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OBSERVATIONS ON THE LEUCOCYTOSIS OF PNEUMONIA.

The discovery of the white corpuscle in the blood of man is credited to Nasse in the year 1835. Since that date these wandering cells of the blood and the closely related cells of the lymph and the fluid of the body cavities have occupied the attention of many able observers, in the endeavour to throw more light on their morphological characters, functions and life history.

Of late years much has been done in connection with, and growing importance attached to, the condition termed leucocytosis in which there is observed an increase in these cells in the blood. In order then to form some definite conception as to what ought to be regarded as an increase and what not, it is necessary to consider what is the average number of white corpuscles or leucocytes, as they are termed, occurring in the blood as a state of health.

Different observers give somewhat varying estimates regarding this point. According to Hayem, they number 6000 per C m m. Von Limbeck gives the average number as being 8-9000, but a difference of 1000 above or below these figures, he says, is not to be regarded as having any special significance. Osler computes the normal number in adults as being about 5-7000. Rieder gives the average in the case of 20 adults as 7680, and in that of 12 children aged from 9 to 15 years as being 9660 per C m.m.

From these observations and those of others it is evident no rigidly fixed standard can be assigned as the normal, the numbers in health varying considerably in the case of different individuals. Limbech's observations go to show that the average count of leucocytes in the blood of a well nourished individual is as a rule higher than that in a poorly nourished person, although the latter be "sound". Thus, for instance, 10,000 leucocytes may be counted per C m.m. in the case of a robust adult and the number not deemed excessive, while if a like number be counted in an ill-nourished individual, a pathological

increase may be considered to have taken place. As a rule, however, these varieties are not sufficiently great to cause much difficulty in determining whether an increase exists or does not exist in a particular case.

But further, as in leucocytes there is not only to be observed an increase in the total number of haemal leucocytes, but also a disturbance in the relative proportions of the different varieties to each other, it is next necessary to mention briefly the various forms of these cells found in the circulating blood, along with the various classifications proposed by different observers.

It was Wharton Jones who, in the year 1846, first discovered that the white cells of the blood and lymph were not all of one kind. He divided them into "granular" and "nucleated" cells. His observations, together with those of Rindfleisch in 1863, were confirmed a year or two later by Max Schultze, who further differentiated the white cells of the blood into the following four groups:—

(1). Small round cells with round nucleus and little clear protoplasm.

(2). Larger cells with round nucleus and more clear protoplasm.

(3). Cells with finely granular protoplasm and one, two, or more nuclei.

(4). Cells with coarse granules in the protoplasm .

Ehrlich in 1878 and following years more particularly examined by means of aniline dyes the granules of the corpuscles and classified them according to their elective affinity for basic, acid, or neutral dyes. He made out the existence of five forms of granulation associated with as many varieties of wandering cells. His table of cells according to these granules is:-

α- granulation, - Eosinophilic - present only in small numbers in human blood; grnaules c coarse, stain readily with acid dyes.

β- granulation - Amphophilic - cells frequent in rabbits and guinea-pigs in blood; in man in medulla of bones; stain both with acid and basic dyes; granules fine.

γ- granulation - Large cells found in connective "Mastzellen", in blood of man only in certain cases of Leukaemia; stain only with basic dyes; granulations coarse.

δ- granulation - Fine basophilic, mostly "mononuclear"; stain with basic dyes.

ε- granulation - Neutrophilic - the most frequent leucocyte of human blood; polynuclear; stain only with neutral dyes.

Metchnikoff, basing his classification on the action of the different cells towards microbic and other foreign particles introduced into the organism, distinguishes the following forms:-

1. Lymphocytes - immature leucocytes.
2. Large hyaline cells, mononuclear, phagocytic, "Macrophages".
3. Smaller neutrophile cells, polynuclear, "microphages".
4. Eosinophilic cells - not phagocytic.

Kanthack and Hardy in 1893 showed that neutrophilic and amphophilic cells did not exist as such, the so-called neutrophilic and amphophilic granules in reality being faintly oxyphilic, or, in other words, having a feeble affinity for acid stains.

Other classifications have been proposed by Lowit, Hayem, Bizzozero and Heyl; but those given above are generally regarded as types, and have been recently admirably collated in tabular form by Adami (see next page). To the table I have added the aver-

Collation of the different Classifications of the Varieties of Leucocytes (Adami)

	Ranthack and Sandy.	Ehrlich	Metchnikoff	Max Schultze	Wlassitsch & Sacs.
20-30%	Lymphocyte.	Lymphocyte	Lymphocyte	Small round cell I	Non-granular nucleated cells.
2-6%	Hyaline Cell		Macrophagocyte	Large round cell II	
1-6%	Coarsely gran. eosinophile cell	Eosinophile cell.	Eosinophile cell	Cells with coarsely gran. protoplasm	Granule cells — Coarsely gran.
60-75%	Finely gran. neutrophile cell.	Neutrophile / Amphophile	Microphagocyte	Cells with finely gran protoplt.	Granule cells finely granular.
0	Coarsely gran. basophile cell.	Basophile cell with "γ"- granulation			
?	Finely gran basophile cell	Basophile cell with "δ" - granulation		Cells with finely gran-prot.	? Granule Cells. finely granular.

age relative percentages of the different forms of cells occurring in the blood of the healthy adult.

I shall discuss more in detail the various cells and their classification later. We are now placed in a better position to shortly consider the different forms of leucocytosis described, and deal with the various definitions of the term advanced by the several authors who have specially studied the conditions.

Since both in leukaemia and leucocytosis there is observed an increase of white cells in the blood, it is not surprising that there should have existed some confusion b etween them. Virchow embraces leucocytosis under leukaemia when he defines the latter term as representing that condition in which the white corpuscles are increased, which increase appears to be due to irritation of the blood-forming glands, especially the lymph glands. Eichorst, V. Jaksch, Jurgensen, Seifert and Müller, Strumpell, O.Vierordt, and Gowers & Taylor draw a distinction between leukaemia and leucocytosis, the distinction consisting in this, that in leucocytosis

the increase of the white blood cells is transitory (symptomatic) and of not so high a degree as in the case of leukaemia. Pee, in his work on leucocytosis (1890) expresses himself in similar terms as regards this point. Hamilton says:- "A mere increase of a temporary nature in the number of colourless corpuscles, unaccompanied by any splenic tumour, general enlargement of the glands, or ~~decrease~~ disease of the ~~line~~ bone marrow is known as leucocytosis."

Cases, however, have been reported of leucocytosis which, on account of the large number of leucocytes counted, were regarded as cases of leukaemia, and which subsequently proved not to be such. To make the distinction between the two conditions a mere numerical one is, according to Muir, wholly inaccurate and unscientific; Ehrlich and Einhorn support this contention. The difference is not merely a quantitative, but a qualitative one. In leukaemia there are observed cellular elements not present in healthy blood, while in leucocytosis the increase is due to augmentation in number of the white cells normally found in the blood, and usually,

although not universally, to a specially large increase of the polynucleated (finely granular oxyphilic) forms relatively to the other leucocytes in the blood. This important point is recognised by Eberth in his definition of leucocytosis:-

By leucocytosis is understood a disproportional increase of the polynuclear leucocytes or such (white) elements as normally are present in healthy blood." The definition which Von Limbeck gives in the recent edition of his work on the blood is substantially the same. As Rieder's work on leucocytosis is generally recognised as the standard, a certain amount of weight must be attached to his definition which is as follows:-

"Leucocytosis is a transient condition, probably dependent on temporary changes in the blood-forming organs, sometimes of shorter, sometimes of longer duration, accompanied, as a rule, by not a very high increase in the number of white blood cells and occurs in various physiological and pathological conditions. The white blood cells are (in contra-distinction to the condition in leukaemia) generally similar

in size and character to those normally found in the circulating blood. One finds, (in the case of man) an almost invariable and usually excessive increase of these cells which are characterised by possessing polymorphous nuclei and finally granular, very mobile protoplasm, namely the neutrophilic cells of Ehrlich or the finely granular cells of Max Schultze - at all events in those forms of leucocytosis which are associated with pathological conditions."

Various forms of leucocytosis have been described. They have been classified by Rieder and v. Limbeck after this manner:-

I. Physiological Leucocytosis.

(a) Digestive Leucocytosis.
(b) Leucocytosis of Pregnancy.
(c) Leucocytosis of the New-born.

II. Pathological Leucocytosis.

(a) Post-haemorrhagic leucocytosis.
(b) Leucocytosis associated with malignant tumours.
(c) Agonal, or premortal leucocytosis.
(d) Inflammatory Leucocytosis.

III. Leucocytosis due to medicinal agents or otherwise experimentally produced.

Of the physiological forms the digestive

sub-variety need only be referred to here, as it might possibly influence clinical observations undertaken in cases of inflammatory leucocytosis. From one to six hours after the principal meal the number of leucocytes circulating in the blood is said to be increased, diminishing soon after to normal. The increase, however, is not so great as some authors, notably v. Jaksch, would have one to suppose, and as a rule is only evident when an individual, who has previously fasted for some considerable time, partakes of a full meal. The increase is said to be due to an excess in the number of lymphocytes or small mononucleated cells and to a less extent of the basophilic cells of the blood (Kanthack and Hardy). On the other hand Rieder finds no increase in the percentage of mononucleated cells in digestive leucocytosis, but finds a marked diminution of the eosinophilic cells under the same conditions. Sherrington is also of the opinion that fasting increases the number of eosinophilic cells in the blood. Further investigations are required to throw light upon these points.

Of the pathological forms the agonal or pre-mortal leucocytosis first described by Litten probably does not occur as such, but, as Limbeck points out, - and my observations are in accordance with this view -, it is to be explained as due to some inflammatory or other condition, such as is ordinarily associated with an increase of leucocytes, complicating the illness towards its close. Of the form of leucocytosis accompanying malignant tumours and of that occurring after a large haemorrhage, the latter is more constantly observed; but as neither tends, except in very rare cases, to interfere with observations directed towards inflammatory leucocytosis, these varieties need not further be considered here.

The experimental form will be referred to later, when various points regarding leucocytosis of pneumonia are discussed.

As regards inflammatory leucocytosis, if Virchow's view were correct, one would expect to find the occurrence of a leucocytosis in all diseases attended with irritation of the lymph glands, pro-

vided that irritation was not so great as to cause destruction of the gland substance. Therefore in these diseases specially associated with enlargement of the lymph glands, such as typhoid, erysipelas, pneumonia, an abnormal increase of the white corpuscles would occur.

Halla refers inflammatory leucocytosis to disease of the whole lymph system, especially of the spleen, lymph glands, and bone marrow.

Escherich is his sketch on cachectic leucocytosis supports Virchow's view and cites the experimental work of Lassar who found that, through irritation from without, inflamed and swollen lymph glands produced lymph in greater quantity, more concentrated and richer in cell elements.

Next comes the sweeping assertion of Böckmann who avers that in acute fevers the count of the red corpuscles varies inversely, and the count of the white corpuscles varies directly, with the height of the temperature.

When, however, these theories were put to the test by clinical observations it was found that

none of them held good!

Acute phthisis, a disease associated with high temperature, showed as a rule a normal number of colourless corpuscles. Typhoid fever, a disease associated preeminently with glandular enlargement was found to run its course without leucocytosis. Further, in those inflammatory conditions associated with increase of white blood cells, a high degree of fever did not necessarily imply a high degree of leucocytosis.

Rieder's explanation of such seeming discrepancies is that the increase of the white blood-corpuscles is much less dependent on the temperature than on the localisation of the process and the entry of certain chemical substances into the blood.

Lastly, comes von Limbeck's assertion that acute diseases attended with fever and exudation (with the exception of those of a tubercular nature) are regularly accompanied by a leucocytosis, while in those infectious diseases associated with no exudation (typhoid, intermittent fever, sepsis) leucocytosis is as regularly absent. He maintains, further,

that, although the degree of leucocytosis is largely dependent on the amount of exudation and its richness in cell elements, ~~the~~ of chief influence in this connection are the amount and virulence of the infecting agent and the resistant power of the individual infected.

With these points before us, it were well, before passing on to the consideration of the special blood phenomena observed in croupous pneumonia, briefly to summarise the results of clinical investigations directed towards the computation of the white corpuscles in various acute diseases.

Most observers are agreed that acute non-tubercular inflammation of the serous membranes (pleura, peritoneum, meninges) such as are accompanied by exudation, are generally associated with leucocytosis, which reaches a high degree in those cases in which the exudation is purulent. In tubercular inflammations of those membranes, on the other hand, it is said that leucocytosis is generally absent. A high degree of leucocytosis is found too in all other acute suppurations, where the exudate is at all extensive,

also in erysipelas, in scarlatina, and in osteomyelitis. In diphtheria the leucocyte count, though still high, is rather less than in the last named diseases. A moderate increase is observed in most cases of acute articular rheumatism during the febrile period. Authorities are practically unanimous that typhoid fever is attended with no leucocytosis; and if such appear it is due to some complication occurring in the course of the disease. In pulmonary phthisis, acute or chronic, a normal number of white cells is usually observed. Quite recently Stein and Erbmann have stated as the result of a series of observations that leucocytosis occurring in pulmonary tuberculosis is not due to tubercle bacillus but to the a secondary infection leading to breaking down of the substance of the lung - a septic process due to the activity of various virulent bacteria and cocci. A normal number of leucocytes is also, as a rule, counted in typhus fever, measles, variola, catarrhal bronchitis, and acute nephritis. In malaria, quite apart from the administration of drugs, most observers are agreed that an appreciable diminution of leucocytes

takes place in the blood of the general circulation.

Of all the inflammatory affections attended with leucocytosis the one that has attracted most observers is croupous pneumonia, and those who have studied this disease from the standpoint of the blood are unanimous in their opinion that it is attended in the great majority of cases with marked increase in the number of colourless corpuscles.

Piorry, early in the century, has remarked on the so-called "Buffy-coat", "Crusta Phlogistica" of the blood of the pneumonic patient, a phenomenon usually observed towards the seventh or eighth day of the disease, and refers its occurrence to ~~the~~ & special feature of the disease, viz. "Haemitis".

Virchow noted in pneumonia a greater or smaller increase of the so-called white blood. He accounts for the occurrence of the continued leucocytosis to a swelling of the bronchial lymph glands, and says that in cases where the lymph glands do not swell there will be observed no leucocytosis.

From Virchow's time up to a comparatively recent date, the literature on the subject is relativ-

ely scanty.

Of more recent observers first in order comes the names of Halla, Hayem and Gilbert, and later among others, those of Tumas, v.Jaksch, v.Limbeck, Pick, Rieder, Maragliano, Tschistovitch, Kikodse, Laehr, Sadler and Osler.

In 14 cases of pneumonia reported by Halla leucocytosis only twice was absent and both were very severe cases which terminated fatally. Of the other 12 cases only 3 died. The intensity of the fever does not usually affect the leucocytosis. Reinert agrees with the views of Halla.

Hayem and Gilbert report that in two cases of typhoid pneumonia (la pneumonie typhoide) there was observed no close fibrinous reticulum or increase in the number of white blood corpuscles such as is characteristic of ordinary cases of acute pneumonia.

According to v.Limbeck and Pick the leucocytosis comes on early in pneumonia, persists during the whole course of the febrile period and disappears at the crisis. The parallel between the leucocytes and the temperature is, however, not always so con-

stant, for in some cases the leucocytosis outlasts the fever by a few days; in the case of a lysis there may be observed a gradual decrease in the number of leucocytes.

If a so-called pseudo-crisis occur in the course of the affection it is accompanied by no diminution in the number of white cells. He has observed in cases terminating fatally an increase of the leucocyte count towards the end. There are also to be observed cases of croupous pneumonia, in which, during the whole course of the disease leucocytosis is absent; these are said to furnish a worse prognosis. Limbeck, however, comes to the conclusion after studying the experimental work of Tschistovitch and reviewing the clinical literature on the subject that the appearance or non-appearance of leucocytosis in pneumonia affords no sure prognostic sign regarding the course of the disease. A direct dependence of the degree of leucocytosis on the extent of the infiltration in the lungs does not exist; on the contrary it depends clearly on the degree of virulence of the infecting material and the constitution of the infec-

ted organism.

According to Tumas the increase of the white blood corpuscles outlasts the crisis by about one to three days.

Pee gives expression to his astonishment at the high degree of leucocytosis occasionally found in pneumonia.

Von Jaksch finds a relatively greater leucocytosis in the case of children suffering from acute pneumonia than in adults affected by the same disease. He has lately observed that the prognosis in cases of acute pneumonia running its course without an increase in the number of white blood-cells is very unfavourable. He believes that where there is an absence of leucocytosis in cases of severe croupous pneumonia, means for the increase of the leucocytes by the administration of drugs (antipyrin, antifebrin, pilocarpin, nuclein) should be adopted. In one of his cases a day after the administration of pilocarpin an increase of leucocytes was apparent.

On the other hand Pichler has still more recently reported the result of the effect of pilo-

carpin, nuclein, and antipyrin on the count of the leucocytes in pneumonia and typhoid fever. Twenty-four cases of pneumonia were observed. Neither the administration of pilocarpin nor nuclein was invariably attended by an increase in the number of leucocytes; nuclein, however, usually caused an increase. When a rise occurred, the number only exceptionally reached a high figure. In the case where Antipyrin was tried, observations showed a sinking in the number of white cells. Pichler's conclusion is that, as a spontaneous high degree of leucocytosis, so also the artificial increase of leucocytes, in no way warrants a favourable prognosis. Similar results were arrived at as regards typhoid.

Sadler has recently observed 21 cases of pneumonia in the clinique of w.Jaksch. In 16 of these cases there was a leucocytosis and three died. In 5 cases there was no leucocytosis. Three of these died and the sectio showed in two of these cases infiltration of both lungs, and in the third case nearly the whole of the left lung. In the cases which recovered the fall in the leucocytosis corresponded to the

fall in the temperature. The count of the red blood corpuscles in most of the cases was normal; the haemoglobin, in all cases where the red blood corpuscles were normal in amount, was perceptibly diminished.

Kikodse states the relative and absolute increase of the white blood corpuscles to be about twice up to three times the normal. Only in severel cases in which death resulted could he find no increase of the same. According to this observer the leucocytosis appears before the change in the lung (? is apparent) and remains up till the crisis. The rise in the number of leucocytes is accounted for by the great increase in the mature (polynuclear) leucytes, which, according to Kikodse's view, become mature in the lung alveoli. Simultaneously with the temperature crisis there comes a blood crisis in which a fall of the leucocytes takes place to or below the normal level.

Maragliano finds no relationship between the intensity of the leucocytosis and the severity of the infectious disease. He does not agree with the shortly expressed opinion that leucocytosis betters the

prognosis in pneumonia. He has seen pneumonic patients with a high degree of leucocytosis (of over 40,000 leucocytes) die, while others, without leucocytosis have recovered. He further regards it as useless to artificially promote leucocytosis in those cases where none exists. His views are thus in accordance with the before mentioned later observations of Pichler.

Laehr finds an unmistakeable connection between the temperature and the leucocytosis, in this, namely, that the acme of fever shows the highest leucocytosis; at the fall of the temperature there occurs a quick fall of the leucocytes. He cannot agree, along with Halla, Reinert and v.Limbeck, with the assumption of Böckmann's that the degree of leucocytosis is dependent on the height of the fever. In numerous cases where pseudo-crises occurred the leucocytosis still continued. Of his 16 cases all showed leucocytosis and two died. As regards the variation in the relative proportions of the different varieties of white cells, the polynuclear forms are increased, the eosinophilic cells relatively diminished.

The number of the red corpuscles and the percentage of haemoglobin sink during the course of the disease to rise again to normal after the crisis.

Rieder reports the results of observation on 26 individuals of different ages and sexes. He finds no parallel exists between the extent of the infiltration and the degree of leucocytosis in the different cases observed by him. Further, in the self-same case with increase of infiltration of the lung, an increase of the leucocytes in the blood cannot alwyas be detected. He corroborates the statements of other observers that the leucocytosis appears early. In three cases Rieder was able to make blood-examinations within 6, 14, and 16 hours respectively from the occurrence of the rigor and found at that period in all those cases a very high degree of leucocytosis. The fall in the temperature curve took place in almost all the cases recorded by him prior to the fall in the leucocyte curve. He also gives a few cases of croupous pneumonia in which the total leucocyte count is compared with the relative proportion of the different forms of leucocytes present.

The eosinophilic cells could only in one case of pneumonia be observed. Rieder adds that it ought not to be said on this account that they are generally deficient in this disease, but that only on account of the increase of the other forms in there observed a relative diminution of these. The percentage ratio of the mononuclear sank, varying from 4.4 (17600 leucocytes in 1 C m.m. to 17.3% (29,200 in 1 C.m.m.) One sees, in this connection, he goes on to say, that no parallel can be drawn between the leucocyte count and the percentage increase of the polynuclear cells in the blood; when also a rare case is met with where no noteworthy increase is observable in the leucocyte count, there is yet observed in the blood the characteristic condition found in leucocytosis, - decrease of the eosinophilic and increase of the polynuclear cells.

What Osler says in the recent edition of his book as regards the question of the blood changes in pneumonia may perhaps be taken as a fair resume of the opinions of the majority of observers on the subject:-

"Anaemia is rarely seen. There is in most cases a leucocytosis, which appears early, persists, and disappears with the crisis. The leucocytes may number from 12 to 40 or 50,000, even more per C.m.m. The fall in the leucocytes is often slower than the drop in the fever, particularly when resolution is delayed. Of considerable prognostic importance is that in malignant pneumonia, the leucocytosis is absent; and in any case the continuous absence may be regarded as an unfavourable sign. A striking feature in the blood-slide is the richness and density of the fibrin network. This corresponds to the great increase in the fibrin elements, which has long been known to occur in pneumonia, the proportion rising from 4 to 10 parts per thousand. Hayem describes the blood plates as greatly increased."

Although abundant observations have thus been made on the variation of the total number of leucocytes occurring in the blood of the pneumonic patient from day to day the changes which take place during the same period in the relative numbers of the different varieties of those cells have been, so far

as I know, but little investigated. It is true that it has been affirmed and generally admitted that the polynuclear cells are increased, the eosinophilic cells diminished during the course of the affection, but little is known regarding the period and mode of that increase, the time and the degree of that decrease, and the subsequent return to the normal. My observations were directed to the daily comparison of the total with the relative numbers of the different varieties of the leucocytes during the course of the attack, and the further comparison of the figures obtained with the main clinical facts in each case. The expectation was entertained that thereby more light might possibly be thrown on certain points connected with inflammatory leucocytosis not yet clear, and possibly some information gained in regard to the life history of the leucocytes themselves and the mutual relationships of the different forms of the cells.

Towards this end the following methods were adopted. The total number of leucocytes per C.m.m. was first ascertained by means of the Thma-

Zeiss leucocyte pipette and counter. According to the degree of leucocytosis the blood was diluted 10 to 20 times (As a rule where it was expected that the count would exceed 15,000 it was found more convenient to use the latter dilution.) The diluting fluid was the ordinary solution of methyl green with .3% acetic acid. The number of leucocytes on 400 squares of the counter (1/10 C.m.m. of the diluted fluid) was ascertained, and that number multiplied by one or two hundred according to the dilution; this gives sufficiently accurately the number of white blood corpuscles per C.m.m.

Cover-slip film preparations of the blood were also taken at the same time. As a rule these were allowed to dry in the air and afterwards fixed by heat, corrosive sublimate, or other fixing re-agent. In certain cases where it was specially desirable to have the cells as little altered as possible, the films were immediately placed in the fixing solution. Lately, the new method recommended by Gulland was employed. The films were stained in a variety of ways. In the majority of the preparations, however,

either haematoxylin and rubin and orange, or methylene blue - eosin stains were employed. The forms of cells differentiated by me were four in number and I have referred to them by the old name of (1) polynuclear, (2) large mononuclear, (3) small mononuclear, and (4) eosinophilic. (In the cases and charts these are respectively denoted as P., L., S., E.). Although in my earlier observations many more were enumerated, I afterwards found it necessary only to count on an average 300 cells in order to calculate sufficiently closely the percentage ratio of the different forms. Where, however, the percentage ratio of cells occurring in very small numbers, e.g., eosinophiles, was required to be accurately estimated, a very much larger number of corpuscles was counted.

There follows collected in tabular form the records of 22 cases of pneumonia with the results of my observations on the leucocytes in each case. The total number of white cells is reported, and in succeeding columns the relative percentages of the polynuclear, large and small mononuclear, and eosinophilic cells to the total number of leucocytes occurring in the blood of the general circulation is shown.

28 A

Case. 1. M. Thomas, aet 20.

Croupous Pneumonia (Lower Lobe L. Lung); Recovery.

Date 1897	Day of Dis.	Temp. F	Total Leucocytes	P	L	S	E	Remarks.
Jan 4	1	e. 104·8						Jan 4. 1897. Rigor on the morning of this day. On Admission to R.E.I Pulse 120 Resp 33. Slight dulness l. side below sp. of scapula.
" 5	2	m. 104·8	20700	91	6	3	0	
		e. 102						
" 6	3	m 104·8	22200	89	7	4	0	
		e. 103·6						Jan 5. Rusty Sputum. Fraenkel and Friedländer's organisms in sputum.
" 7	4	m 102	14100	90	5·5	4·5	0	
		e. 104·6						Jan 7 - Pulse 90 v. discretus. Resp 40.
" 8	5	m 103·2	6600	84	9·5	5·5	0	Marked dulness rere l. lower lobe; br. amphoric; crepitations.
		e. 102						
" 9	6	m 103	9600	81	13	6	0	Jan 8 - Patient very weak and delirious.
		e. 100·2						Jan 9 - Patient quieter pulse better 98, discretus.
" 10	7	m 100·6	20900	90	6	4	0	Jan 10 - Pat. much stronger; pulse better.
		e 102·4						
" 11	8	m 99						Jan 11 Crisis. Resolution commenced. After Jan 12. temp remained normal with exception of transient rise even of Jan 15 to 102°.
		e. 98·8	12500	79	9·5	10·5	1	
" 12	9	m 98·4						
		e. 99	9600	78	9	13	0	
" 14	11	\	12000	79	7·5	13	·5	Feb 6 - Patient dismissed; resolution complete.
" 18	15	Normal	15600	78	7	15	0	
" 23	20		8500	65	8	22	3	

Case 2. F. Matilda, aet 31.

Croupous Pneumonia of L. Lung: Recovery.

Date 1897	Day of Dis.	Temp	Total Leucocytes	P	L	S	E	Remarks:
Feb. 5	(?) 8	e. 101·2	20000	91	4·5	4·5	0	Jan 29. Felt ill; rigors; pain in side.
" 6	9	m 102·6	25000	91	4	5	0	Feb 5. Adm. R.E.I. Marked dulness l. side, abs. in axilla below 5th rib.; br. tubular -
		e 101·2						
" 7	10	m 100·8	18000	88	6	6	0	Herpes. Slight jaundice; rusty sputum.
		e. 100·2						Feb 9 - High pitched resp. in axilla; br. tubular at apex. at base fine crepitations.
" 8	11	m. 100·2	17200	78	11	11	0	
		e. 98·4	22000					Slight Albumen in urine
" 9	12	Normal or Sub-normal.	13800	82	7·5	10·5	·5	Feb 24 - Slight dulness in l. axilla and behind at
" 11	14		7800	85	4	11	0	l. base. Vr. Fren in crd. Few crepitations.
" 15	18		-	74	9	17	0	Mar. Sent out well; phys. signs of consolid. dis appeared.
Mar 3.	19		4500	77	5	16	2	

Case 3. A. Mrs., aet. 25.

Croupous Pneumonia of Rt. Lung: Recovery.

Date 1897	Day of Dis	Temp	Total Leucocytes	P	L	S	E	Remarks.
March 17	5	e. 103·8	~~20600~~					March 13. Pain in rt. side; shivered.
" 18	6	m 99·2	20600	85	9	6	1 in 300	Mar. 17. Dulness; crepit. rt. axilla.
		e. 102·4						Mar. 19. Hyper. infra-clav. reg. rt. side.
" 19	7	m. 98	7800	79	10	9	2%	Dulness bel. sp. of scap. behind Br. bronchial.
" 20	8	normal after.	5600	72	15	10	2·5%	Vr. Res. incrd.
" 22	10		6400	67	14	14	4·5%	Mar. 20 - Dulness apex to base behind; crepit. in rt. axilla. &c.
								Mar 31 - Discharged Rt. side clear.

Case 4 F. James, aet. 13.

Croupous Pneumonia. Lower Lobe Rt. Lung : Recovery

Date 1897	Day of Disease	Temp. F	Leucocytes per cmm	P	L	S	E	Remarks.
								Had pneumonia a year previously.
Feb 6	2	e 104·4						Feb 5 - Felt unable to work; hot and cold by turns.
" 7	3.	m 105. e. 103·6						
" 8	4	m. 103·8	14,800	84	8	8	0	Feb 6. Began to cough.
		e. 102						Adm. R. C. D.
" 9	5	m 101·6	6300	77	11	12	0	Pulse 110. Resp 40.
		e. 102·6						Dulness; fine crepitations rt. base behind
" 10	6	m 101·6	7000	73	14	13	0	Friction in front 4th space.
		e. 103·6						Auscultation -
" 11	7	m 100·7						High pitched bronchial breathing behind; below
		e. 101	8500	80	11	12	0	sp. of scapula;
" 12	8	m 100·8						Vocal. Res +. Fraenkel's diplo. in sputum.
		e. 100	12000	80	9	11	0	Urine - chlorides scanty - No albumin.
" 13	9	99·6						Feb. 13. Phys. Signs of resol.
" 14	10	98	10000	67	8	24	1	Feb 20 - Resol. process complete.
" 18	14	98	6000	58	6	35	1	

Case 5 A. Helen aet. 10.

Croupous Pneumonia - mid. & low. lobes Rt. Lung : Recovery

Date 1897	Day of Dis.	Temp. F	Leucocytes per cmm	P	L	S	E	Remarks.
								Rigor. Feb 28.
Feb 26	4	e. 103·6						Adm. Feb 26 - Feb 27 - Mar 3.
" 27	5	m. 104	29200	90	5	5	0	Very ill; delirious. Crisis occurred
" 28	6	m 104						Mar 3 - good recovery.

Case. 6 F. James.

Croupous Pneumonia: Recovery.

Date 1897	Day D. Dis	Temp. F.	Leucocytes	P	L	S	E	Notes.
Feb 26	3	e/101·8	~~20800~~	~~82~~	~~12~~	~~6~~	~~0~~	
"								Feb 24. Shivered vomited; pain in side.
27	4	102·2	20800	82	12	6	0	
"		104						
28	5	98	19400	82	5·5	12	·5	Feb 26. Sl. Dulness resp. b. rt. upp. lobe. resp'd.
		103·8						
Mar 1	6	97	13800	63	12	25	0	
"		97						Feb 28. Temp. fell. pulse, resp. rate fell - appearance crisis - no pain in side.
" 2	7		9000	60	9	30	1	
" 3	8		6800	64	10	21	5	Feb 28 - night - pulse resp. temp - gone up.
"		Subnormal afebrile.						
" 4	9							Diagnosis: Croupous Pneumonia -
" 5	10		5400	65	7	24	4	upper Lobe. Rt Lung.

Case 7 E., Peter aet 9.

Croupous Pneumonia. (lower lobe rt lung.): Recovery.

Date 1897	Day of Dis	Temp. F°	Leucocytes per cmm	P	L	S	E	Notes.
Mar 6	2	m 102·4						
" 7	3	m 103 e 104						Mar 5. Rigor, vomiting, pain in head
" 8	4	m 103 e 102						Same night — pain in rt side [illegible].
" 9	5	m 101·8 e 102·2	17600	90	4	6	0	Adm R.I.H. even March 6th Resp 48 Pulse 126.
" 10	6	m 101·8 e 100·2	18000	89	4	7	1 in 500	Consolia p l. lobe rt side. Br. tubular.
" 11	7	m 100 e 101·2	13300	83	9	7	4 in 500	Sputum rust coloured.
" 12	8	m 98·2 e 100·6	[~~15000~~ ↓	~~69~~ ↓	~~13~~ ↓	~~15~~ ↓	~~2%~~ ↓]	Herpes on upper lips and submasc. reg.
" 13	9	Remains subnormal	15000	69	13	15	2%	
" 14	10		8000	67	11	16	5%	Patient made a good and quick recovery.
" 15	11		10700	67	10	20	3%	
" 18	14		7800	71	10	18	1%	

Case 8 Bell S. act 22

Lobar Pneumonia (R. Lung) : Recovery.

Date 1897	Day of Dis	Temp. F	Leucocy	P	L	S	E	Notes.
Mar 21	6	e. 102	15700	86	7	6	.5	Mar 21. Has been ill since Mar 5. Cough.
" 22	7	101.4	15000	83	6	8	3	Sense of in rt side.
		100.2						Phys. signs cons of whole rt side.
" 23	8	99.8	15000	76	7	11	.5	Resp. w Quiet RB Bronchitis.
"		99.4						
24	9	99.8						Sputum - vis cons.
25	10	98						Fraenkel's diplococci found.
26	11	97.4						Mar 24. Cons of. at base - friction.
27	12	98	12200	73	8	12	6	Resol proceeding.

Case. 9 H. Donald aet 19.

Lobar Pneumonia. (L. Lung. L Lobe): Recovery.

Date 1897	Day of Dis	Temp. F	Leucocy	P	L	S	E	
Mar								Mar 17. Pain in rt side. Shiverings.
20	4	100.6	28600	91	5	4	0	
		101.4						Mar 19. Sputum tinged slightly
21	5	98	10600	74	14	12	0	Mar 20 Apn. R. 21.
		98						Diagnosis - Lobar Pneumonia - L. lower Lobe.
22	6	101 / 98	7600	68	10.5	20.5	1 0/0	
23	7	97 / 97						Resol - slow.

Case 10 D.,— aet 45.

Lobar Pneumonia. Recovery.

Date Mar.	Day of Dis	Temp	Leucocytes per cmm	P	L	S	E	Notes.
27	2 5	F 103·6	26800	91	5	4	0	Case only examined once. Clinically was a very typical case of Lobar Pneumonia.

Case 11 C., Charles aet 23.

Croupous pneumonia R. Lung: Recovery.

Date 1897	Day of Dis	Temp F	Leucocytes per cmm	P	L	S	E	Notes.
Mar 29	5	103·4 102·6	16200	86	9	5	0	Mar 25. Severe pain in "stomach"; vomited; rigors.
" 30	6	101·4 102·6	32000	89	7	4	0	Mar 27. Sputum blood stained. Mar 28. Adm. R.I. Phys. signs behind
" 31	7	103·2 100·4	33000	92	5	3	0	complete consolid. L. lung apex to base. Inf. Bronch. Voc. Res +
Apr 1	8	97·2 99·8	18000	83	7	10	0	
" 2	9	98·6 100						Apr 1. Pat. delirious towards night.
" 3	10	99 100·4						Apr 4. Temp normal.
" 4	11	98·2 98·6	15500	69	19	12	0	Consol. still marked. Crepit.
" 5	12	98						
" 6	13	19800	12800	55	20	25	0	Recovery speedy.
" 10	17	98	9800	60	16	22	1	Resolut. quick.

Case 12.

M. Archibald. act 14.

Croupous Pneumonia - Lower Lobe. l. lung: Recovery.

Date 1897	Day of Dis	Temps. T	Leuc per cmm	P	L	S	E	Notes.
Mar 29	? 4	ℰ 103	27000	89	5	6	0	
" 30	5	ℳ 103.8	16000	87	8	5	0	Adm. R.E.I Mar 29.
		ℰ 100.2						No definite rigor pain began 4 o'clock on Mar 26; remained in bed.
" 31	6	ℳ 100.6	15 200	85	8	6	0	
		ℰ 102						Mar 30. Phys. signs cons. l. lower lobe. Cough; no expect.
Apr 1	7	ℳ 97.6						
		ℰ 98						Apr. 1. delirious at night.
" 2	8	ℳ 98.8	6400	63	10	23	3	P. 96. Resp. 44.
		ℰ 97.8						Apr. 3. Lung resol.
" 3	9	97	5600	67	7	22	4	—
" 4	10	97.4						Patient made good recovery.

Case. 13. A., Thomas., aet. 20

Rt.-sided Croupous Pneumonia; Pleurisy with Effusion: Recovery.

Date 1897	Day of Dis	Temp F	Leucocytes per c.mm	P	L	S	E	Remarks.
Mar 29	–	4pm 105	18000	87	7	6	0	Adm. R.21. Mar 29.
– 30	–	m. 99.4 e. 101.8	15600	85	6	8	.5	Mar. 17 Unable to work, felt ill; shivered. Stayed in bed two days; went back to work;
– 31	*1	m 99.4 e. 103	13400	83	7	8	1.5	
Apr 1	*2	m 102 e. 105	38000	92	5	3	0	Mar 24. Noticed some blood in sputum; pain in l. side of chest; cough.
2	*3	m 103.8 e. 105.6	54000	93	5	2	0	Mar 28. Felt very ill, pain in chest worse
" 3	*4	m 102.4 e. 102.2	40000	91	4	5	0	Mar 29. On admiss. Dulness at l. side, phys. signs of effusion; aspirated 30 z clear sero-fibrinous fluid withdrawn.
" 4	*5	m 101.8 e. 103.4	32000	93	3	2	0	Rt. side, dulness slight in infra-clav. reg. Behind slight dulness above sp. & scap. Sputum – Tenacious – Fraenkel's pneumococci.
" 5	*6	m 101 e 103	35000	90	6	4	0	
" 6	*7	m 98.2 e. 101.4	30400	87	6	7	0	Mar 30. Dulness at rt side cleared up consid.
" 7	*8	m. 98	15600	80	8	10	0	Apr 1 Slight dulness at l. base.
" 8	*9	m. 100.8						Extensive dulness rt. lung front and behind. Poster.r tube when breathing. Pulse 124. Resp 40
" 9	*10	m. 98	15800	87	6	7	0	
" 10	*11	m. 99						
" 11	*12	m 97.4	22600	75	9	15	0	Apr. 7. Hypodermic inserted at l; base no fluid withdrawn.
" 14	*15	m 98	15800	71	7	21	0	Apr. 20. Dulness diminishing l. base; rt. lung resolving.
" 20	*21	m 99	10400	76	5	18	0	

Case 14 W. James. aet. 19.

Left-sided Croupous Pneumonia: Empyema.

Date 1897	Day of Dis	Temperature F	Leucocytes per cmm	P	L	S	E	Remarks.
Mar 30	4	e. 102.2	20800	88	9	3	0	Mar. 27. Took ill; shivered; severe pain in l. side.
" 31	5	m 101.6 e 101.8	21300	86	10	4	0	
Apr 1	6	m 100 e 101	16000	88	7	5	0	Mar 30. Adm. N.Y.H. Severe p. in l. side. Bl. streaked sputum.
" 2	7	m 99 e. 100.8	24000	86	8	6	0	Dulness almost abs. apex to base, front and behind l. lung. Behind bl. sounds distant tubular.
" 3	8	m 99 e. 99.2	—	—	—	—	—	Mar 31. L. lung abs. Dull behind and in front; hypodermic needle inserted & withd l. base no fluid.
" 4	9	m. 99 e. 99	18400	84	9	6	0	
" 5	10	m 98 e. 98	—	—	—	—	—	Apr. 3. Bony note superclav. region in front. Dull l. base behind; bl. sds. absent.
" 6	11	m 100 e. 100.6	14800	84	9	6	0	
" 7	12	m 99.8 e. 100						Apr. 8. L base aspirated. Very sero-purulent fluid removed.
" 8	13	m 99 e. 101.2						
" 9	14	m. 98 e. 100	7200	78	11	10	0	Apr 14. 25 c.c. pus removed.
" 10	15	m. 98.2 e. 101						Apr 19. Portion of rib resected. Pleura found not to be much thickened at operation. Pneumococci (encapsulated) again found in pus.
" 11	16	m 99.6 e. 100.2						
" 12	17	m 98.6 e. 102						
" 13	18	m. 99.4 e. 102	13200	86	8	5	0	
" 17	22	m 101.6	7600	72	17	11	0	

Case 15. S. William.

Acute Lobar Pneumonia. Emphysema.

Date 1897	Day of Dis.	Temp.	Leucocy	P	L	S	E	Notes.
Mar 16	3	103	27200	92	6	2	0	
17	4	102	17000	91	6	2	0	Mar 14. Pain in l. side.
"		100·2						Sick; vigor.
18	5	100·2						
"		100						Mar. 16 Rdn R 21
19	6	99·6	14400	79	15	6	0	Temp 103. Resp 36. P. 90
"		99·8						
20	7	99·6						Phys. signs consol. at l. side.
"		99·2						
21	8	98·4	23000	72	18	10	0	Mar 20. Phys. signs fluid. sputa. rusty.
"		100						60 m pus aspir.
22	9	100·6						Fraenkel's pneumo- in great numbers in pus.
"		100·6						
23	10	99·8						Mar 23. 35 fl. m. pus. aspir.
"		98						Pneumococci. — Sent to Surgical Side.

Case 16 G. James aet. 59.

Croupous Pneumonia (Rt Lung upper and Mid lobes) Acute Pericarditis : Death.

Date 1897	Day of Dis	Temp. F	Total Leucocytes	P	L	S	E	Remarks:
								Jan 9; Adm. R.E.I.; delirious, ill 4 or 5 days. Fraenkel's pneumococci in great numbers in rusty sputum. Death Jan 10 6 a.m. Seeks diagnosis :- Croupous Pneumonia. Grey hepatisation upper and middle lobes Rt lung; acute pericarditis.
Jan 9	? 5	4 pm. 100·6	15000	93·5	3·5	3	0	
" 10	? 6	4 a m 100						

Case 17 M. Robert aet. 26

Croupous Pneumonia (Rt Lung) : Death.

Date 1896	Day of Dis	Temp. F	Total Leucocytes	P	L	S	E	Remarks.
Nov 6	1	e. 105						Nov 6. Pain in Rt side; rigor. on admission Nov 6 Pulse 124 resp. 38
" 7	2	m. 102·4 e. 103	13000	72	24	3	0	
" 8	3	m. 100·8 e. 100·8	14200	-	-	-	-	Nov 8 - Rusty Sputum. Phys. signs consolid; great pain in Rt side. Nov 10 ? Fluid at base Rt. lung.
" 9	4	m 101·6 e 101·8	14400	-	-	-	-	Nov 11. - Escape of blood 10.30 a.m. after this pulse quickly failed Death occurred at 9 p.m. Pain in Rt. side continued until death.
" 10	5	m 102·6 e. 102·6	14000	90	5	4	0	
" 11	6	m 101·4 e. 102	15000	92	5	2	0	Clinical Diagnosis :- Croupous pneumonia (consolid. of whole of Rt lung)
" 12	7	m 101·8 e 102	16300	95	3	2	0	? Rt-sided Empyema.

28 M

Case 18. F. Philip. aet 37.

Croupous Pneumonia. (Rt Lung).

Rt. Hemiplegia.

Death.

1897	Day	Temp	Leuc.	P	L	S	E	Notes.
Apl 16	? 6	102						Apl 16. adm Rt. 1. Rigor sick, vomited.
" 17	7	102.8	28600	90	5	4	0	on Apl 11.
		103						Apl 14. Hemiplegia came on gradually.
" 18	8	102.2	30000	92	4	4	0	
		103.6						Apr. 17. Marked signs consol. Rt. axilla.
" 19	9	104	29600	91	4	5	0	Rt. Lung. Rusty sputum.
		104.6 (12 noon)						Apl. 19. Death 3 p.m.

Case 19. G. James aet. 59.

Croupous Pneumonia. Acute Pericarditis Death

1897 Jan	Day Dis	Temp F	Leuc.	P	L	S	E	Notes.
								Admitted in dep. alcoholic.
9	? 5	12 noon 100.6	15000	93.5	3.5	3	0	Adm. Jan 9.
		8 p.m 100.2						Dia. early on Jan 10
								Sectio -
10	6	12 a.m 100						Grey hepatic. Rt. upper lobe.
								Acute Pericarditis

28 N

Case 20. B. Henrietta aet 27.

Croupous Pneumonia. Rt Lung.

Death.

Date Apl	Day	Temp	Leuc	P	L	S	E	
16	7	102·6						Adm. Apr 16. 7th day.
"		103	17000	90	4	5	0	
17	8	103·6						Apl 10 – Shivers. Sick 2 weeks.
"		103·6	17800	92	3	4.		Pain in Rt side
18	9	102·8						
"		103·2						Apl 16. On admission pat very weak.
19	10	103·8						
"		103·8 (12 noon)						
								Apl. 19. Death occurred 12 noon.
								Section – Early grey hepat. whole Rt lung, no other changes.

Case 21 B. Matthew aet. 39.

Croupous Pneumonia. Death

Date.	Day	Temp.	Leuc.	P	L	S	E.	
Apr.								Adm. Apr. 16.
16	5	103·2						Section –
"		103	4600	87	10	2	0	Grey. Hepat. Rt. Lung. (L. Lobe.)
17	6	100·2						Smears hyaluted cocci in lymph

Case 22 W. Henry aet. 51.

Acute Pneumonia (Cerebral Tumour) : Death.

Date 1897	Day of Dis.	Temp. F	Total Leucocytes	P	L	S	E	Remarks.
Feb 1	0	m 97·6						Adm. R.D.I. Oct 21. 1896. Diagnosis: Cerebral tumour.
		e. 98						
" 2	1	m 99·4						Temp. normal up to Feb 2. 1897 when had rigor; temp became elevated.
		e. 102						
" 3	2.	m 101·4						Pulse and resp became rapid. Pulse scarcely perceptible at time of blood exam. 11 a.m.
		e. 104	*4400	35	42	23	0	
" 4	3.	m 103·8	*7400	94		6	0	Death occurred Feb 4. 6 p.m. Secto diagnosis: Small area of caseat. inflam. rt. mid and lower lobes.
		e. 104·4 (4 p.m)						

* See special note p. 52.

Case 23. C. David aet 42.

Croupous Pneumonia. : Death

Date 1897	Day of Dis	Temp. F	Total Leucocytes	P	L	S	E	Remarks
								Adm. Mar 22. Had a "fit" on Mar 21. Drinking heavily for some time.
Mar 22	2	e. 103	6200	61	29	10	0	
" 23	3	m 103·6						On admission found to be suffering from del. tremens.
		e. 102·8	5500	46	34	20	0	phys. signs lobar pneumonia.
" 24	4	12 a.m. 103·4						Death occurred Mar 24. 4.30 Secto diagnosis: L. a.m. Acute pneumonia. Rt. Lung. Rea passing into grey hepatisation.

GENERAL SUMMARY OF CASES.

Of the foregoing 23 cases the last three on the list showed no leucocytosis and all three died. The first of these cases (case 21) was that of an alcoholic patient, whose condition, moreover, at the time of blood examination (performed a few hours before death) apart from slight tremor of the tongue, was not such as in any way to indicate a speedy lethal exit; the sectio revealed the lower lobe of the right lung in a state of grey hepatisation. Case 22 was that of a patient suffering from cerebral tumour; the sectio showed only a small amount of consolidation The last case was, like case 21, that of an alcoholic patient in whom the pneumonia was accompanied by delirium tremens and the post-mortem examination showed consolidation of the whole of one lung. I shall refer more particularly to the blood examination in those cases at a later stage.

Of the 20 cases which were accompanied by leucocytosis, 5 died. Case 16 was one of so-called traumatic pneumonia in an alcoholic subject, it was complicated by very extensive acute pleurisy. In the

next two cases there was no sectio. In one the clinical examination pointed to consolidation of the whole of the right lung, and possibly right-sided empyema. The other was complicated by right-sided hemiplegia with aphasia (? cerebral thrombosis) occurring during the course of the pneumonia; the leucocyte count in this case was the highest of those terminating fatally, viz., 30,000, which number remained for three days, never showing any marked variation up to within a very short time of death. Case 19 revealed acute pericarditis with effusion. Case 20 showed grey hepatisation of the whole of the lung, but no changes of importance in any of the other organs.

Of the remaining 15 cases occurring with leucocytosis, two of them were peculiar in this, that the leucocytosis which was present at an early stage, disappeared for two to three days during the acute stage, reappeared just before the crisis, again to decline with the fall of the temperature. In one case (the first of the series) the patient was extremely weak and collapsed during the stage of no...

leucocytosis, and coincidently with the rise in the number of the leucocytes his condition improved. The second patient in which this phenomenon occurred, was a boy aged 13 (case 4.) whose condition did not at any time afford ground for anxiety; he had had an attack of croupous pneumonia a year previously.

Of the other cases 10 made a good recovery, while in three, convalescence was delayed owing to such complications as pleurisy with effusion and empyema (Cases 13, 14, 15).

CHANGES IN THE TOTAL NUMBER OF LEUCOCYTES.

I have already mentioned that Rieder has asserted that the leucocytosis of pneumonia begins early, within a few hours after the occurrence of the rigor. V.Limbeck states that leucocytosis always commences prior to the occurrence of the exudation; the exudation is a result of the leucocytosis. Löwit on the other hand, would expect a diminution in the number of leucocytes in the circulating blood to precede the leucocytosis - a condition of hypoleucocytosis or, as he has termed it, leucocytopenia. Sherrington has proved experimentally that such a phase does take place at an early stage, after the establishment of the lesion in non-bacterial inflammations of an acute local character. It is most probable that such a diminution in the number of leucocytes also occurs at the very earliest stage of a pneumonic attack, a circumstance of which the proof is not yet forthcoming, however. If it exists, it must be transitory.

The condition of leucocytosis, or hyperleucocytosis, as it has been also termed, accordingly

begins early. In most cases it persists during the whole course of the affection. In my observations it outlasted the fever from one to six days. The duration of the leucocyt~~es~~osis is generally ~~tardy~~ prolonged in those cases in which there is no sudden and complete fall of the temperature to normal, or where, this occurrence having taken place, the temperature curve thereafter shows certain minor elevations above the normal. If another acute inflammatory process be superadded to the primary disease it has the effect of causing the leucocyte curve to remain more or less highly elevated for a longer or shorter period, according to the variety and duration of the complicating affection.

The degree of leucocytosis varies. It is as a rule considerable in acute pneumonia. My highest count was 54,000 in a case complicated with pleurisy. Still higher counts have been recorded. The period in the course of the affection at which the highest degree of leucocytosis is to be found, varies; sometimes it occurs early in the process; at other times just before the crisis.

I have found no direct connection to subsist either between the height of the fever or the severity of the attack (apart from cases where no increase of leucocytes occurs) and the degree of leucocytosis. That a continuous leucocytosis occurring after the temperature has come down to and remains at normal always implies a delay in the resolution of the pneumonia I cannot affirm. In case 2 there was considerable delay in resolution and the leucocytosis remained less than a week after the crisis.

What connection there exists between the extent of the consolidation and the degree of leucocytosis I shall have to discuss later, as also the reasons for the non-appearance of leucocytosis in certain cases, and in others the disappearance of a leucocytosis previously existing in the blood.

Following the method adopted by Sherrington in his paper on Inflammatory Leucocytosis I shall next discuss the

<u>Disturbance of the Numerical Ratios normal between the Various Kinds of Haemic Leucocytes</u>.

Much more interesting, far more constant, and I believe vastly more important, both from the developmental point of view as regards the blood-cells and also from a purely clinical standpoint, than the consideration of the variations in the total numbers of leucocytes, is the observation of the numerical ratios which the different forms of leucocytes bear to one another at different periods in the course of pneumonic process.

Of each of the four chief varieties of haemic leucocytes I shall now give a brief description. Of their many designations I have referred to them in this paper by the terms Polynuclear, Large and small mononuclear, and Eosinophilic.

(a) Polynuclear.Cell.

They are also referred to as polymorphous or polymerous. They correspond to the neutrophilic cells of Ehrlich. Kanthack and Hardy term them finely granular oxyphilic. Durham refers to this cell as the "microxyphil cell" or "microxycte".

The typical cell (plate II. Fig.1b) is smaller than either the eosinophilic cell or the

large mononuclear cell. The nucleus is an exceedingly irregular structure branching throughout the cell. The lobes are usually united by fine bonds of chromatin. The irregularity is undoubtedly, as Arnold first suggested, a sign of the amoeboid activity of the cell; this fact has since been corroborated by Heidenhain, Metchnikoff, Gulland, and others. When at rest the nucleus assumes the spherical aspect, also in the slowly killed cell it becomes spherical but here it takes up an eccentric position with regard to the cell body (Sherrington); later it becomes fragmented.

The cell body is finely granular; these granules stain ~~freely~~ feebly with eosin and other acid dyes. Durham says that in specimens made from the human subject shortly before death the granules do not appear. Hankin considers he has noted a loss of granulation in these cells in the presence of microbes, etc., and he supposed the granules are the source of the alexins, or natural bactericidal substances. Hahn and Durham assert they have never observed the process in their investigations. I have never noted

loss of granulation in these cells in cases of croupous pneumonia, or other acute inflammatory conditions.

They are present in the blood of the healthy adult in the proportion of 60-75% of all the haemic leucocytes. They form by far the greater proportion of the cells found in acute inflammatory exudations and constitute the overwhelming majority of all cells found in the consolidated lung of croupous pneumonia. Here, however, owing to degenerative changes, they are often only with difficulty recognised.

I have, moreover, observed them in great numbers in the sputum of patients suffering from croupous pneumonia. At an early stage of the affection, when the microscope may reveal the cellular elements of the expectoration as being made up almost exclusively of these cells, their recognition therein is a matter of considerable diagnostic importance.

(b) Large Mononuclear Cell.

This cell is rather larger than the preceding cell (Plate II. Fig.1.c.) The nucleus typically is spherical or kidney shaped. It shows a more or less open chromatin network, which is often more

condensed at one or more situations. It has been termed hyaline, but the name as Durham points out, in an unhappy one, for in many cases a reticulum may easily be made out, showing nodal points of unequal size. This reticulum, I have found, often stains well with a saturated watery solution of methylene-blue, it also stains with haematoxylin. In the same film, however, other large mononuclear cells are frequently met with whose protoplasmic network refuses to take up the stain.

These cells represent in the circulating blood from 2-6% of all the leucocytes present.

(c) Small Mononuclear Cell.

This cell has also been termed the lymphocyte, from the fact that it has been supposed to originate in lymphatic glands. It is a small cell, spherical in shape, possesses a deeply staining spherical nucleus, and little cell substance (PlateII, Fig.1.d.) Kanthack and Hardy represent the cell substance to be free from granules. I may, however, say that I have observed frequently granules in the cell protoplasm in film preparations stained with

agneous methylene-blue; this appearance was generally associated with the occurrence of the same phenomenon in the large mononuclear cells. Buchanan has also observed that in many lymphocytes amphorous points of basophile matter can be made out. Their percentage in the blood of the general circulation is from 20 to 30% of all the wandering cells. They are said to be increased during the process of digestion (Okintschitz; Kanthack and Hardy).

(d) Eosinophilic Cell.

This cell is also known as the coarsely granular oxyphile cell, as the "megoxyphil cell" or "megoxycyte".

In man this cell is larger than the poly-nuclear cell. The nucleus is horse-shoe shaped or lobed; in the latter case the lobation is usually not so marked as in the case of the typical poly-nuclear cell. (Plate II. fig.3.e.). A nuclear net-work may generally be made out. The cell granules are relatively large, spherical, or slightly ovoid bodies and have a strong affinity for acid dyes. Recent micro-chemical tests have demonstrated that the granulation is albuminoid and as it is of stable composition, resists decomposition, and is not digested in the gastric juice, Weiss places it among the nucleo-albumins and proteids.

As regards the province of the eosinophilic granules there exist various views. Hankin and Kanthack promulgated the theory that these granules produced alexins. Siawcillo, as the result of his observations, cannot confirm the hypothesis, nor has he been able to see any change either in quantity or in the form of the granules of these cells found in the exudate provoked by the injection of bacteria. Neither can Durham find that it plays a prime part in

the tissue-battle against micro-organism nor can he trace any indubitable or apparent loss of granulation as a result of contact with bacteria. Sherrington also has noted in a series of experiments the highly resisting power of the coarsely granular leucocyte to various chemical agents.

The number of those cells according to various observers is from 2 to 4% of the total number of leucocytes; in the blood of children according to Reider, Cannon, Zappart, they are present in a considerably higher proportion. They are greatly increased in the blood in leukaemia. The expectoration of asthmatics is chiefly made up of these cells, Among other conditions they are said to be increased in skin disease, intermittent fever, etc. Zappart has observed the diminution of eosinophilic cells in most of the infectious diseases (croupous pneumonia, septicaemia, erysipelas, etc.) but after the temperature falls, the number of eosinophilès becomes often grèater than normal. Ehrlich says they are decreased in every acute leucocytosis.

Eosinophilic cells are also present in

numbers in bone marrow, in the coelomic fluids, and in the lymph spaces throughout the body. In different situations, however, they exhibit certain differences in form and character (Muir, Kanthack & Hardy, Hardy and Wesbrook).

Having thus differentiated these four varieties of leucocytes and described certain leading features in regard to each of them I shall now proceed to an account of the variation in their numerical ratio during the course of acute pneumonia. For this purpose I divide all cases of croupous pneumonia into two groups.

I. Cases occurring with Leucocytosis.

II. Cases occurring with no Leucocytosis.

I. The cases occurring under the first head form the great majority of all cases of acute pneumonia and will be considered first. Three stages or phases of the leucocytosis will be described; those may be conveniently termed:-

1. Early Stage.
2. Later Stage.
3. Stage after Crisis.

1. Early Stage.

This stage begins soon after the initial rise of temperature and usually lasts 3 or 4 days.

If the blood is examined at an early period in the course of the affection, e.g., the second day, it will be found that there is marked leucocytosis. On examination of the blood films it will be found that the polynuclear cells are relatively to the other forms as yet but slightly increased, if increased at all. The large mononuclear cells are absolutely and relatively to the small mononuclear cells very greatly increased. The latter are generally absolutely diminished; their relative percentage ratio is always greatly diminished. The eosinophilic cells are absent. To give an example, let us suppose a healthy man has 7000 leucocytes per C.m.m., he is seized with an attack of croupous pneumonia and on the second day of the attack 20,000 leucocytes are counted in his blood. The relative percentage of the various forms in a typical case might be as follows.

	Before the attack.	Second day.
Polynuclear.	72%	79%
Large mono(nuclear)	5%	15%
Small mono(nuclear)	20%	6%
Eosinophilic.	3%	0%
	100%	100%

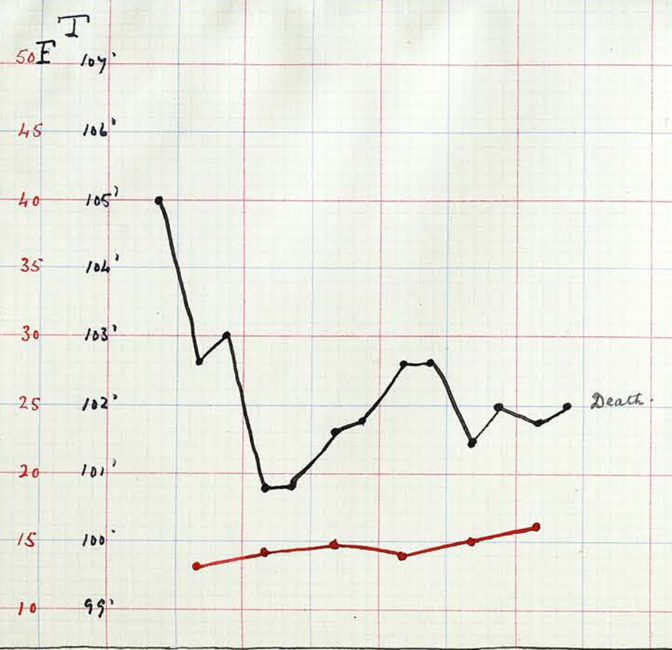
What strikes one most forcibly on examining a film preparation of the blood at this stage is the great relative increase of the large to the small mono-nucleated cells. The latter, instead of being much more numerous than the others, as in health, are are usually much fewer in number. As the disease progresses we find that the large mono-nuclear cells have diminished until they come to equal, or nearly equal, the small number. The polynuclear cells are proportionately augmented in numbers.

From a very early stage in the process the eosinophilic cells are diminished not only relatively, but absolutely in the blood and the diminution of these cells continues to the end of Stage 2. In fact, it is rare to come across an eosinophilic cell in the blood film taken during the acute febrile period of croupous pneumonia. Plate I., fig.1. is a photo microgram representing a typical blood field in the early stage of croupous pneumonia. Plate II., fig. 1. is a coloured diagramatic representation of the blood at the same stage . Both figures show an increase of the large as compared with the small

M. Robert aet. 26 Croupous Pneumonia. : Death.

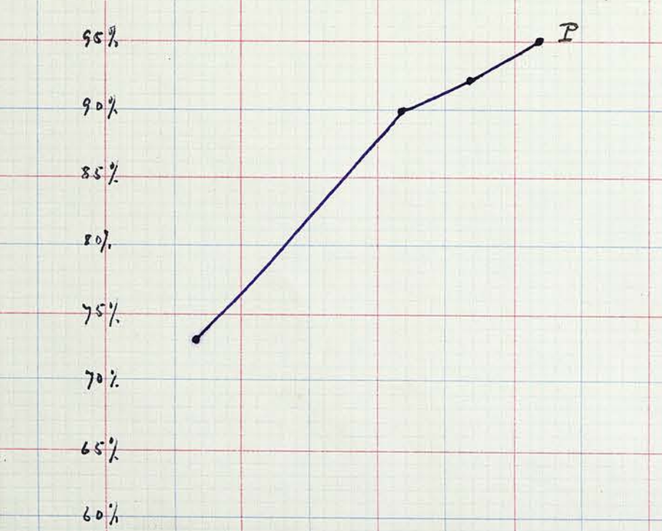
Leucocytes - Thousands per c.m.m.

Day of month	1896 Nov	6	7	8	9	10	11	12
Day of Disease		1	2	3	4	5	6	7



Temperature Curve - Black.

Curve of Total Number of Leucocytes per c.m.m - Red.



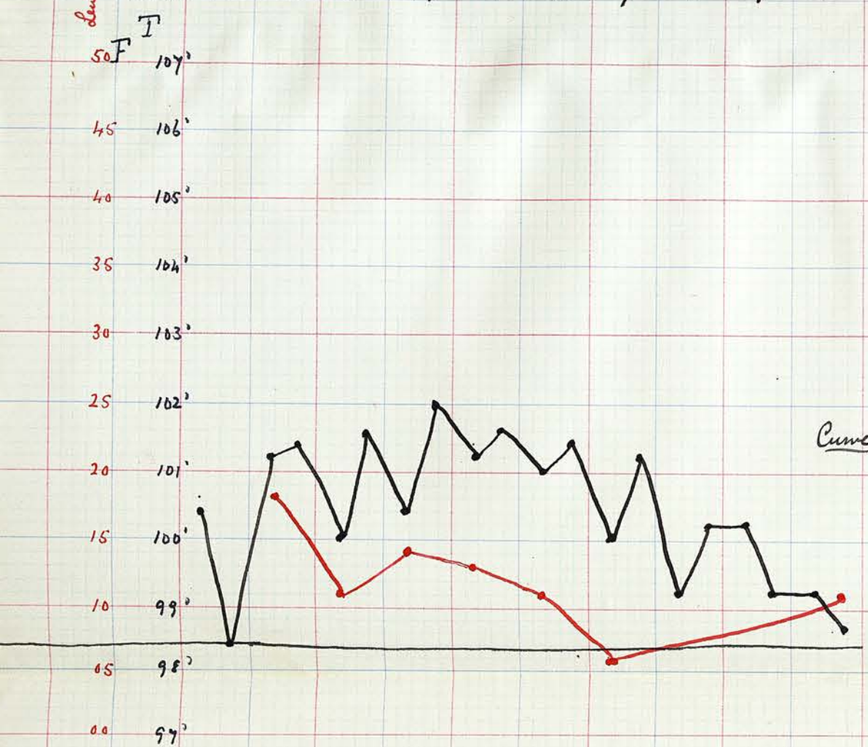
Curves of Relative Percentages of different varieties of Leucocytes -

Violet = Polynuclear.
Blue = L. Mononuclear.
Red = S. Mononuclear.
Black = Eosinophilic.

S. James act 46 Septic Pneumonia. Recovery.

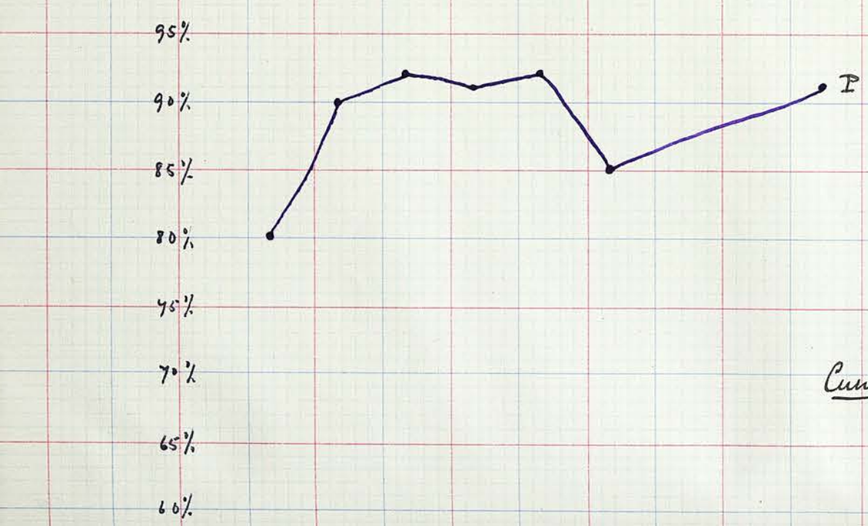
Leucocytes – thousands per cmm.

Day of Month	1896 Dec 1	2	3	4	5	6	7	8	9	10
Day of Disease	1	2	3	4	5	6	7	8	9	10

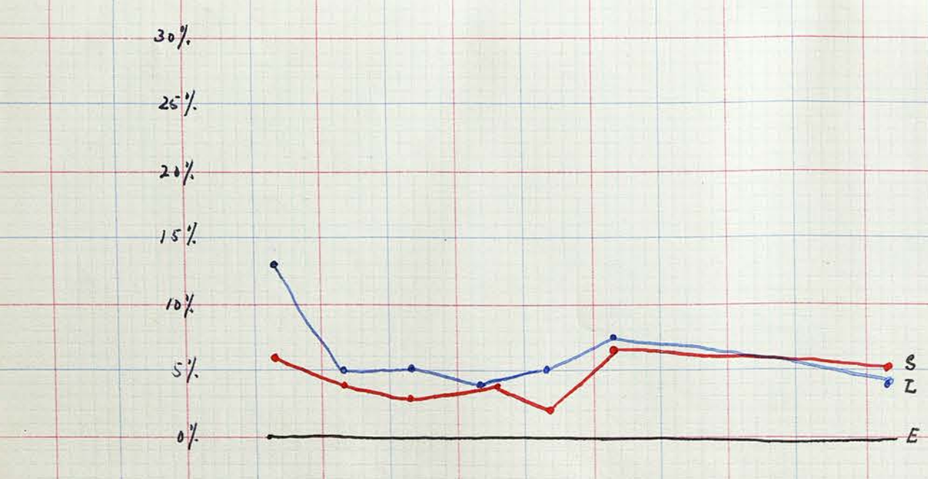


Temperature Curve - Black -
Curve of Total Number of Leucocytes per cmm - Red -

Observations not continued further - Temp. oscillated up and down till Jan 24.97 after which it remained normal.



Curves showing Relative Percentage Ratios of different varieties of Leucocytes -
Violet - Polynuclear -
Blue - Large Mononuclear -
Red - Small Mononuclear -
Black - Eosinophilic -



mononucleated cells, and an absence of eosiniphiles. Chart I. is the result of the blood examination in case 17. The curve of the large mononucleated cells is seen indicating at first a high percentage of these cells which quickly falls until it closely approaches that of the small cells. The curve of the polynuclear cells shows a progressive increase in their relative percentage ratio. A high relative increase of the large to the small mononucleated cells is, as far as my observations go, a characteristic feature of the blood at the commencement of all acute inflammatory conditions.

Chart II. represents the same phenomenon as occurring in a case of septic pneumonia following excision of a portion of the tongue.

2. Later Stage.

There is no strict dividing line between this stage and that just described. It corresponds to the period of maximum increase of the polynuclear cells; it is the stage of great relative diminution of both forms of mononuclear cells together as compared with the polynuclear cells. The latter cells

reach their highest relative percentages as a rule from about the third to the fifth day of the affection. At this time they generally number over 85%, usually about 90%, and twice in my observations reached the high figure of 95% of all the haemic leucocytes (Cases 12 & 17). The small and large cells in fairly equal proportion make up the remainder.

These relative percentage ratios are maintained with surprisingly little variation up to the critical fall of the temperature notwithstanding frequently the occurrence of slight oscillations in the total number of leucocytes per unit vol. of blood. Plate I., fig. 2. is from a case at the fifth day and shows great increase of the polynuclear cells. Plate II., fig. 2. also represents the same stage.

3. Stage after the Crisis.

With the occurrence of the critical fall of temperature a remarkable series of changes takes place in the relative percentages of the cells, and, what is of greater importance, these alterations in the relative percentage ratios occur whether or not there coincidently occurs any appreciable diminution in the total

number of leucocytes per unit of blood. If the blood be examined within a few hours of the crisis, it is found that there is a great reduction in the polynuclear cells, corresponding increase of the mononuclear, and perhaps the appearance of a few eosinophiles.

Let us suppose the individual referred to above in Stage 1, had a typical attack of croupous pneumonia, that his blood was examined on the eighth day of ~~his~~ the affection and the leucocytes numbered 22,000; in the afternoon of that day the crisis occurred. Suppose next morning it was found the leucocytes were slightly reduced, say 18,000 in number; changes very similar to the following would probably be revealed on examination of the blood films:-

	Stage 2. (8th day).	Stage 3. (9th day)
Polyn.	90%	79%
Large Mono.	5%	10%
Small Mono.	5%	10%
Eosinop.	0%	1%
	100%	100

On the following day the polynuclear cells would be found to be still more decreased, the small

mononuclear cells on the other hand still further increased, and for the first time in the course of the affection these cells would outnumber the large mononucleated cells. In other words the increase in the number of the large cells occurring at the crisis is transitory (sometimes it is not noticed to occur) the increase of the small mononucleated cells continuous and progressive. For clinical examples of these changes see especially cases 7, 8, 9, 12 and Charts III. and IV. See also Plate I., fig. 3, which is from a film preparation taken a day after the crisis; also Plate II, fig.3., which represents typically what occurs after the crisis.

A quick relative increase of the small to the large mononucleated cells, especially when the change is associated with a speedy return of the eosinophilès is a favourable sign. It indicates a true crisis.

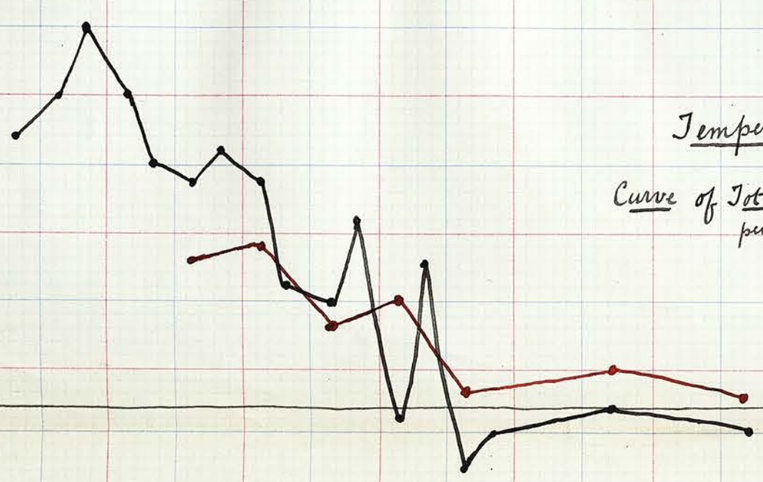
In the case of a lysis the same events occur, but the return to normal is slower,the stage of increase in the large mononucleated cells being of relatively longer duration. In these cases the re-

E., Peter, aet 9. Croupous Pneumonia (Lower Lobe Rt Lung) Recovery

Day of Month 1897 March	6	7	8	9	10	11	12	13	–	15	–	18
Day of Disease	2	3	4	5	6	7	8	9	–	11	–	14

Leucocytes per c.mm. (thousands)

50	F 107°
45	106°
40	105°
35	104°
30	103°
25	102°
20	101°
15	100°
10	99°
05	98°
00	97°



Temperature Curve = Black

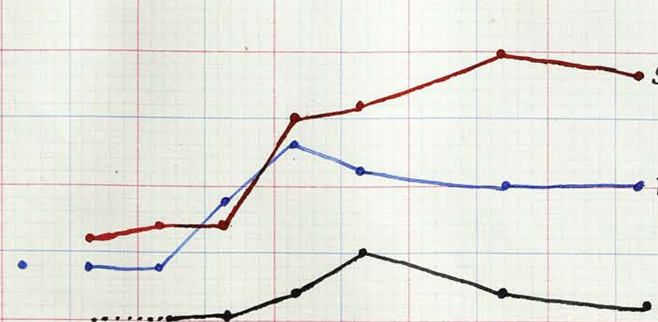
Curve of Total Leucocytes per c.mm. = Red.

95%
90%
85%
80%
75%
70%
65%
60%

Curves showing Relative Percentages of different varieties of Leucocytes –

Violet = "Polynuclear"
Blue = Large mononuclear.
Red = Small mononuclear.
Black = Eosinophilic.

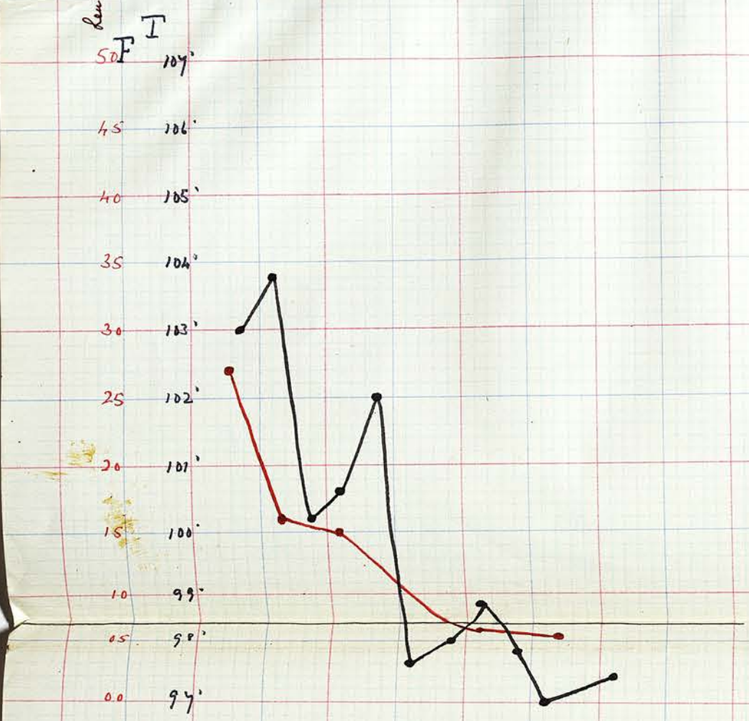
30%
25%
20%
15%
10%
5%
0%



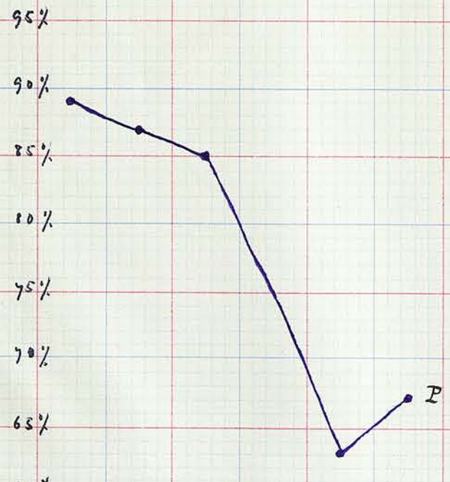
M. Archibald aet 14 Croupous Pneumonia. Recovery.

Day of month	1897 mar 29	30	31	apr 1	2	3	4
Days of Disease	? 4	5	6	7	8	9	10

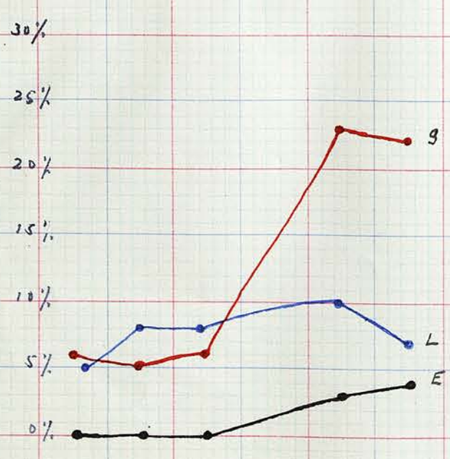
Leucocytes - thousands per c.m.m.



Temperature Curve - Black.
Curve of Total Number of Leucocytes per cmm - Red.



Curves showing Relative Percentage Ratios of different Varieties of Leucocytes -
Violet - Polynuclear.
Blue - Large Mononuclear.
Red - Small Mononuclear.
Black - Eosinophilic.



appearance of the eosinophiles is also later.

In cases terminating by crisis the last named cells are found to occur in something like their normal relative proportion in from one to six days after the fall of the temperature. After slight attacks they seem to appear earlier that in cases where the patient was severely ill.

In from three days to a week on an average, after the occurrence of the crisis the relative numerical ratios of the different cells have resumed something like the condition found in health.

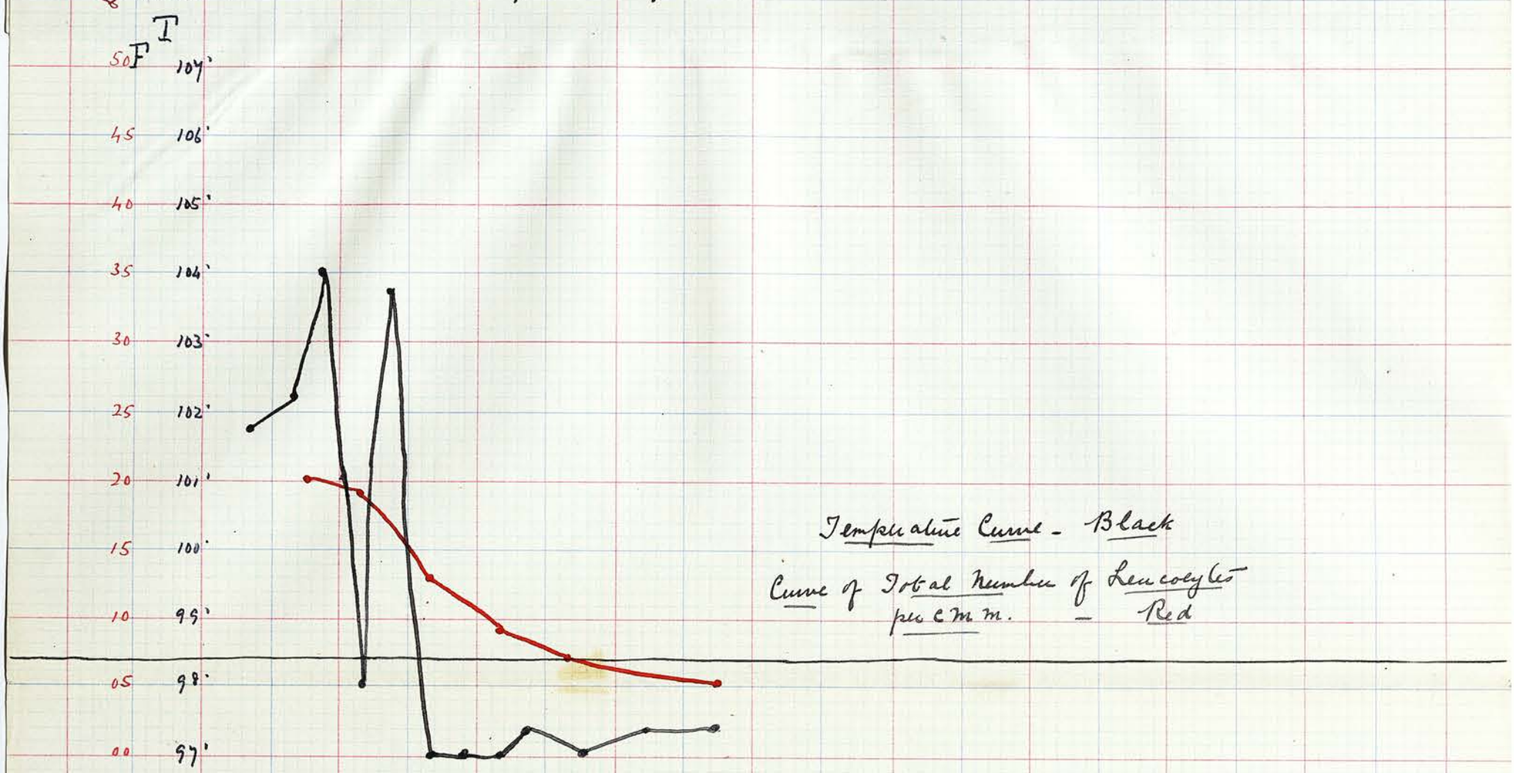
A pseudo-crisis is attended with but little change in the relative proportions of the cells.

Case 6 (Chart V.) is an apparent exception to this in so far that there was a decided change occurring after the first fall of temperature. At the time I thought a true crisis had occurred both from a clinical point of view (the pulse, respirations and general symptoms indicated it), and from the examination of the blood. At night, however, the temperature went up again and there was every appearance of the occurrence of a relapse. Next morning the

Fr James aet 10 Croupous Pneumonia - Recovery.

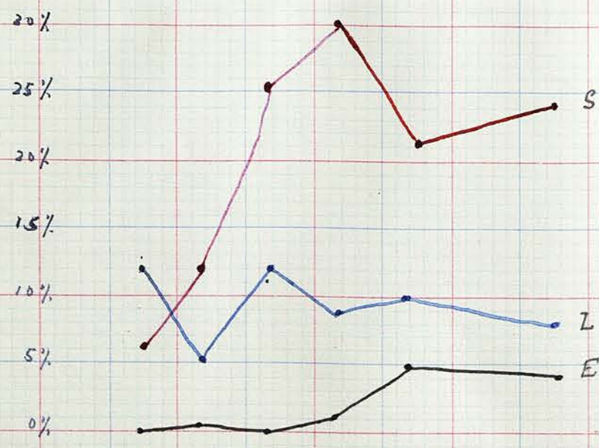
Leucocytes per c.m.m. – thousands

Day of Month	1897 Feb 26	27	28	Mar 1	2	3	4	5
Day of Disease	3	4	5	6	7	8	9	10



Temperature Curve - Black

Curve of Total Number of Leucocytes per c.m.m. - Red



Curves showing Relative Percentage Ratios of different Varieties of Leucocytes -

Violet - Polynuclear.
Blue Large Mono.
Red Small "
Black - Eosinophil.

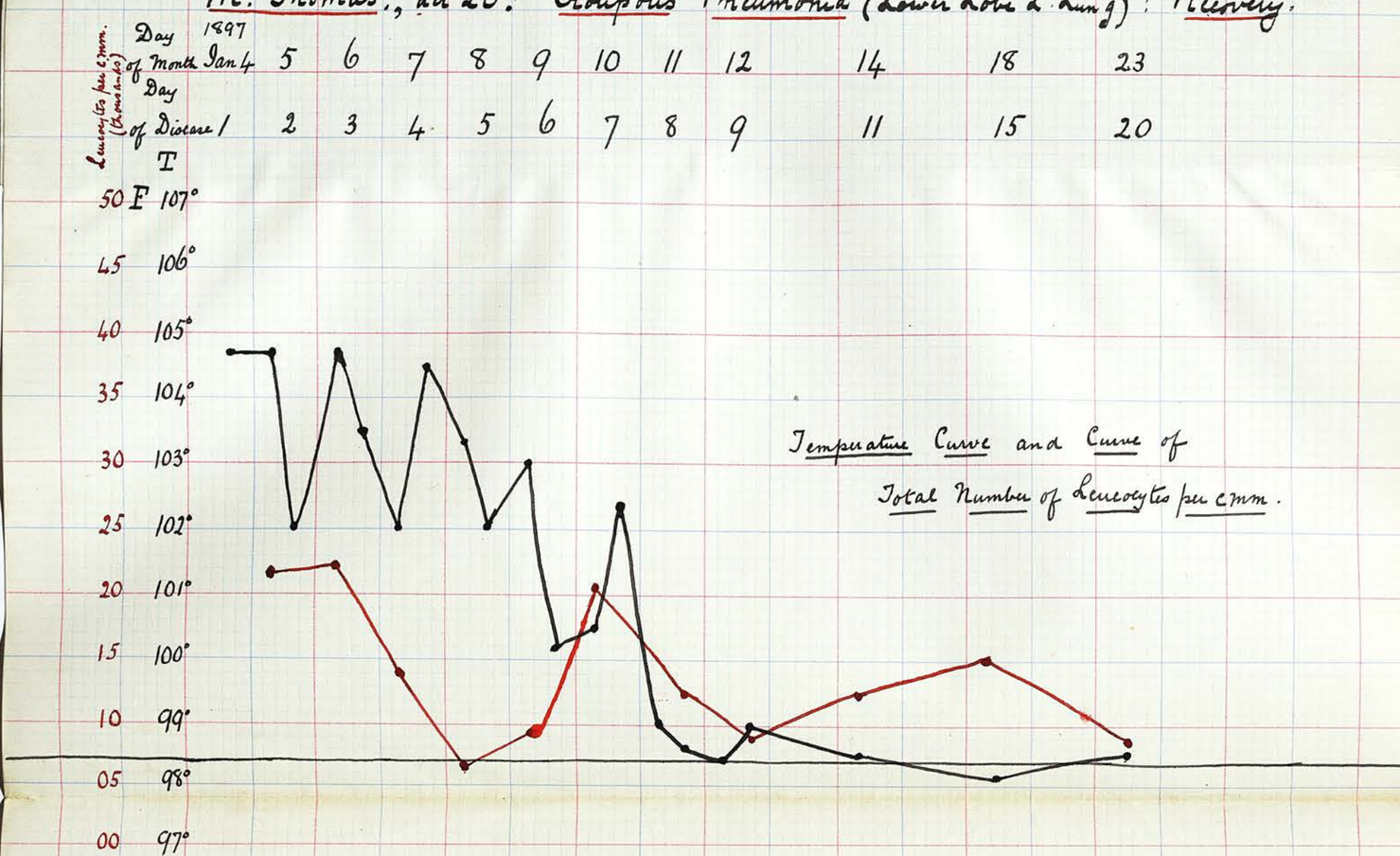
temperature again fell to normal and the blood examination revealed this time an unmistakable "leucocyte-ratio" crisis. The temperature remained and continued subnormal.

A decided fall in the total number of leucocytes during the acute attack as in cases 1 & 4 (Charts VI and VII) is accompanied by a considerable decrease in the percentage ratio of the polynuclear cells, and a relative increase of the mononuclear cells. In fact, the decrease in the total number of leucocytes in the blood is mainly to be attributed to a diminution of the polynuclear cells alone.

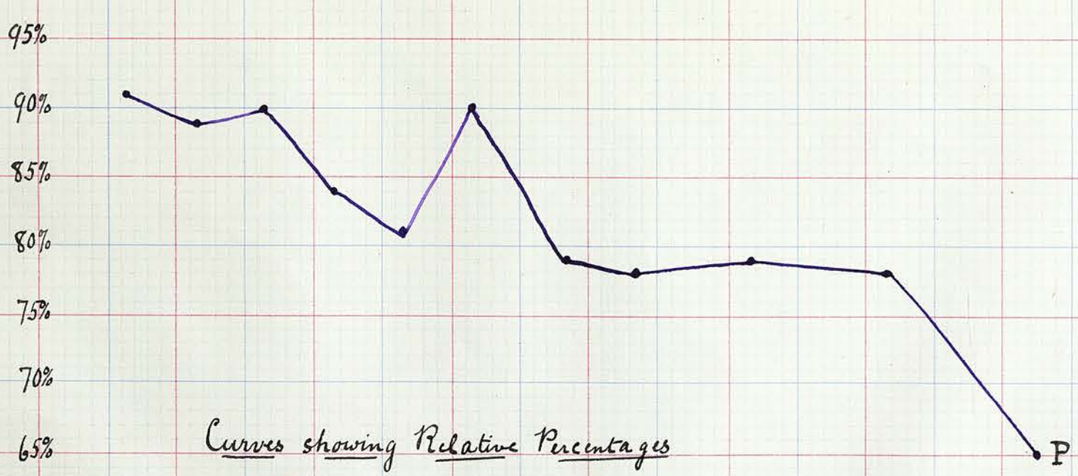
This condition is differentiated from what occurs at the crisis by the fact that the temperature still remains high, that there is continuous great relative increase of the large to the small mononucleated cells, and the eosinophilic cells remain absent.

A continued relative increase of the large mononuclear cells particularly when accompanied by a continued absence of eosinophiles, and especially after the temperature has fallen to some extent, is a condition very often associated with the superaddi-

M. Thomas., act 20. Croupous Pneumonia (Lower Lobe L. Lung); Recovery.

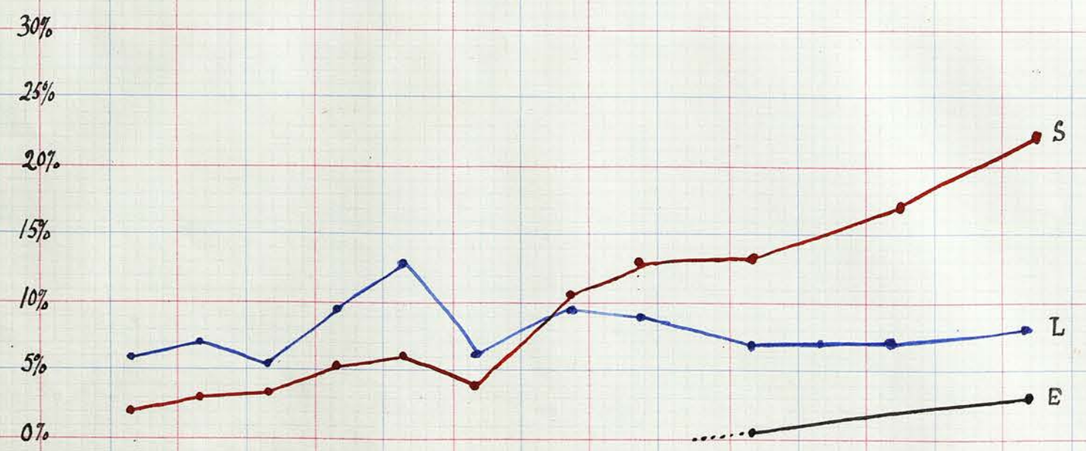


Temperature Curve and Curve of Total Number of Leucocytes per c.mm.

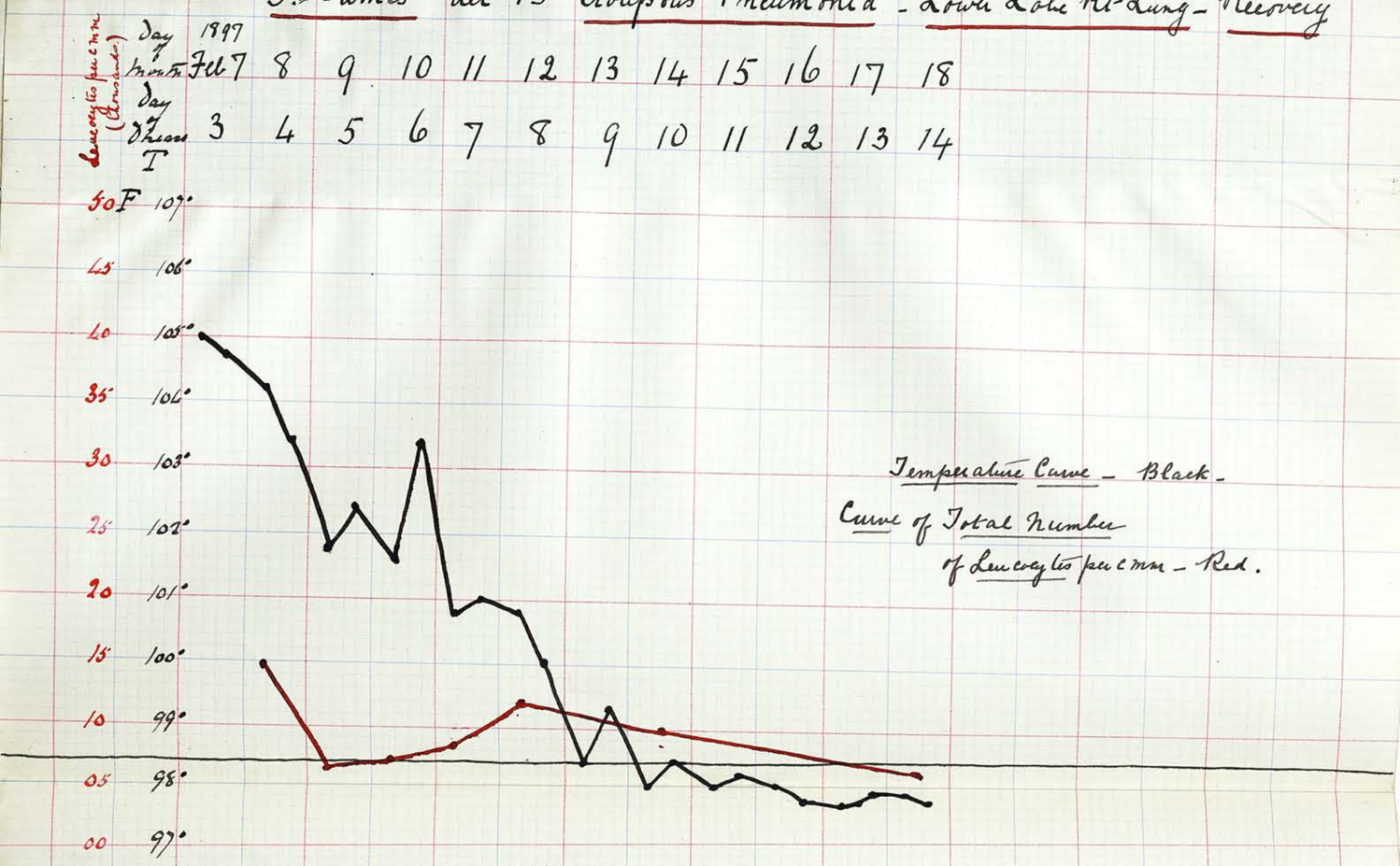


Curves showing Relative Percentages of Different Varieties of Leucocytes.

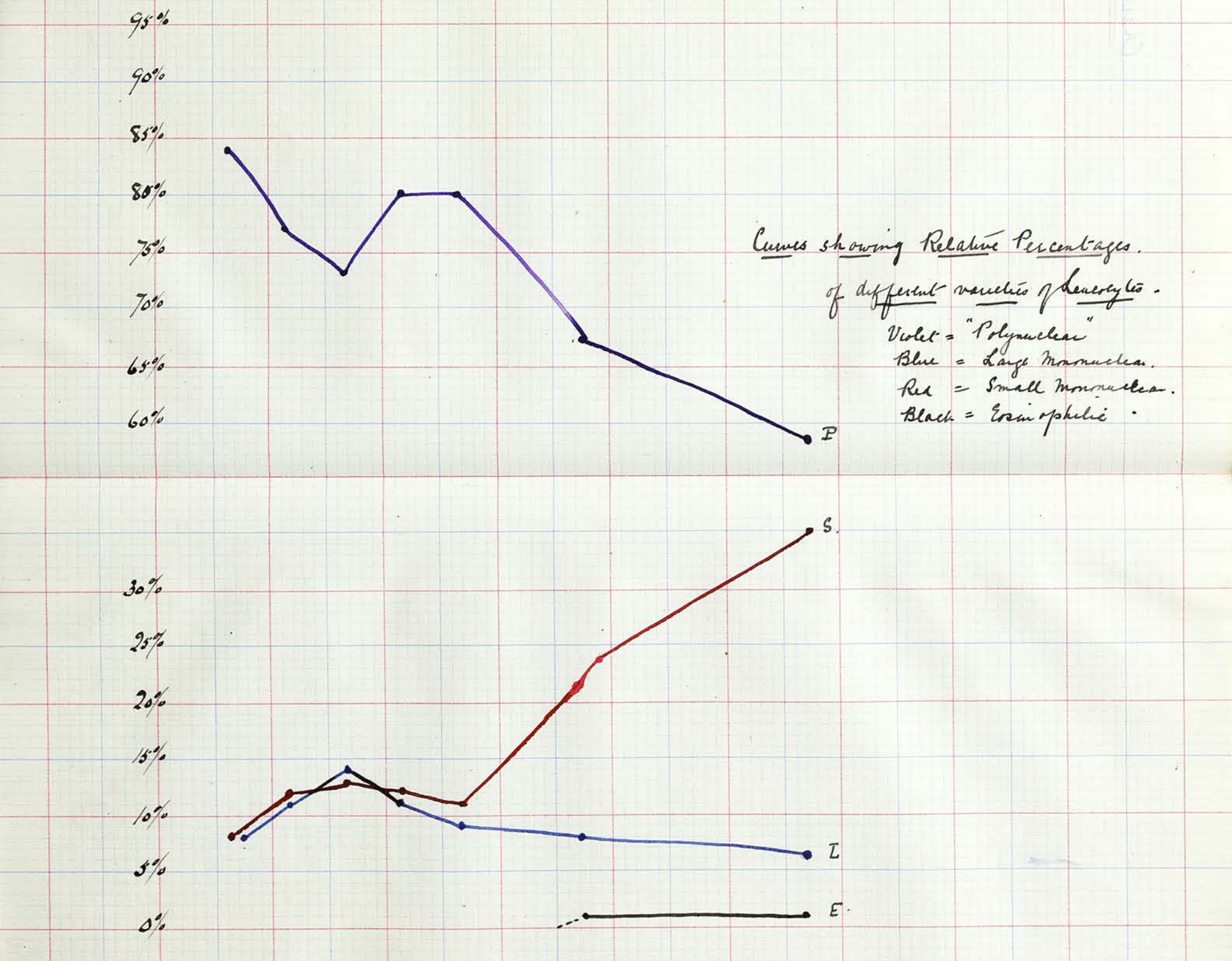
Violet = "Polynuclear".
Blue = Large Mononuclear.
Red = Small Mononuclear.
Black = Eosinophilia.



F. James aet 13 Croupous Pneumonia - Lower Lobe Rt-Lung - Recovery



Temperature Curve - Black -
Curve of Total Number
of Leucocytes per c mm - Red.



Curves showing Relative Percentages
of different varieties of Leucocytes.
Violet = "Polynuclear"
Blue = Large Mononuclear.
Red = Small Mononuclear.
Black = Eosinophilic.

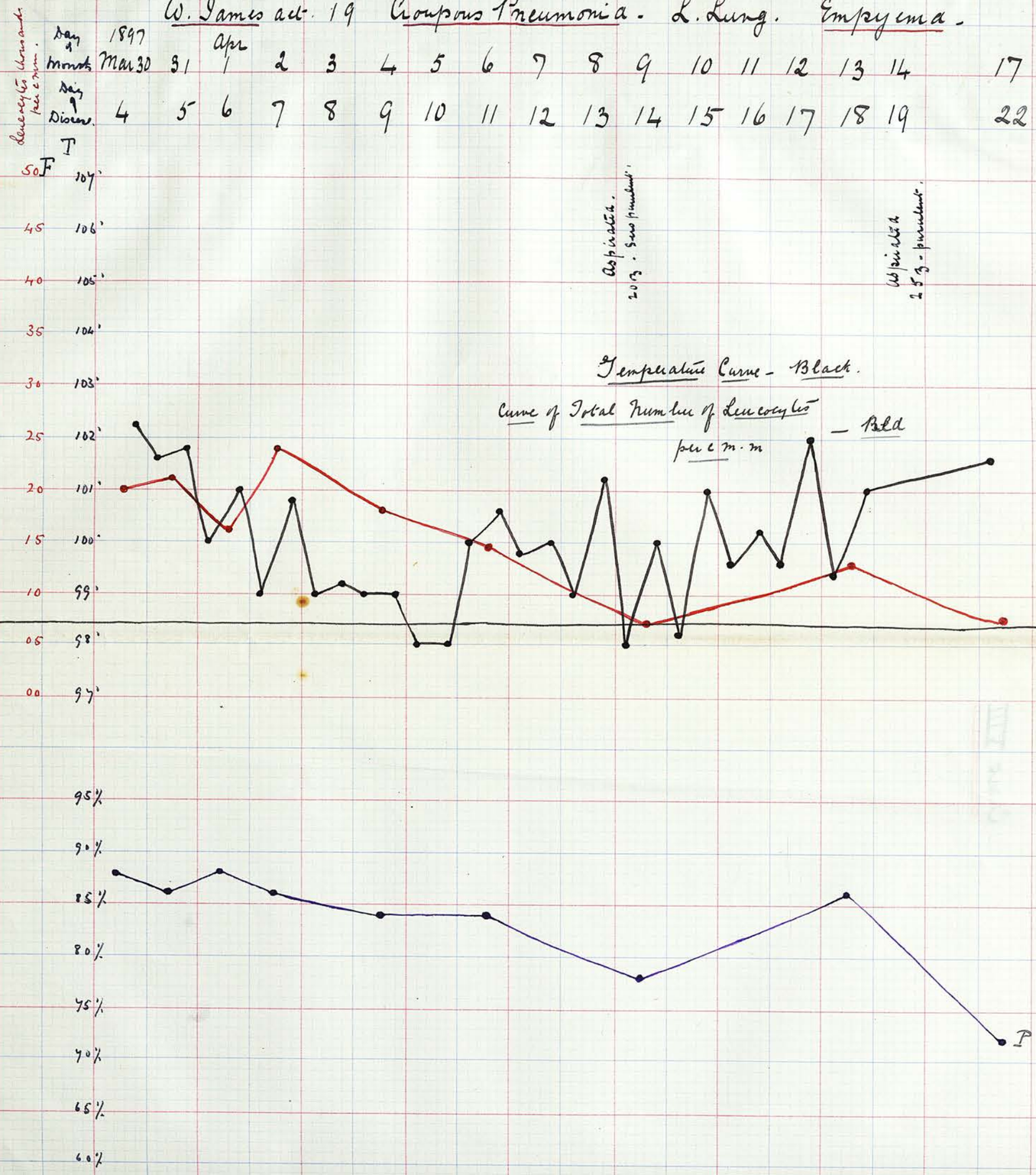
tion of an acute inflammatory complication (See cases 13, 14, 15 and Chart VIII). The microscopic ~~fluid~~ film in those cases bears a striking resemblance to that seen in stage i.

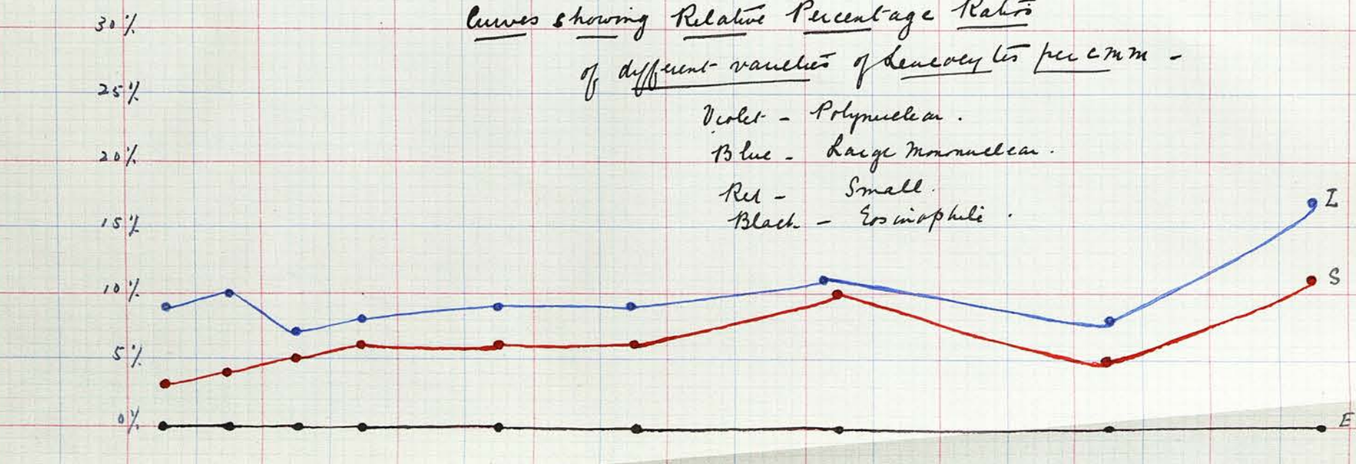
In Chart IX, I have constructed what I conceive to be a typical diagramatic representation of the leucocyte variations in croupous pneumonia. But it must be borne in mind that just as in pneumonia, scarcely two cases are alike in their clinical signs and symptoms, so we can hardly expect to find the blood conditions to be exactly similar in two cases. Clinically, however, there are described certain classical signs and symptoms in croupous pneumonia and these as occurring in a definite order, and so therefore, after a similar manner, it may be permissible to give a typical schematic representation of the blood examination in this affection.

II. Pneumonia occurring without Leucocytosis.

The absence of leucocytosis was noted in three cases, all of which terminated fatally. In all

W. James act. 19 Croupous Pneumonia. L. Lung. Empyema.





Diagrammatic Representation of Temperature and Leucocyte Curves.

Leucocytes = thousands per c.mm.

Day of Month 1897

Day of Illness

0 1 2 3 4 5 6 7 8 9 10 11 12 13 14

I

50 F 107°
45 106°
40 105°
35 104°
30 103°
25 102°
20 101°
15 100°
10 99°
00 97°

Blue - Temperature Curve.

Red - Curve of total number of Leucocytes per c.m.m.

Leucocytopenic Stage. — Early Stage — Later Stage — Stage after the Crisis.

95%
90%
85%
80%
75%
70%
65%
60%

P

Curves showing Relative Percentage Ratio of Different Varieties of Leucocytes.

Violet - Polynuclear.
Blue - Large mono-nuclear.
Red - Small mono nuclear.
Black - Eosinophiles.

30%
25%
20%
15%
10%
5%
0%

S
L
E

the cases there was found to be present a remarkable change in the characters of the white blood corpuscles. If I said that in film preparations from case 21, there were present 87% finely granular oxyphilic cells, 10% hyaline cells, and 2% lymphocytes, my statement of the facts, while tolerably accurate, would convey no proper impression of the cells observed. In Plate II., fig. 3., three cells are respectively lettered b. c. d. Cell b. is a large mononuclear cell possessing a large spherical nucleus with a comparatively open nuclear network which is stained by the methylene-blue. Cell c. shows one of much the same size, but the nucleus is slightly more condensed and irregular; the protoplasm of the cell-body shows a few fine granules stained with eosin. Cell d. is a further stage of the same. In e. and f. we have the nucleus still further condensed and fragmented, and the protoplasm shows the fine oxyphile granules as being much more numerous and closer together than in the previous cells. In short these latter cells are typical finely granular oxyphile cells in everything but size, being much larger than the ordinary cell.

In case 22, there were present in my first examination 35% polynuclear cells, 14 hours afterwards and 7 hours before the death of the patient, scarcely a typical polynuclear cell with fragmented nucleus could be found in film preparations. In this case the cells were rather smaller than in either the preceding or following case, but there occurred the same difficulty in strictly separating the polynuclear (finely granular oxyphilic) from the large mononuclear cells. There appeared to be cells in all stages of transition between these forms. Yet the great percentage of cells found in the consolidated portion of the lung was apparently made up of typical polynuclear leucocytes. Plate I., fig.4, is a photomicrogram taken from a blood film from case 23. Here the cells were also of a large size; there were a relatively larger number of the typical large mononucleated cells ~~were~~ present than in the other cases.

EXPERIMENTAL LEUCOCYTOSIS.

Before attempting to explain the occurrence or non-occurrence of the leucocytosis in pneumonia let me briefly review the experimental work on the subject.

The Intravenous or subcutaneous Injection of a great variety of drugs, e.g. hemialbumose, pepton, pepsin, nuclein, tuberculin, and various extracts, causes at first a diminution in the number of leucocytes in the blood of the circulation. Löwit on purely theoretical grounds believed it was due to a "leucolysis" or destruction of the polynuclear cells, which are those diminished in number. Other observers have gone far to prove, however, that the cells are not destroyed, but that they are simply arrested in the capillaries of the lungs, liver and spleen. Sherrington notes a leucocyto-penic phase in the non-bacterial acute inflammations. He finds that the diminution here also is due to a decrease in the polynuclear cells.

A stage of hyper-leucocytosis follows the

decrease. In Sherrington's experiments it occurred ¾ of an hour after the establishment of the local lesion, its duration varied, it was occasionally prolonged for days. In his experiments it was the polynuclear leucocyte which was increased in this stage. After injection of bacterial products there is also leucocytosis, and though most observers say that the increase here too is due to increase in the granular leucocytes (v.Limbeck, Rieder, Kanthack, Wilkinson) it is doubtful whether it be of the same nature as inflammatory leucocytosis. As regards the special experimental work on Croupous pneumonia, Tschistovitsch has shown that inoculation of rabbits with a virulent culture of Fraenkel's diplococci produced no leucocytosis, on the contrary there was a decrease of those cells in the blood, and the animals succumbed to the infection. Attenuated cultures provoked a leucocytosis and the animal overcame the infection. These experiments, however, are unsatisfactory, in so far as they do not indicate whether or not those inoculations were attended with acute inflammatory processes in some region of the body.

The same objections hold, as regards v.Limbeck and Rieder's experiments.

Morse (1895) would explain the variation of the leucocytes in acute diseases in man as due to the influence of chemiotaxis.

Jacob (1896) as the result of his latest experimental studies in the production of leucocytosis believes that in the haemo-poietic organs there exists not only a reserve of leucocytes but also of bactericidal substances, prehaps free, perhaps enclosed in white blood corpuscles. At the moment of infection leucocytes and bactericidal substances the first strengthening the second, quit their place of reserve, in order to battle against the bacteria or their toxins.

CONCLUSIONS REGARDING THE OCCURRENCE OF THE LEUCOCYTOSIS IN CROUPOUS PNEUMONIA.

It is difficult in the midst of confusing and more or less contradictory theories and experiments to arrive at any definite conclusion regarding this matter.

In considering the subject it is necessary to bear in mind two essential features of the affection.

1. Febrile symptoms due to the specific action of the pneumotoxin or pneumotoxins.

2. Inflammatory exudation.

It is extremely doubtful if the action of the pneumonic poison directly produces leucocytosis or at all events any high degree of leucocytosis. Rabbits inoculated with Fraenkel's diplococci die of acute septicaemia and there is observed no leucocytosis; further that no specific action in this respect can be attributed to the pneumococci, as compared with other organisms, as is shown for instance by the fact that septic pneumonia often presents as high

a degree of leucocytosis as that occurring in true croupous pneumonia. Sherrington in his experimental work has definitely proved that an acute inflammatory leucocytosis, similar in all respects to what occurs in pneumonia, can originate altogether apart from the action of organisms.

The occurrence of the leucocytosis in pneumonia and the inflammatory exudation are closely connected as regards their origin; in other words the general and local leucocytosis are due to the same cause. The action of the organisms on the lung tissue produces irritation products, these cause a local leucocytosis due to an action of a local positive chemiotaxis, but at the same time these irritants find their way into the blood stream and cause a haemic or general Leucocytosis, occasioned by the action of a haemic positive chemiotaxis.

The extent then of the general leucocytosis of pneumonia is dependent on (1) the degree of absorption into the blood stream, of irritants due to local action of the pneumococci, (2) it is also dependent on the local exudation in another way.

The inflammatory exudation in pneumonia is exceedingly rich in haemal leucocytes. In one case where the right upper lobe was alone ~~and~~ consolidated, the fluid scraping of the consolidated portion showed nearly 500,000 cells (mostly leucocytes) per C.M.M. That this was probably a low estimate of the number of leucocytes per C.m.m. of lung tissue may be surmised when one remembers that in leukaemia there is present frequently 500,000 leucocytes per C.m.m. and that in the fluid blood.

On the assumption that there were present half a million leucocytes per c.m.m. in the above case, on a rough calculation, it was computed that there were present in the consolidated portion more than ten times the number circulating in the blood in health. The great loss in number of the haemic leucocytes by this inflammatory exudation must accordingly be taken into consideration in pneumonia. It may be inferred from this that there may be a great increase in the inflow of leucocytes into the blood of the general circulation, though, on account of the excessive emigration, no increase in their numbers

is observed in the blood.

(3) The degree of leucocytosis is dependent on the nature of the infection and the resisting power of the individual. Clinically in some cases it is noted that there is a great amount of consolidation and slight general symptoms; in other cases the converse is true. Otherwise stated, in one class of cases the local action of the pneumococcus is the predominating feature, in another class the general toxic effect is infinitely greater as compared to the local effect, in another class of cases large extent of consolidation is accompanied by general symptoms of marked severity. These facts must be taken into consideration in seeking for an explanation of the occurrence of the leucocytosis and its degree. In severe cases owing to the virulence of the toxins ~~incubating~~ circulating in the blood, coupled with weak resisting power of the individual, and perhaps an impoverished blood supply to the leucocyte producing centres, there is no output of fresh leucocytes in corresponding ratio to the number of those lost from the blood stream.

The febrile process is accompanied by a quickened rate of development of the lymphocyte, through the stage of the hyaline cell, to the fully formed polynuclear leucocyte which process ceases along with the arrest of the fever. That such a transition occurs is disputed. Most observers are agreed that the lymphocyte develops into the hyaline cell (large mononuclear); Ehrlich, Ous~~/~~koff, Metchnikoff, Gulland and others believe that the lymphocyte develops into the hyaline cell, and further by a process of condensation and crowding together of the chromatin network together with certain alterations in the cell ~~of the~~ body of this corpuscle, there is formed the typical polynuclear cell.

To this last hypothesis certain of my observations in pneumonia would appear to lend support and with the aid of this hypothesis the events taking place in pneumonia can be best explained.

1. The relative low percentage of the polynuclear leucocytes in the first stage as compared with Stage 2, is firstly due to the fact that they are being rapidly lost from the blood; secondly that

they are in the process of development.

2.) The relative high percentage of the mononuclear cells in Stage 1, notwithstanding that they are also, though to a less extent, lost from the blood, is due to increased rate of development from the lymphocytic condition.

3.) In stage 2 the process of exudation is over, or if not, the production of the leucocytes is proportional to the loss; the large cells are often relatively diminished as compared with Stage 1, because they have developed into fully formed polynuclear cells.

4. At the crisis the agents which are the cause of this increased rate of development are antagonised, and a sudden arrest takes place of the progress. This is evidenced first by increase in the number of large mononuclear cells, an arrest of their process of development into the polynuclear first taking place, later by a greater relative increase of the lymphocytes due to a further arrest of development, the conversion of the lymphocyte into the hyaline cells being apparently a simpler and more quickly

accomplished process, than the other.

On no other theory than this can I explain the absolute increase in the number of the mononuclear cells which is often seen at the crisis.

5. A quick decided fall of the leucocyte count during the acute attack is to be explained as due to a sudden increased exudation into the lung, which the haemic leucocytosis is not capable of meeting.

6. Cases occurring without leucocytosis may be explained by (1) very rapidly extending inflammatory exudation, (2) failure in the production of leucocytes either due to extreme virulence of the poison, or a want of proper blood supply to the leucocyte producing centres. In such cases most of the polynuclear cells disappear from the blood. They are probably not destroyed; their loss may be accounted for by emigration. The cells which remain in the blood are mostly cells in a transitional stage between the large mononuclear and polynuclear forms. In these cases, even the largest hyaline share in the process of rapid development, and the result of this

is the production of polynuclear cells of a larger size than normal.

Clinical Importance of the Blood Examination in Pneumonia.

I. Diagnosis.

From a diagnostic point of view the examination of the blood is often of the greatest importance. At an early stage, where the history and symptoms would indicate croupous pneumonia, but physical signs are not present, the occurrence of a leucocytosis, especially of high degree, (say above 15,000) would be greatly in favour of pneumonia.

On the other hand, if an hour or so after the occurrence of a rigor, the blood of the patient is examined, and there is found to be no leucocytosis, and further, that the small cells are not decreased in number, as compared with the large cells, and especially if eosinophilic cells are present, it may be definitely asserted that no acute inflammatory process of any extent, and accordingly no pneumonia, is present.

Pneumonia may thus be diagnosed from, besides other diseases, Acute Phthisis and Typhoid.

In connection with the serum diagnosis of typhoid it is often useful. To cite an actual case:-

A patient with indefinite history and suffering from high fever, with physical signs of bronchitis, and impaired resonance at the base of one of his lungs, was supposed to be suffering from pneumonia. The blood examination showed 7,000 leucocytes per C.m.m. On film examination the polynuclear, large and small mononuclear cells appeared in a fairly normal proportion, the small mononuclear cells, greatly surpassing the large mononucleated cells in number. Pneumonia was therefore excluded. The serum test showed a well marked reaction; and the case finally turned out to be one of typhoid fever.

The occurrence of leucocytosis complicating typhoid fever indicates the occurrence of an acute inflammatory complication, possibly pneumonia.

By the blood examination we may accordingly now be able to more easily differentiate between typhoid fever, typhoid fever complicated with pneu-

monia, and typhoid pneumonia.

I have already referred to the fact that a tardy fall in the total number of leucocytes, especially when associated with continued relative increase of the large mononuclear cells, occurring towards the end of a pneumonic attack, may lead one to suspect the occurrence of a secondary acute inflammatory complication.

By the blood examination alone, a true lobar pneumonia (due to Fraenkel's pneumococcus) cannot be well separated from a septic pneumonia. In the case of the latter affection, however, there is usually greater variation both in the total number and relative percentage ratios of the different forms of cells per C.m.m. of blood.

II. Prognosis.

From this point of view the blood examination is of less value. The following conclusions may however be arrived at:-

(1) The absence of a leucocytosis is usually an unfavourable symptom (especially where the exam-

ination of the blood film shows a condition similar to that occurring in the three cases which I have described).

(2). On the other hand the presence of a leucocytosis does not necessarily indicate that the affection will pursue a favourable course, nor that the patient is not liable to suffer from one of the many complications of the disease (e.g. pericarditis, empyema, etc.).

The above observations were carried out during part of the time of my tenure of the Stark Scholarship. The clinical portion of the work was done chiefly in connection with the University Clinical Wards of the Royal Infirmary; and I have to thank the Professors of Clinical Medicine for affording me every facility in the carrying on of the work.

My thanks are also due to Professor Chiene, Dr. Gibson, and others for like facilities. I am specially indebted to Professor Greenfield for placing the Pathological Laboratory at my disposal and for many valuable suggestions. I am also indebted to

Dr. Leith and Dr. Muir, Pathologists to the Royal Infirmary. To Dr. Muir, who suggested the particular subject of these observations, and was ever ready to direct and counsel me in carrying them out, I owe much. I am indebted to Mr. Richard Muir for the excellent manner in which he has executed the plates which accompany this paper.

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Plate I

Explanation of Photomicrograms.

Fig. 1.

Represents Early Stage of Pneum.a with Leucocytosis. Notice increase of Large Mononuclear (=2) to Small Mononuclear (=1)

Fig 2.

Late Stage of Pneumonia. Shows great relative increase of Polynuclear forms (=18) to other forms (=1)

Fig 3.

Taken from a Case one day after the Crisis. Shows one Eosinophile (in centre of field), 7 Polynuclear, 2 L. mono., & 3 small mon.

Fig 4.

Pneumonia without Leucocytosis. Shows large mononuclear and large Polynuclear forms From Case 22.

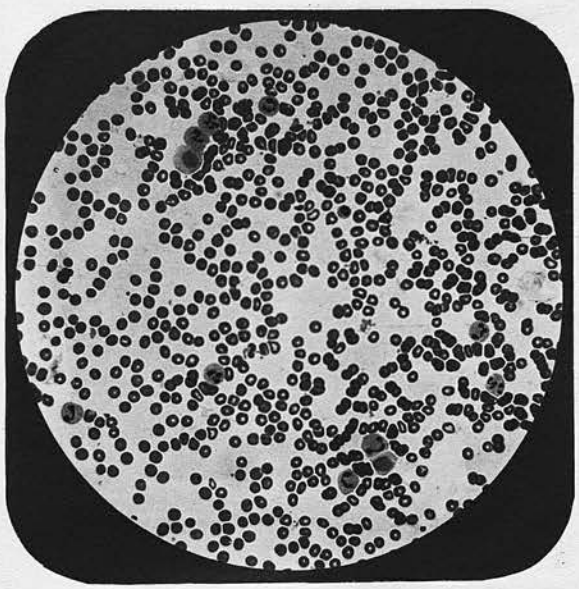

Fig 1

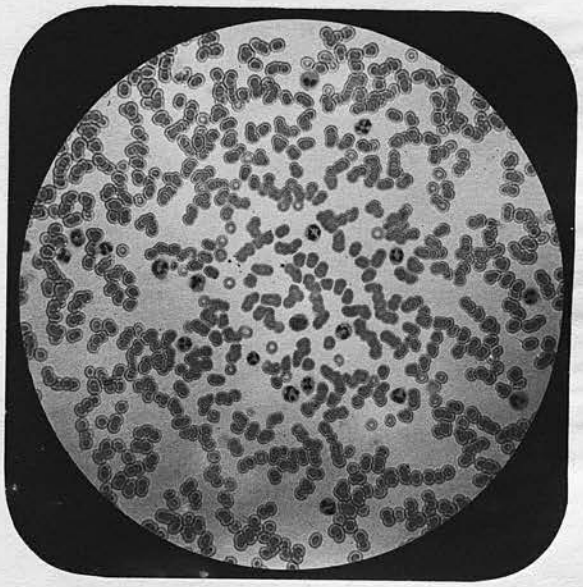

Fig 2.

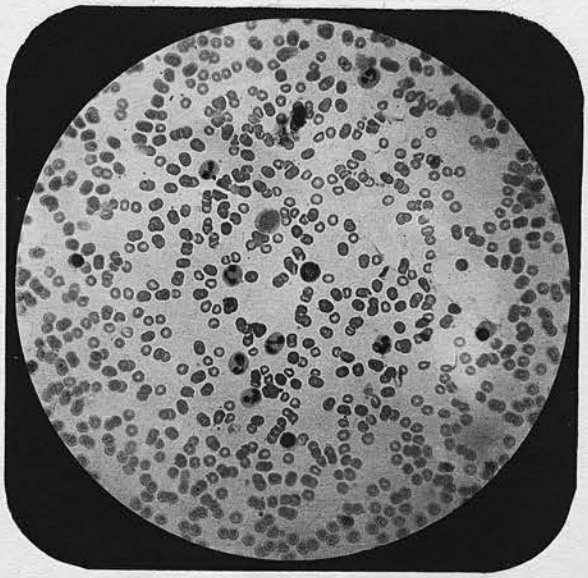

Fig. 3

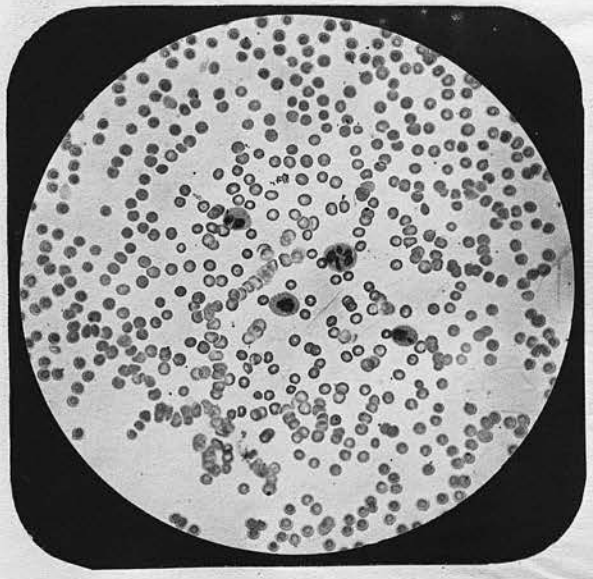

Fig 4.

×220, diam.

Plate II

Explanation of Coloured Figures

Fig 1. Fig 2. Fig 3

a = red blood corpuscle
b = polymuclear leucocyte.
c = large mononuclear.
d = small mononuclear
e = eosinophilic.

Fig 1. Fig 2. Fig 3 represent Pneumonia occurring with Leucocytosis, Stages 1. 2. 3 respectively.

Fig 4.

a = red blood corpuscle.
b - typical large mononuclear cell.
c, d } - large transitional cells.
e, f } large polymuclear cells.

Fig. Represents typically a field in a case of Pneumonia occurring without Leucocytosis.

Fig. 1.

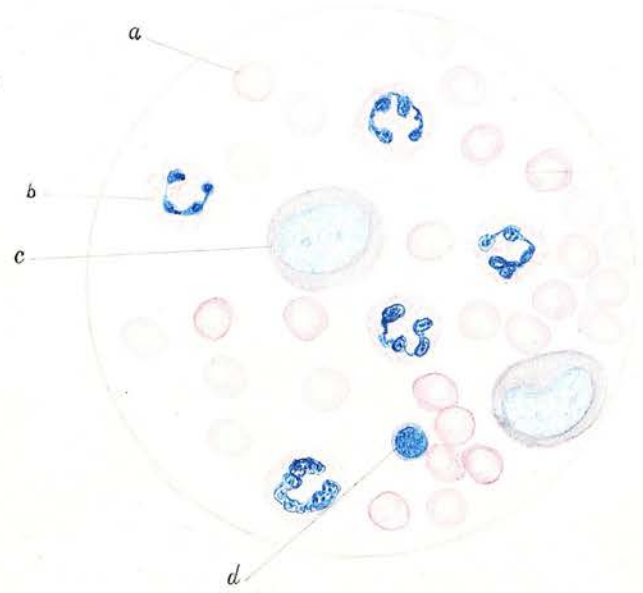

Fig. 2.

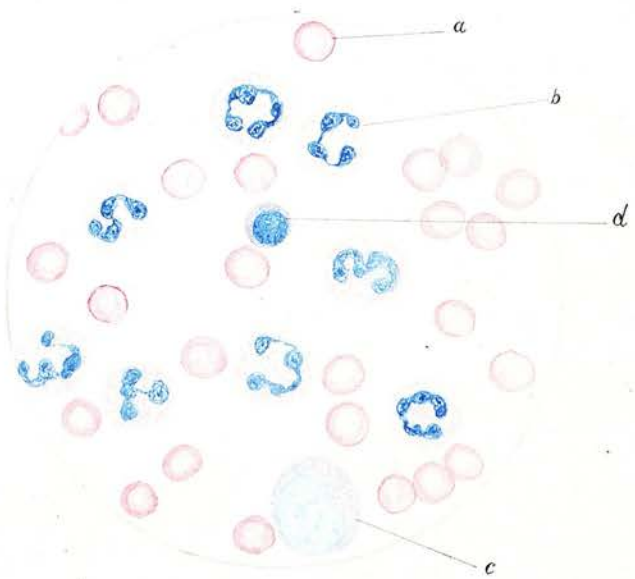

Fig. 3.

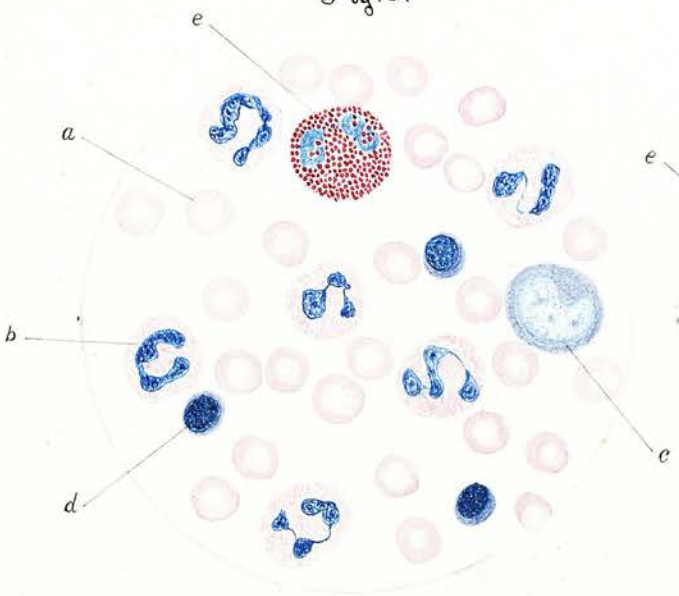

Fig. 4.