48, admitted on 4th. day. A very ill patient who was moribund during the first 2 weeks. Severe pleuritic pain was a marked feature and the consolidation was very massive. The sputum was copious throughout but in the second week increased from 7 ozs. to 15 ozs. and became very necrotic (chocolate rust) and then gradually altered till it resembled bronchiectatic sputum. Convalescence was very slow. The leucocytes were moderate but improved after serum. Active tuberculosis. Bronchiectasis. The patient looked like death during the whole of the 2nd. week but was not delirious, had reasonable heart sounds and maintained a leucocytosis.

Case No. 230. Female, aet. 30, admitted on 4th. day. A sharply ill young woman. Patchy consolidation of R.3. She had no serum and the curves decreased on the 7th. day. She was grossly anaemic (secondary, post-puerperal).

TYPE III.

Case No. 55. Male, aet. 47, admitted on 3rd. day. Died.
He was admitted moribund with complete consolidation of the L.2 lobe and +++ bronchitis throughout the chest. A large quantity of black tarry-looking spit was put up till he died. This was not explained by the P.M. findings. ? Haematemesis or haemoptysis. Organism cultured from spit.

Case No. 92. Male, aet. 58, admitted on 5th. day. Died.
An emaciated old-looking man. There was consolidation of R.1 and 2 with considerable bronchitis elsewhere in the chest. One dose of serum was given. The pulse which was very poor on admission began to fail shortly after midnight and he became very delirious. P.M. Consolidat. R.1 and R.2. R.1 advancing to suppuration.

Case No. 117. Male, aet. 65. Died.
This patient was moribund on admission. The date of onset was obscure. There was no reaction and he sank under an overwhelming infection.

TYPE III.

Case No. 118. Male, aet. 41, admitted on 3rd. day. Died. A rather scraggy man. On admission the signs of consolidation were poorly developed and he did not appear to be very ill. Two doses of serum were given. Following the bacteriological report, non-specific measures were intensified. For a time he seemed to improve a little but the spit became increasingly copious and necrotic. Lung tissue could be identified in the spit for 5 days before he died. Toxaemia was severe throughout but, it is noteworthy, there was no delirium till the very end.

Case No. 132. Male, aet. 23, admitted on 4th. day. Our first III to recover. The illness lasted 16 days and pneumonia wandered about the chest, L.1, R.1, R.3?, L.2. A non-reactive illness, moderate curves and low leucocytes. Serum reaction.

26/11/31. Mouse alive on 7th. day.

18/12/31. Group "X" scanty.

6/1/32. Mouse not dead in 6 days.

X-ray:- 17/11/31. Shows complete consolidation R.1.
Lesser complete opacity R.3.
Shadow L.1.

20/11/31. Consolidation R.1, R.3, L.1.

TYPE III.

Case No. 152. Female, aet. 38, admitted on 6th. day. Died. 2 doses of serum were given before she could be typed. She collapsed on the following day. Unusually high leucocytes.

Case No. 155. Female, aet. 44, admitted on 1st. day. Died. A stout woman admitted early in her illness. The signs of consolidation progressed rapidly after admission. There was no delirium and the only sign of severe intoxication was severe progressive anoxaemia. Otherwise it resembled a Type II illness in the early stages with good reaction, very high temperature, maintained blood pressure, leucocytes not unduly depressed. In spite of the good reaction everything failed at the 7th. day. Fairly good leucocytosis. Reactive illness.

Case No. 170. Female, aet. 20, admitted on 4th. day. Admitted reacting well. A high temperature was maintained till the termination by crisis. It resembled a severe Type II illness.

GROUP "X".

Case No. 7. Male, aet. 24, admitted on 3rd. day. A sharp attack but not severe. There was no real delirium. The effects of the serum could not be judged. Pneumonia unresolved on 2/4/30. Dismissed on 18/4/30 well.

Case No. 9. Female, aet. ?, admitted 24 hours after onset. A somewhat perplexing case. Admitted with all the general symptoms of pneumonia but the physical signs at the L. base were those of small pleural effusion and no large pulmonary or pleural lesion developed. Puncture was negative. Sputum practically absent and only mucoid. Toxaemia was slight. Serum reaction.

Case No. 10. Male, aet. 34, admitted on 5th. day. A simple pneumonia in a healthy adult. He was very 'well' during the course of the illness and there was no sign whatever of toxaemia. It is to be noted that this was a second attack. The temperature came down by lysis.

GROUP "X".

Case No. 13. Male, aet. 33, admitted on 4th. day. Died. A recurrent attack after 12 months in a young man of poor physique. The disease was of the 'creeping' type and of marked severity. Toxaemia declared itself from the onset but seemed to be under control till a day before the end. The heart began to fail. Three lobes affected. Creeping pneumonia.

Case No. 15. Female, aet. 42, admitted on 3rd. day. An abortive attack in a woman bedridden and crippled with R.A. After one dose of serum the temperature fell by crisis. Signs of consolidation were not well developed. On the 6th. day all the curves rose a little. A second dose of serum was followed by subsidence and progress was uninterrupted. A Group "X" was present in pure culture.

GROUP "X".

Case No. 20. Male, aet. 20, admitted on 2nd. day. The illness ran a normal course to begin with but the curves had a second rise on the 12th. day and puncture showed a slight effusion incipiently purulent. Some fluid was withdrawn and progress thereafter was slow but uninterrupted. Pleural effusion.

Case No. 21. Male, aet. 19, admitted on 2nd. day. An acute ill-defined attack. Mainly the R.3 lobe was involved but definite consolidation failed to develop. The temperature was low and he had a pseudo-crisis on the 3rd. day and thereafter convalesced normally.

Case No. 22. Male, aet. 14, admitted on 1st. day. A mild attack in a healthy boy. No sputum was obtained. There was ? indication for serum.
Readmitted to ward 3 on 5/12/30; he had a short febrile illness with no pulmonary signs.

Case No. 25. Male, aet. 33, admitted on 2nd. day. A moderate attack involving mainly the L.2 lobe. Toxaemia was marked on admission but the illness ran a moderate course.

GROUP "X".

Case No. 33. Female, aet. 24, admitted on 5th. day. The physical signs on admission were simply of a diffuse bronchitis. Two days later the R.3 was definitely consolidated.

Case No. 34. Female, aet. 62, admitted on 3rd. day. A low pneumonia with ill-defined physical signs mainly confined to R.3. There was a well marked scoliosis affecting the lower dorsal spine. She progressed normally.

Case No. 35. Female, aet. 30, admitted on 3rd. day. A severe illness in a fairly healthy woman. Signs of consolidation well marked only at R.3 but there was an initial profuse bronchitis. The illness ran a normal course. Slight aortic regurgitation.

Case No. 36. Male, aet. 22, admitted on 4th. day. A severe illness characterised by much dyspnoea and cyanosis. Cyanosis was noted for 3 days after the crisis. Consolidation of the L. lower was accompanied by ++ friction.

GROUP "X".

Case No. 43. Male, aet. 34, admitted on 2nd. day. A rather severe illness affecting mainly the R. upper lobe but also to some extent the R. lower lobe. Toxaemia was mild. After 2 days of serum the curves declined. Syphilitic.

Case No. 48. Male, aet. 28, admitted on 2nd. day. A fairly severe attack involving completely L.2 and to a lesser degree R.3. He responded well to treatment and convalesced normally.

Case No. 57. Male, aet. 44, admitted on 2nd. day. Died. Admitted very cyanosed with a frequent small pulse and B.P. 88/74. General progress uniformly unsatisfactory. Leucocyte count 6,000. Cardiac weakness and toxic symptoms were progressive. Impoverished circumstances.

Case No. 60. Male, aet. 49, admitted on 2nd. day. An acute attack of lower left lobe pneumonia in a healthy adult. There was a fairly typical crisis on the 5th. day.

Case No. 61. Male, aet. 65, admitted on 7th. day. Died. An old man admitted moribund with R. 60, P. 140, T. 98°F. The R.2 and 3 lobes were solid and there was coarse friction. There was no sputum. The blood culture was negative.

GROUP "X".

Case No. 63. Female, aet. 28, admitted on 4th. day. A mild pneumonia involving mainly the L.2 lobe but later spreading to the R.3 lobe. She was rather distressed on admission by considerable pleurisy. Cyanosis and toxaemia were mild. A ketosis developed on 14th. (urine : ferric chloride test) and persisted till 28th. in spite of counteractive measures. Convalescence was uneventful.

Case No. 65. Male, aet. 20, admitted on 4th. day. A mild attack; admitted probably just when the crisis was due. The R. upper and R. lower lobes were involved but there was no story of delirium although cyanosis and dyspnoea were acute.

Case No. 66. Male, aet. 34. Treatment begun 2nd. day. He made a good recovery. Consolidation confined to L.2 lobe. Evening 20/12/30 fevered. Temperature began to fall 24/12/30. 25/12/30. 100°F. Rose again but settled on 29th. Never seriously ill.

Feb. 1934. He had a second attack again in L.2. Very bloody spit but not clinically so ill. The organism was "X" and did not belong to any type from 1 - 22.

GROUP "X".

Case No. 67. Male, aet. 26, admitted on 4th. day. A fairly severe attack involving the whole left lung. The curves came down by lysis 2 days after admission. There was persistent mild cyanosis; he failed to tolerate the mask.

Case No. 70. Female, aet. 27, admitted on 6th. day. Evidently a fairly acute attack nearing crisis when admitted. The R. upper lobe was solid and resolved slowly.

Case No. 71. Male, aet. 30, admitted on (?) 2nd. day. On admission the curves were those of an acute respiratory condition although the lungs were only characteristic of a generalised bronchitis. Tubercle B were later found in the sputum. Tubercle.

Case No. 72. Female, aet. 40, admitted on 4th. day. She had a consolidation of the L.2 lobe on admission but the illness was not severe. Convalescence was uneventful but the L.2 lobe failed to resolve completely. No serum given.

GROUP "X".

Case No. 73. Female, aet. 26, admitted on 10th. day. The symptoms were those of pneumonia but apart from some scattered râle there was no sign of lung involvement on admission.
No serum.
N.B. Diaphoretic given at the end of the illness changed the reaction in 2 days.

Case No. 74. Female, aet. 36, admitted on 6th. day. Died. On admission she was very cyanosed and dyspnoeic and there was pneumonia of the whole R. lung. Five doses were given at short intervals with no effect whatever. The cyanosis was relieved by oxygen at first but later was not affected (cardiac failure). For the last 24 hours she was very toxic. Alcohol.
N.B. Here was a case in an apparently healthy woman. No previous respiratory illness; infected with a specific organism in relatively pure culture yet although she makes a good fight the organism wins. We had no serum to help and adjuvant methods of treatment were unavailing.

Case No. 75. Male, aet. 25, admitted on 2nd. day. He was not acutely ill but there were signs of commencing pneumonia of the R. lower lobe. The most conspicuous thing was the widespread pleurisy. Probably not a pneumonia.

GROUP "X".

Case No. 77. Female, aet. 21, admitted on 2nd. day. A fairly acute illness involving R.3 and L.2. Cyanosis was severe but responded to oxygen. The illness slowly subsided during 5 days.

Case No. 82. Male, aet. 42, admitted on 2nd. day. This man was in Belvidere in Oct. 1930, 4 months before, with a Type II pneumonia. He made a slow recovery and was in indifferent health till this illness developed. He was not very ill on admission but the chest was full of râle, and cyanosis and dyspnoea increased later. The curves were high. There was no evidence of consolidation. 'Not a pneumonia' A.W.H.

Case No. 87. Male, aet. 16, admitted on 2nd. day. A typical acute pneumonia in a healthy boy. Serum 2 doses were given but discontinued after bacteriological diagnosis. He ran a typical course with well maintained fever accompanied by progressive lung spread and leucocytosis and terminating by crisis on the 8th. day.

Case No. 88. Female, aet. 25, admitted on 3rd. day. A typically severe illness. There was a pseudo-crisis on the 5th. day, the illness terminating on the 8th. day. A rising leucocytosis. Unaffected by serum.

GROUP "X".

Case No. 89. Male, aet. 55. Watched from commencement. A terminal R.3 pneumonia in a case of uraemia. No serum. Termination by profuse bronchitis, pulmonary oedema.

Case No. 94. Female, aet. 44, admitted on 3rd. day. She was sharply ill from a profuse bronchitis. An old chronic bronchitic with emphysema. A pneumococcus was isolated from the spit.

N.B. Although a severe illness, no marked general reaction:- leucocytes only 12,000.

Case No. 97. Male, aet. 38, admitted on (?) 5th. day. He had a well developed L.2 pneumonia on admission. The curves settled rapidly in the succeeding 24 hours. Resolution was unusually rapid.

GROUP "X".

Case No. 101. Male, aet. 34, admitted on 2nd. day. This was a 5th. attack in a healthy man. On admission there was consolidation of R.1 and all the symptoms of a sharp illness 2 days old. After a dose of serum everything subsided and convalescence supervened. Yet the organism was reported as Group "X" throughout. although from the clinical appearance one would have ventured a diagnosis of Type I infection responding to Type I serum.

There are 3 possibilities: —

(1) A spontaneous termination uninfluenced by serum.

(2) A non-specific effect.

(3) Bacteriological error.

In view of our previous experience the 3rd. is untenable. Non-specific effect is usually simply a temporary subsidence of the temperature curve. We do not think there is any effect on the ultimate course of the illness. This was a 5th. attack in a patient young and full of vigour. He probably had a large degree of acquired resistance, e.g. on admission the leucocytes were already 32,000 and remained high but gradually fell after serum.

GROUP "X".

Case No. 111. Male, aet. 17, admitted on 5th. day. A simple pneumonia running a normal course in a healthy boy. He had a crisis the day after admission.

Case No. 113. Male, aet. 43, admitted on 7th. day. Admitted severely ill with severe dyspnoea and cyanosis. He was very depressed and convinced he was about to die. The whole R. lung was involved but spit was moderate and there was a reasonable leucocytosis. He made a rapid and satisfactory recovery.

10/6/31. Differential count:-

Poly.	61·0%
Band.	28·3%
Lymph.	10·0%
Mono.	0·7%

Case No. 115. Male, aet. 11, admitted on 4th. day. A sharp illness with fairly massive consolidation but giving no cause for alarm. A crisis on the 6th. day was followed by rapid recovery.

Case No. 120. Female, aet. 68, admitted on 6th. day. Died. She was moribund on admission. Some serum was given with no effect. The oxygen tent kept the cyanosis at bay but had to be abandoned owing to the delirium of the patient, necessitating constant nursing interference.

GROUP "X".

Case No. 123. Male, aet. 46, admitted on 7th. day. He came in at the termination of his illness. He had no serum as the temperature fell overnight. Convalescence was uneventful.

Case No. 130. Female, aet. 27, admitted on 2nd. day. An acute illness in a healthy young woman. Only R.3 was involved and bronchitis was very scanty; there was no spit during the first 3 days. (Typed from swab.) She was given 4 doses of serum due to a doubtful bacteriological report (? Type II) but there was no response whatever and the illness ran for 8 days, never very serious. There was a very marked drop in the leucocytosis on the 2nd. day after admission, and they were low for the remainder of the illness, 30,000 - 9,000. Headache was very severe. 10 days after the first dose of serum she had a sharp serum reaction. 24 hours' fever with arthritic pain in arms and legs. X-ray:- 11/11/31. Consolidation R.3, especially upper ½.

Case No. 133. Female, aet. 59, admitted on 5th. day. A R.3 consolidation in an elderly woman with old-standing bronchitis. She had one dose of serum, after which the curves subsided. There was a good leucocytosis.

GROUP "X".

Case No. 134. Female, aet. 34, admitted on 3rd. day. A mild attack in a healthy woman. Serum was without effect, and on the 5th. day she had a spontaneous recovery by lysis.

Case No. 140. Male, aet. 17, admitted on 3rd. day. A typical case in a young lad. The response was immediate and convalescence uneventful.
26/1/32. 3 weeks after onset mouse not dead in 4 days.
20/2/32. Mouse not dead after 6 days.

Case No. 142. Female, aet. 25. This was a case of splenic anaemia; she developed a L.2 consolidation which ran a very protracted course. No serum was given.

Case No. 143. Male, aet. 32, admitted on 1st. day. After the 1st. dose of serum the curves which were all low continued to climb. After the 2nd. dose of serum 12 hours later he had a rigor after which a crisis. The curves rose again later in the 3rd. day (reactive rise) and subsided again by evening. It is difficult to believe that the serum did not directly affect the course of the illness here. ? Serum reaction.
20/2/32. 4 weeks after admission, mouse still alive after 6 days.

GROUP "X".

Case No. 147. Male, aet. 18, admitted on 4th. day. A lobar pneumonia in chronic bronchiectasis. The bronchiectasis had been quiescent but was relit by the acute infection. Convalescence was slow, 'unpleasant' but uneventful.

Case No. 148. Male, aet. 31, admitted on 2nd. day. The illness began with pains in the knees and soles of the feet like acute rheumatism and a right-sided pleural rib only appeared 2 days later. The physical signs at the R.3 base did not progress beyond flatness. The serum appeared to help here.
18/1/32. Streptococci and scanty pneumococci.
1/2/32. Convalescent swab 4 weeks later - streptococci only.

Case No. 149. Female, aet. 25, admitted on 8th. day. The story was of pneumonia but on admission there was nothing more than a profuse right-sided bronchitis. She made an uninterrupted recovery.

Case No. 150. Male, aet. 25, admitted on 2nd. day. A fairly acute pneumonia unaffected by serum and running a normal course. Convalescence uneventful.

GROUP "X".

Case No. 154. Male, aet. 11, admitted on 3rd. day. On admission he presented meningitic symptoms (C.S.F. normal) which subsided before the lung condition became evident. No serum was given and he ran a typical 8-day illness ending with crisis. 40 days after first admission, he returned from the convalescent home with tonsillitis and adenitis.

Case No. 159. Female, aet. 32, admitted on 2nd. day. An acute pneumonia (influenzal, A.W.H.) in a healthy woman. The onset was rather indefinite. The spit was not agglutinated by Type I and Type II serum. A very bloody spit, indefinite consolidation changing overnight to a rusty spit with definite consolidation. The leucocytes were very low, although the curves were very high.

Case No. 167. Male, aet. 37, admitted on 3rd. day. A right upper lobe pneumonia of considerable severity which ran a normal course. The curves were normal on the 6th. day but there was some tingeing for 2 more days.

Case No. 168. Male, aet. 50, admitted on 4th. day. A sharp right lower lobe attack in a healthy man. The course was uneventful.

GROUP "X".

Case No. 172A. Female, aet. 25, admitted on 3rd. day. A moderately severe illness at no time causing anxiety.

Case No. 178. Male, aet. 37, admitted on 5th. day. A very severe toxic case, delirium ++. Alcoholic. The whole right lung was involved and the illness ran an acute course for 12 days, and then settled by lysis. The leucocytes at the beginning were low but gradually improved. One dose given through indecision.

Case No. 180. Male, aet. 21, admitted on 3rd. day. An acute illness in a healthy lad. Running a 7-day course to crisis. Convalescence was rapid and uneventful.

Case No. 186. Male, aet. 19, admitted on 2nd. day. A simple acute illness in a healthy boy. Oxygen chamber. He was admitted owing to the distress of dyspnoea although cyanosis was not bad. He felt much more comfortable.

Case No. 188. Male, aet. 25, admitted on 6th. day. An unsteady but not unusual attack. About the 10th. day signs of fluid appeared and tapping produced serous fluid. Pleural fluid: scanty cells, lymphocytes, no organisms. Nil on culture, no T.B. Guinea-pig — negative.

GROUP "X".

Case No. 189. Male, aet. 45, admitted 5th. day. A fairly severe illness. Consolidation was incomplete and illness terminated by lysis. Convalescence was slow and when dismissed resolution was incomplete.

Case No. 191. Male, aet. 47, admitted on 6th. day. An acute illness received at its termination. Convalescence was a little unsteady but the illness was never serious.

Case No. 196. Female, aet. 25, admitted on 4th. day. An acute attack in a healthy woman. Early onset of pleuritic effusion. Pleurisy with effusion.

GROUP "X".

Case No. 204A. Female, aet. 56. This private case was first seen on the 3rd. day; the spit was already very rusty and the whole right lung was involved. Toxaemia ++. Cyanosis ++. The heart failed on the 8th. day. Spit was copious throughout, more broncho-pneumonic than lobar.

N.B. Do the I, II and III pure type pneumonias have a higher number of consolidations than IV which are more broncho-pneumonic?

Case No. 207. Male, aet. 42, admitted on 4th. day. A mild attack in a middle-aged man of poor physique. Convalescence was slow but apparently complete.

Case No. 208. Male, aet. 23, admitted on 2nd. day. A very severe toxic illness in a man of average physique, while R. lung solid. Resolution was extremely slow due to pleurisy and pneumothorax. Extreme leucocytosis. Pneumothorax.

Case No. 209. Female, aet. 25, admitted on 4th. day. A fairly acute illness in a girl who had suffered from chronic bronchitis. R.1, 2, 3 were dull to percussion but fever was never high and the spit never rusty. Mainly acute bronchitis.

GROUP "X".

Case No. 210. Female, aet. 19. 3 - 6 days. An acute illness resembling pneumonia but having irregular curves and a mucopurulent spit. The left lower lobe was dull to percussion. Mainly acute bronchitis.

Case No. 211. Female, aet. 35. Watched from onset. This illness occurred in a patient being treated for mitral stenosis. Consolidation was complete and she had a typical 8-day illness terminating by crisis.

Case No. 217. Female, aet. 25, admitted on 2nd. day. A slow onset in a thick-chested young woman. Began as a pleurisy with rusty spit the following day.

Case No. 218. Male, aet. 54, admitted on 5th. day. On admission he had abdominal and lumbar pain and acute haematuria. Consolidation was commencing and spread to involve ¾ of R. lung. He was never acutely ill. Haematuria.

GROUP "X".

Case No. 220. Male, aet. 36, admitted on 4th. day. A very acutely ill, cyanosed case 'influenza-like' (A.W.H.). Treated in the oxygen chamber which seemed useful. Organisms were numerous. Oxygen chamber. We were satisfied that the oxygen was sufficient to prevent cyanosis and the patient agreed that he was much more comfortable.
It is difficult to maintain the oxygen chamber owing to the frequent need to enter the chamber for nursing attention.

Case No. 224. Male, aet. 46, admitted on 2nd. day. A fairly sharp attack in a healthy man. It ran a normal 8-day course, terminating by lysis.
X-ray:- 8/6/34. L. lower L. consolid.

Case No. 231. Male, aet. 38, admitted on 1st. day. A sudden attack in a chronic bronchitic. Pneumonic consolidation was incomplete and he made a very rapid recovery.