The Rôle of the Polymorphonuclear Leucocyte in the Clinical Pathology of Pulmonary Tuberculosis.

by

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Chapter I

Introductory

No branch of modern medical science has won so many advocates within recent years as Haematology.

It seems almost as if Georges Hayem's dictum "L'avenir appartient à l'hematologie," was being realised more and more; every year since the advent of haematology into the realm of clinical medicine there have been vast strides made in the study of the blood and its cellular elements. The reason for our clinical faith in the blood as a means for diagnosis in disease is due to a combination of circumstances, of which accuracy of detail is one. The term "peripheral haematologist" is an obsolete designation, for we have, in the study of the blood, a clue not only to the content of the vascular system as it is known to the anatomist and physiologist, but also to the more subtle processes in the haemopoietic organs, which constitute the factories where the cells, known to us as Erythrocytes and Leucocytes, are made. We are enabled, as it were, to tell the worth and ability of the factory and its workers from the quality and quantity of the output.

Considering, therefore, the nature of the evidence before us in a blood examination, it is really not surprising that rapid advances have been made in the study of Haematology.

When a tissue is diseased it is of the greatest importance for us to examine it microscopically. Such a procedure is, of course, denied us

in the large majority of cases of disease. The advent of radiography has been a boon to workers in renal, hepatic and pulmonary disorders; we have seen what we had suspected. A literature has been established in radiography and experts in this particular work, are now in a position to verify or modify clinical diagnosis, as the case may be. In other words, a branch of study which was at one time regarded as a valuable adjunct to clinical medicine and clinical surgery, has now become something more,— an invaluable asset, in many doubtful cases. Time was when the study of the blood cells in disease occupied a very inferior position in the routine of medical diagnosis. Gradually, however, the primary anaemias have been placed in the position of "splendid isolation", and have become regarded as clinical entities. There is still an indefinite category of "blood" diseases known as secondary anaemias, which are so-called because of the effect which the primary disease has upon the blood elements. It is on the blood in one particular form of secondary anaemia that my thesis dwells! The gradually increasing,— and oft conflicting,— evidence brought forward in connection with the leucocytes in pulmonary tuberculosis led me to make some observation on the blood of patients suffering from this disease, with the remote hope that a further clue to the clinical pathology of the disease might present itself. How far that hope has been realised remains to be seen, but from the results of the blood examinations herein

detailed, one cannot but conclude that a systemic infection like pulmonary tuberculosis sooner or later makes itself apparent by an alteration in the blood which, until comparatively recently, has received scant recognition from clinical pathologists and diagnosticians.

The Leucocyte Count in Health and Disease.

The total number of white cells in a cubic millimetre of human varies within normal limits from 5,000 to 8,000, but, for all practical purposes, counts up to 10,000 per cub. mm. may be considered normal

The polymorphonuclear leucocytes constitute 40 to 45 per cent. of the white cells of the blood in health, so that there are, approximately, 6,000 polymorphonuclear leucocytes in a cub. mm. of blood containing 8,000 white cells. The nucleus of the polymorphonuclear leucocyte is, as the name implies, polymorphous, i.e., it tends to assume various forms, sometimes being composed of one part, - unipartite, sometimes two parts, - bipartite, and so on.

It is well known that the number of leucocytes is variable in health According to Gulland and Goodall, digestion leucocytosis is a chronic condition which is ever present with us, the increase reaching its maximum four hours after food has been taken These observers claim that an increase of 1,000 to 1,500 per cub. mm. represents the increased leucocyte response to the digestion of food. Leider gives the average increase after the intake of food at 33% Although it does not follow that a similar physiological increase occurs

in disease, one must constantly bear in mind the effect of food in those who may be convalescent from a particular disease, or in those who have but a mild infection.

I have selected the leucocytosis of digestion as an example of an effect which is, more or less, being constantly produced. There are other causes of physiological leucocytosis, eg., pregnancy and parturition, exercise, massage, heat etc., but the digestion leucocytosis serves to illustrate the fact that in health there is a variation in the number of leucocytes in the circulating blood. That the normal increase of 33% in response to digestion may be exceeded is shown by the following table taken from von Limbeck.

TIME	LEUCOCYTE COUNTS.
11-15 a.m.	7,600.
12-15 p.m.	6,000.
1-15 p.m.	8,500.
3-15 p.m.	12,000.
5-15 p.m.	14,000.
7-15 p.m.	10,000.

After a Meal of Nitrogenous and Farinaceous Food.

In disease there is also a daily variation in the number of leucocytes, although the literature confirming this statement is not very abundant. It is an interesting fact that, despite the attention which has been given by haematologists to the physiological variations in the leucocyte count, comparatively little has been devoted to its daily fluctuations in diseased conditions. Jules F. Rey quotes a case of acute appendicitis in which he made the following observations:

Time	Symptoms.	No. of Leucocytes	Polymorphs.	Mononuclears.	Eosinophiles
9 a.m.	Abdominal pain; rigidity; vomiting.	22,400	88%.	12%.	0%.
1 p.m.		23,650	83·5%.	16%.	0·5%.
3 p.m.		20,100	80%.	19%	1%
6 p.m.		18,320	81%.	18%	1%.

In the above case, however, we are dealing with an acute inflammatory focus with a diminishing virulence of the causal organism, or an increased resistance on the part of the patient. In chronic diseases such as pulmonary tuberculosis, Hodgkin's disease, carcinoma of the stomach etc., there is some evidence to show that a variation in the daily count takes place. Martin has made some interesting observations on consecutive leucocyte counts in pulmonary tuberculosis in 40 cases, using the Thoma-Zeiss apparatus. He found that, as a rule, the number of leucocytes was less at night and in the early morning, and that there was a definite fluctuation in most of the cases. By the use of tables he shows that consecutive counts on patients with mitral disease, rheumatic fever, and pneumonia (after the crisis) are remarkably uniform as compared with those done on patients suffering from pulmonary tuberculosis. While he does not, in this paper, make any very special mention of the physical signs in the chests of the patients so examined, one concludes, nevertheless, that even in early cases of phthisis there is a considerable variation in the number of leucocytes found at different periods of the day.
Below are a few tables representing his observations.

Disease: Pulmonary Tuberculosis. Rt. Upper Lobe affected

Tubercle Bacilli present in Sputum

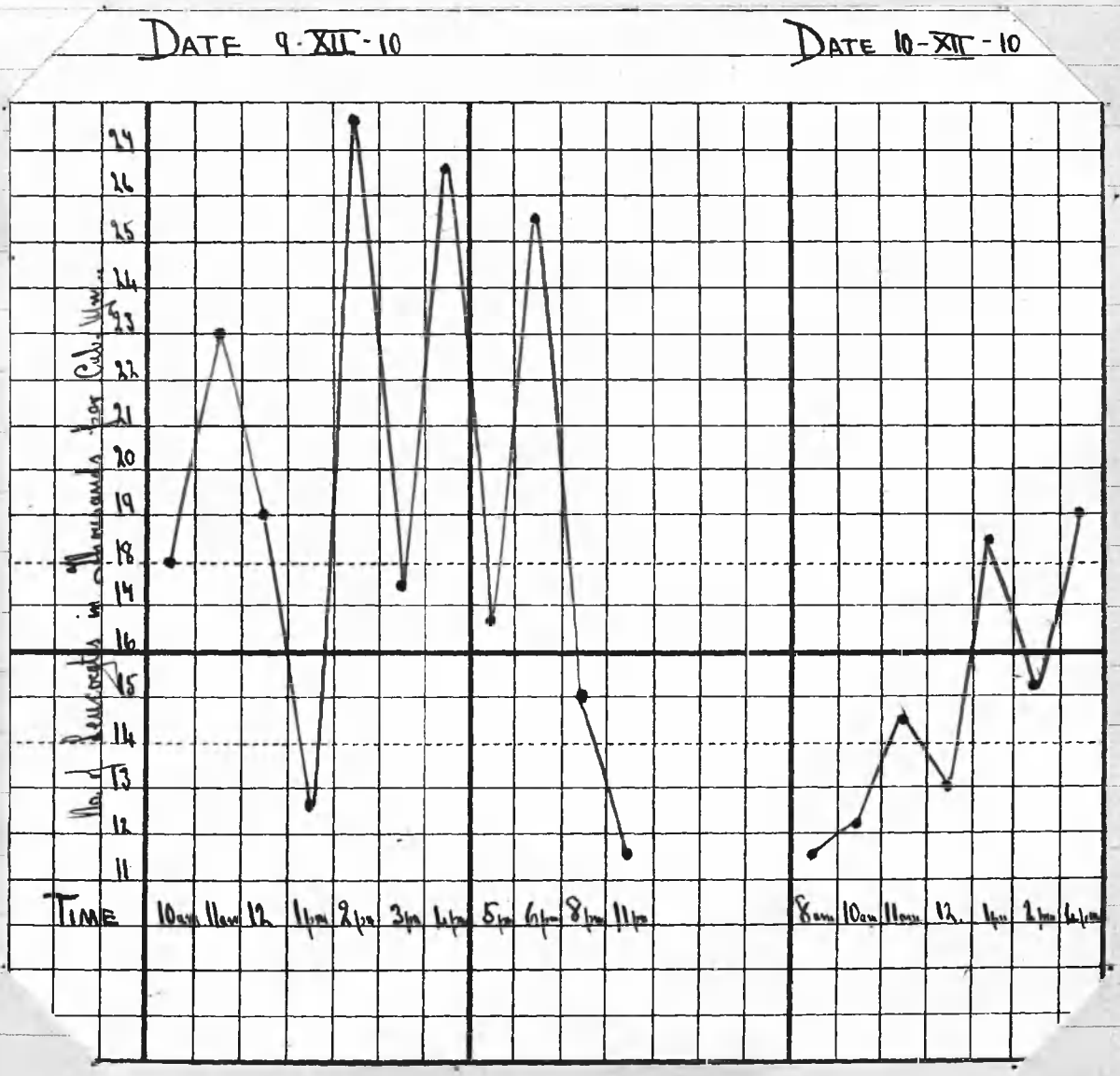
Time	Date	Leucocytes	Polymorphs per cent	Polymorphs per cub mm	Lymphocytes per cent	Lymphocytes per cub mm	Temperature
2 a.m.	28-8-10	9,400	42	6,768	28	2,632	94·0°
10 a.m.	do.	23,000	40	16,100	30	6,900	94·9°
2 p.m	do.	15,000	44	11,550	23	3,450	98·6°
6 p.m.	do.	14,700	44	10,878	26	3,822	98·8°
10 p.m.	do.	12,800	48	9,984	22	2,816	94·0°
2 a.m.	29-8-10	9,400	69	6,480	31	2,914	94·0°
10·30 a.m	do.	18,400	85	15,640	15	2,760	94·6°
2-30 p.m	do.	14,000	85	11,900	15	2,100	98·8°
8 p.m.	do.	13,000	68	8,840	32	4,160	98·9°
Midnight	do.	4,000	69	4,313	31	2,387	98·6°

Table Showing the Daily Variation in the Number of Leucocytes in the Blood (per cub mm.) MARLIN.

Disease: Pulmonary Tuberculosis.

Date	Time	Leucocytes per Cub. mm.
9-12-10.	10 a.m.	18,000.
"	11 a.m.	23,000.
"	12 a.m.	19,000.
"	1 p.m.	12,600.
"	2 p.m.	24,600.
"	3 p.m.	14,400.
"	4 p.m.	26,600.
"	5 p.m.	16,800.
"	6 p.m.	25,500.
"	8 p.m.	15,000.
"	11 p.m.	11,600.

Date	Time	Leucocytes per Cub. mm.
10-12-10	8 a.m.	11,600.
	10 a.m.	12,200.
	11 a.m.	14,500.
	12 noon.	13,000.
	1 p.m.	18,500.
	2 p.m.	15,200.
	4 p.m.	19,000.



A Graphical Representation of the Leucocyte Living in a Case of Phthisis

(MARLIN)

The above chart shows in a concise manner the daily variations occurring in the number of leucocytes in a case of phthisis. Martin's work is the fullest account of the phenomenon to be found in the literature, and it is for that reason I have quoted at length from his findings. Beyond the fact that a leucocytosis follows the injection of Tuberculin (B.E.), he is at a loss to explain this variation in the number of white cells. The only conclusion he comes to is that, although leucocytosis may follow tuberculin injection, yet the total number of white cells is frequently less than one might expect compared with counts on other days when no Tuberculin had been administered. In conclusion, he says, "..... After the injection of Tuberculin (B.E.) usually the patients feel sleepy all the next day; so perhaps, in some way, Tuberculin induces some influence on the blood akin to what may be at work during sleep."

Thomson has urged the advisability of a systematic research on what I have termed the "Leucocyte Living". In cases of carcinoma of the Stomach, Myositis Ossificans and Hodgkin's disease, he found a remarkable departure from normal in the number of leucocytes in the blood. This variation, like the one Thomson found in pulmonary tuberculosis, may have various interpretations, but Thomson does not feel justified in drawing any conclusions from his few observations. He suggests that a series of leucocyte counts, made daily over a considerable period of time, in various diseases, might help to put this remarkable variation on a more solid basis. Below is a chart made by Thomson from his findings in a

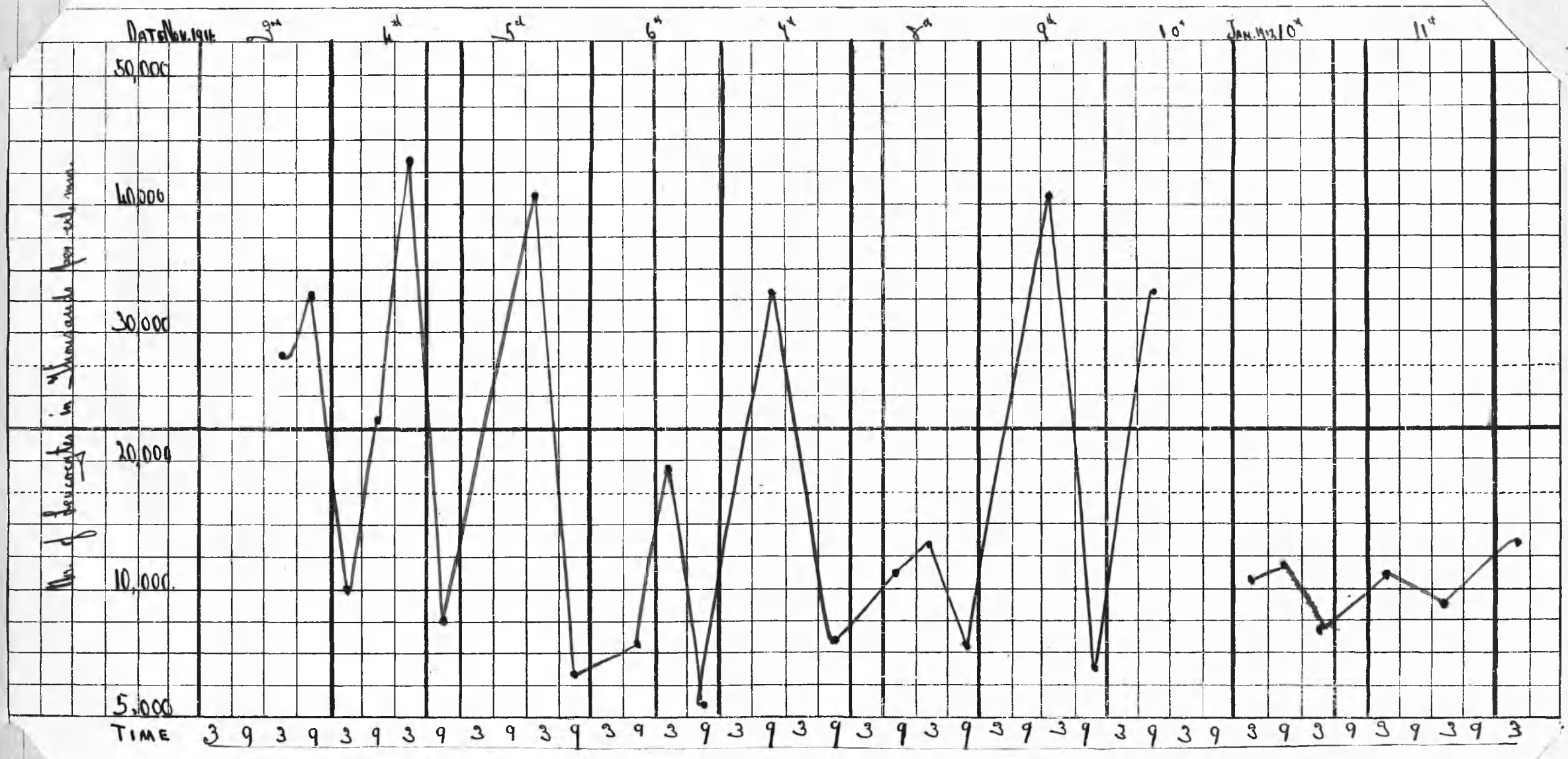
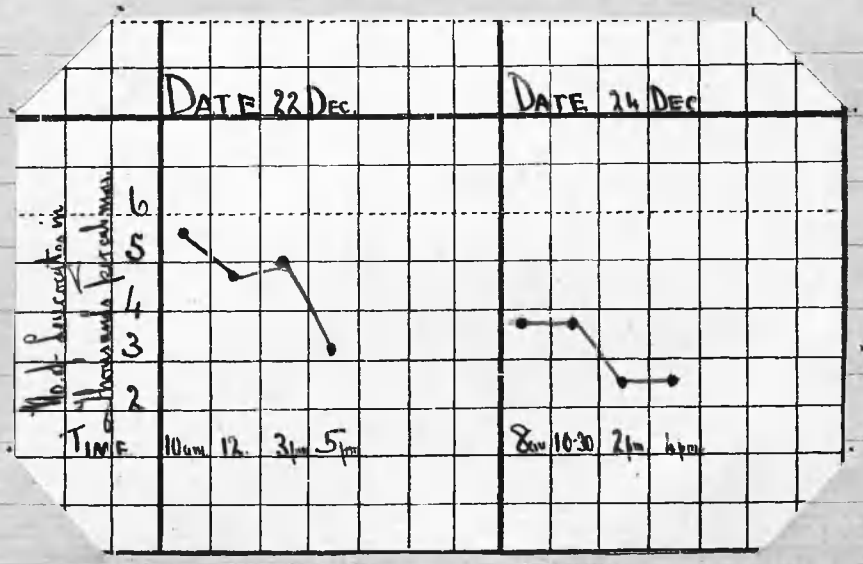


Chart showing the number of leucocytes per cub. mm. of blood taken at intervals daily on successive days. The patient was suffering from Carcinoma of the stomach. (THOMSON)

case of carcinoma of the stomach.

The only other record of consecutive daily estimations of the leucocytes which I am able to find in the literature is in a case of Cabot's, also quoted by Martin. This was a patient suffering from Miliary tuberculosis. I quote the case, not so much for its importance in demonstrating the phenomenon of leucopenia, as for its uniformity in the number of leucocytes. I give Cabot's findings in graphical order below.

DATE.	TIME	LEUCOCYTES per cub. mm.
Dec 22.	10 a.m.	5,625.
"	Noon.	4,425.
"	3 p.m.	5,000.
"	5 p.m.	3,125
Dec. 24.	8 a.m.	3,450
"	10-30 a.m.	3,450.
"	1 p.m.	2,500.
"	4 p.m.	2.500.



Cabot's case of Miliary Tuberculosis

Whatever interpretation we chose to put on the leucocyte count as a weapon for diagnosis in clinical medicine, it is evident that there are, at least, in some diseases, daily variations in the number of white cells found in the blood. The above case of miliary tuberculosis quoted from Cabot, as well as some cases of lymphosarcoma and carcinoma of the caecum registered by Thomson, demonstrate the the "leucocyte swing" is not a constant occurrence in disease.

My investigations on this particular point have been confined to pulmonary tuberculosis in its various stages and clinical manifestations. So impressed was I with the number, and variation in the number, of white cells observed per cub. mm. in some patients presenting sometimes very slight physical signs, that I decided to make observations on persons regarded as healthy. Before detailing my results, I should prefer to give the method I employed in arriving at my conclusions.

The instrument used was the Thoma-Zeiss haemocytometer, and the dilution employed, 1 in 20, for if the dilution be 1 in 10, one has sometimes a difficulty in making an accurate observation when the cells are numerous. All my examinations were made after treating the cells with a solution composed of Glacial Acetic Acid, 1 c.c.; Distilled Water 100 c.c.; and Methyl Green, q.s.; and one could, with a little care proceed to a differential count at the same time, for the nuclei are plainly visable in size and contour. This method of making a differential count, however, I did not employ.

The entire 400 squares were examined, and the total number of white cells enumerated. The counting chamber was now cleaned, and a second drop placed on

the slide; a comparison of the second estimation was then made with the first estimation. If these results differed by more than 300, a third examination was made of a third drop of diluted blood. The average of the three was then taken. Provided one takes care to get the cells uniformly distributed in the counting chamber, a third examination is rarely necessary.

The only point remaining to be mentioned is one which arises on the ethical side of the question. Few patients will tolerate an indiscriminate puncturing of the ear. When one takes into consideration the fact that fourteen and fifteen observations were made during the course of twenty-four hours in some cases, the objection to the routine by the patient has frequently to be tactfully dealt with by the operator. In most cases the difficulty, if such there happens to be, can be surmounted by using the finger as a source of blood, a method which I have used repeatedly. After several hundred examinations of the blood by the method described, I do not recollect a single case which has been complicated by inflammatory trouble, either subjective or objective.

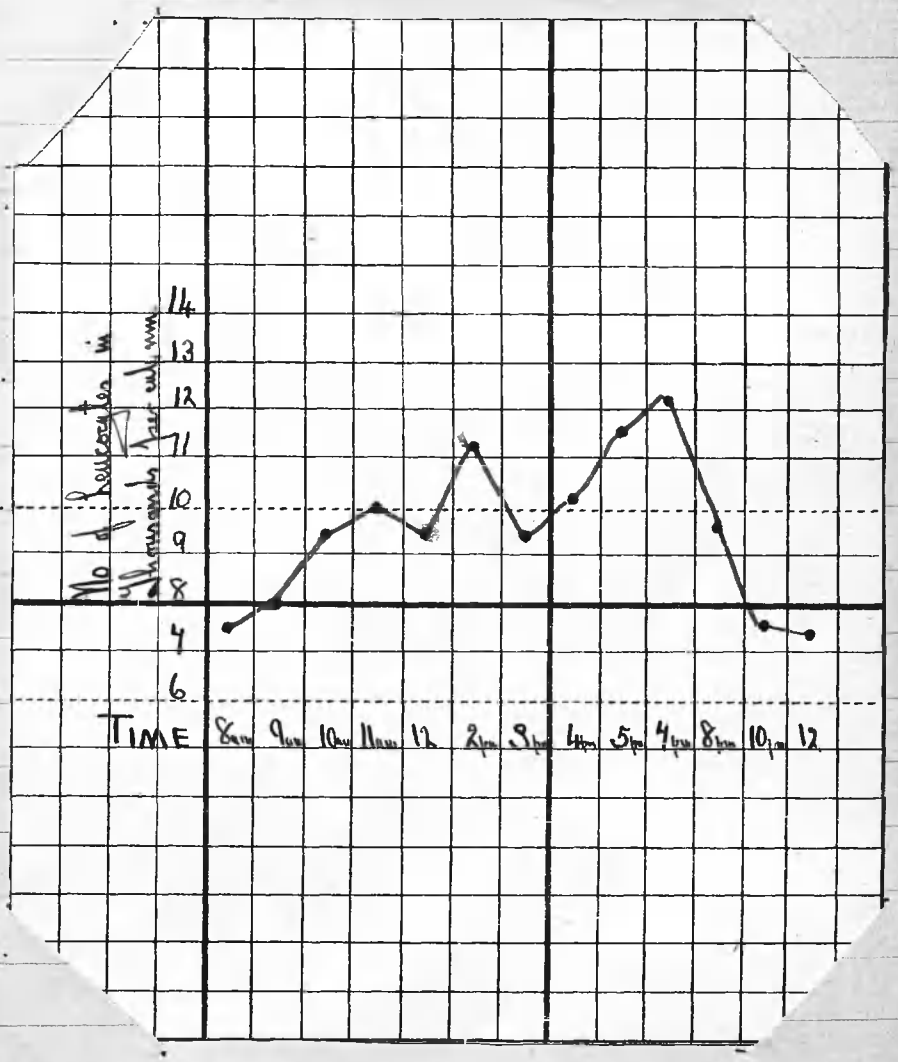
The Examination of the Leucocyte Count in the Healthy.

The first difficulty which presents itself in this connection is the proper selection of the patient. I chose three persons who had splendid past-histories in health and who were, at the time of examination, free from any ailment. Each was subjected to a careful clinical examination, of the chest in particular, and no departure from normal could be ascertained. All three were males; the ages were 25, 18 and 28 years

respectively. On two successive days counts were made at the times specified below, and in this way one was able to pronounce with a fair amount of accuracy, the normal leucocyte content of the blood. Since we are not, for the present, considering the various kinds of cells appearing in the blood, all mention of differential counts is meantime omitted, although it may be stated now that in the cases to be quoted, films were taken at special intervals. (See Chap. V.).

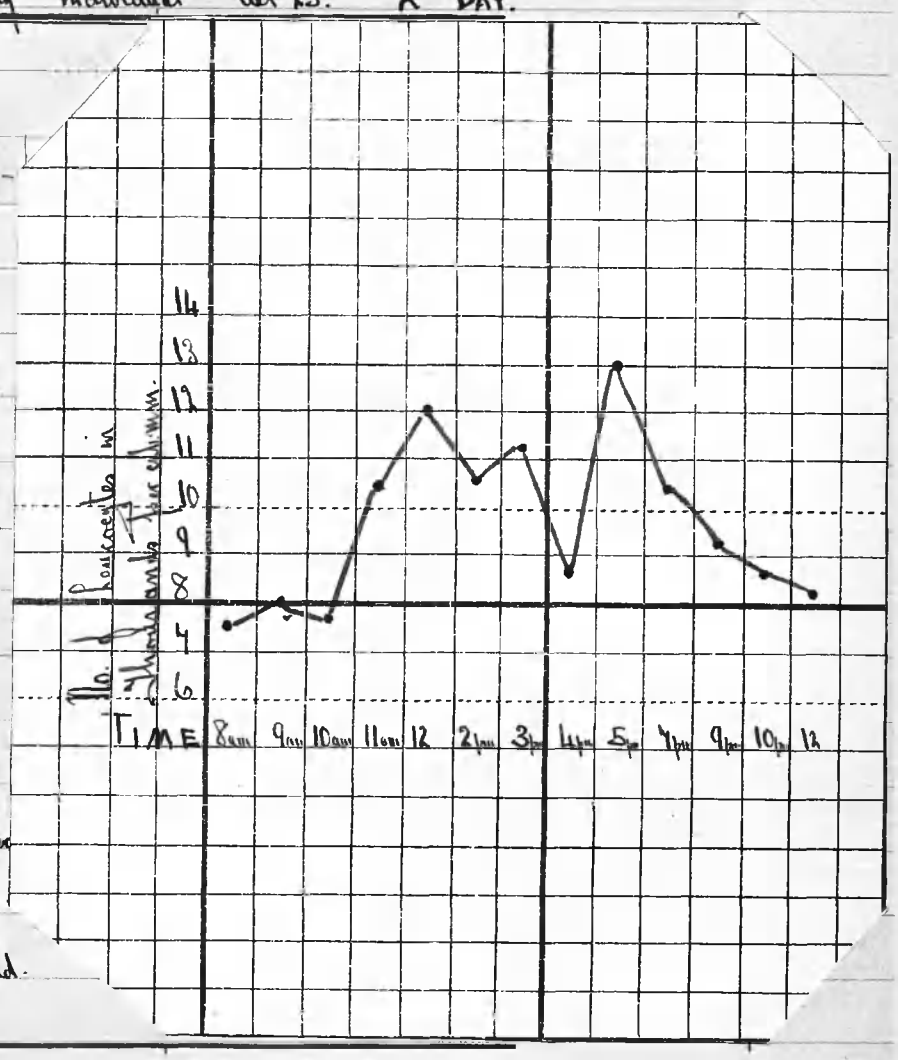
J.M. Healthy Individual Oct: 25. 1st DAY.

TIME	No. of Leucocytes per cub. mm.	NOTES
8 a.m.	7,500.	Before breakfast; up.
9 a.m.	8,000	after "
10 a.m.	9,500	
11 a.m.	10,000.	After 2 miles walk.
Noon.	9,500.	
2 p.m.	11,200	1 hr. after lunch.
3 p.m.	9,400	
4 p.m.	10,200.	After 4 miles walk.
5 p.m.	11,600	After tea
7 p.m.	12,100	After dinner.
8 p.m.	9,700	
10 p.m.	7,600	
Midnight.	7,400	After 1 hr. rest in bed.



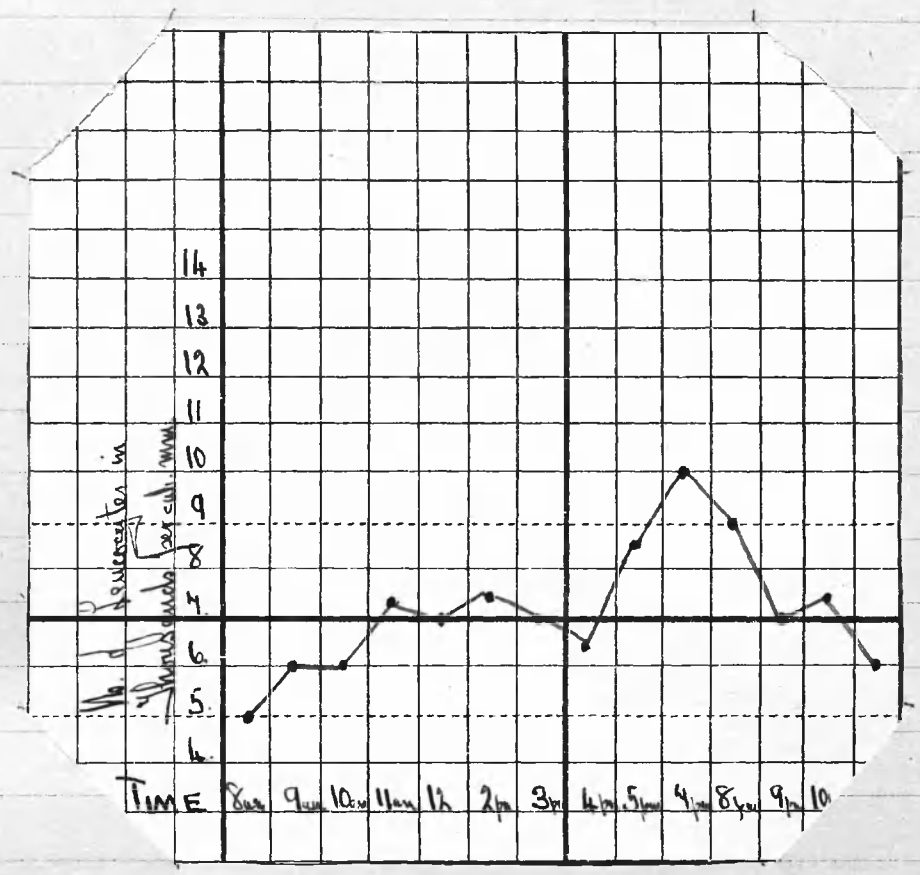
J. M. Healthy Individual Oct 15. 2nd Day.

TIME	No. of Leucocytes per cub. mm.	NOTES.
8am.		Before breakfast.
9am.		After "
10am.		
11 a.m.		After 2 miles walk.
12 noon.		
2pm.		1 hr. after lunch.
3pm.		
4pm.		
5pm.		After 6 miles walk and cold douche
7pm.		
9pm.		3 hrs. after dinner
10pm		After supper.
Midnight.		After 1 hr. rest in bed.

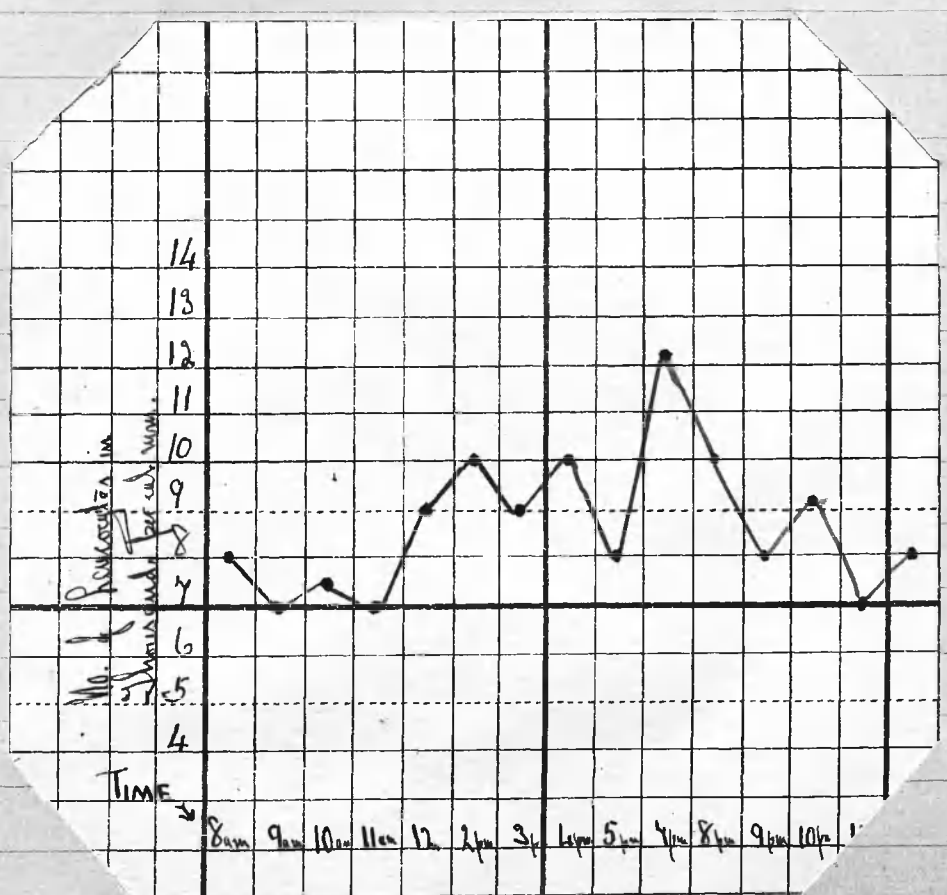


Below appear four charts which are self-explanatory. They represent successive leucocyte counts taken on successive days from two healthy persons. The events governing the daily routine of ~~the~~ ~~the~~ both people were essentially similar to those noted in connection with J. M., see above.

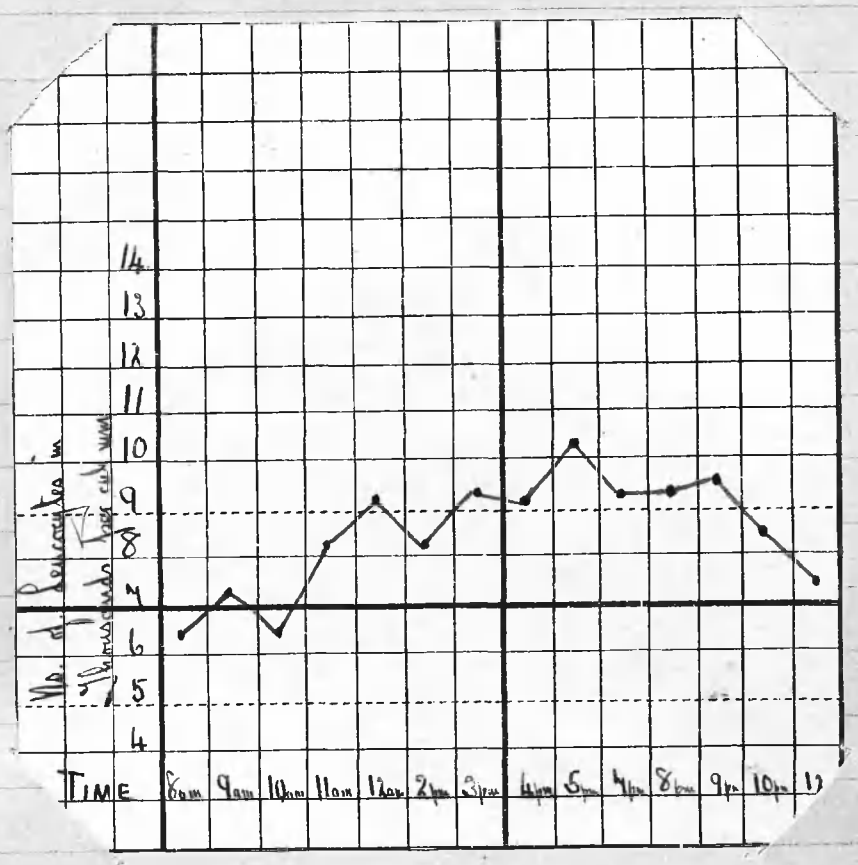
J.S. Healthy Individual. Oct 18. 1st Day.



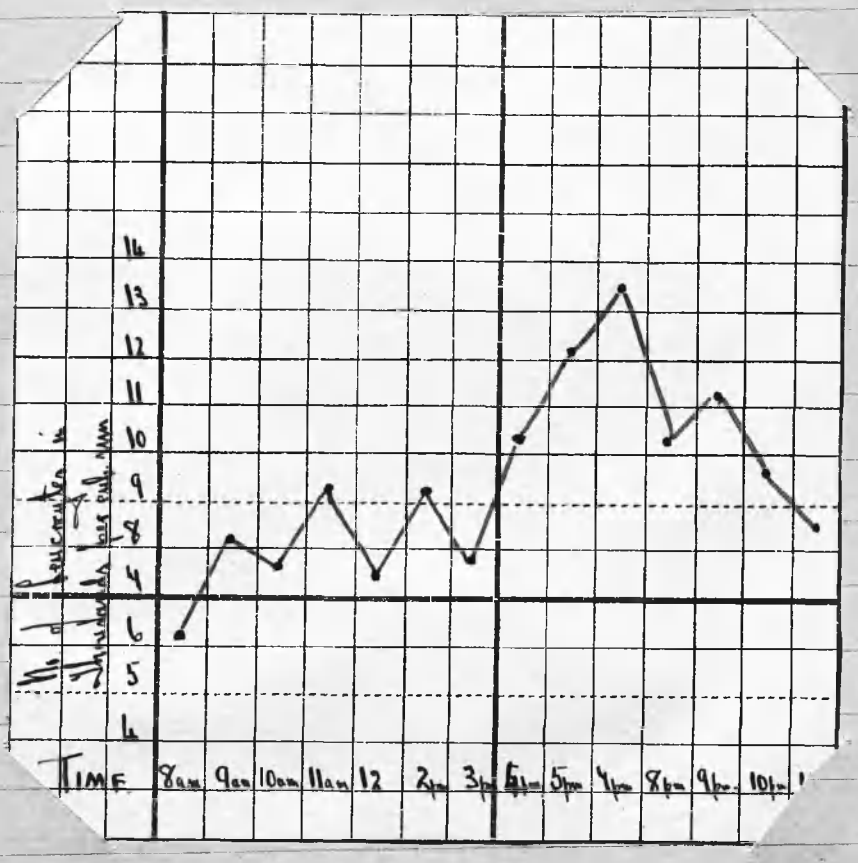
J.S. Healthy Individual. Oct 18. 2nd Day.



K.T. Healthy Individual. Aet 28. 1st Day.



K.T. Healthy Individual. Aet 28. 2nd Day.



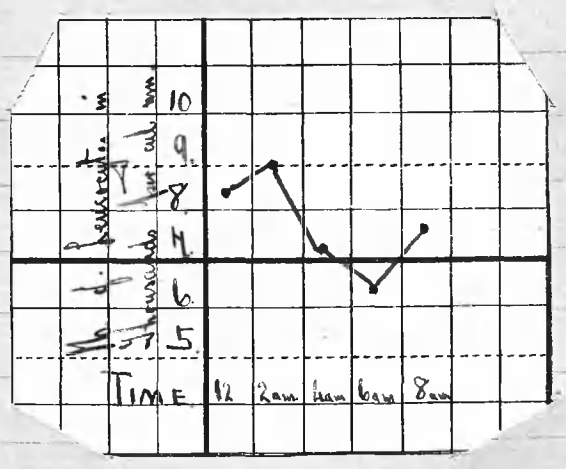
The foregoing tables are, I consider, worthy of reproduction if for nothing else than to serve as what may be taken as the normal leucocyte sizing. There are, however, several points which arise, and which demand some passing consideration. Firstly, there does not appear to be any definite "normal". In other words, each individual even in health, is a law unto himself. It is only a further example of the phenomenon of susceptibility which is characteristic of every tissue in the body. Just as, in some people, different physiological stimuli affect, say, the urinary secretion differently, so also, the stimuli which act as excitors of leucopoiesis have varying effects on the leucopoietic organs of different individuals. Although my results are remarkably constant yet there is no reason for the fact that the leucocytosis in Case I (J.M.) should reach its maximum at 5 p.m. after exercise and douche, and not at 4 p.m. as was the case in J.S. and K.T., the second and third persons respectively. The term "normal" as applied to the leucocyte count is extremely elastic and may lie anywhere between 4,000 at 10,000 cells per cub. mm.. Whatever stimulus or agent excites the leucocyte flow in normal person, it is apparent that it is liable to great variations in strength.

It has been said by some observers (Gallard and Goodall) that "digestion leucocytosis in varying intensity is usually a chronic condition in well-nourished people." This second consideration is shown by the charts preceding, and is merely another way of saying that the leucocyte count is higher during the day than at night and in the early morning. Assuming for the moment that immunity problems are left out of account in dealing with the healthy, (a proposition

which cannot be regarded in its entirety), we notice that at no time in the day does the leucocyte content fall below that registered between midnight and 9 a.m.. There is in fact, a commencing leucocytosis after breakfast which does not have any opportunity of falling owing to the periodical intake of food customary for those enjoying good health. The assertation of the leucocyte count in the very early morning hours has certain apparent inconveniences in its execution in those who are ill, but in order to determine the extent of the count during the usual sleeping hours, I made a few observations which now fall to be recorded. The findings represent the leucocyte counts in the normal healthy person. (J.M. Lit 25.)

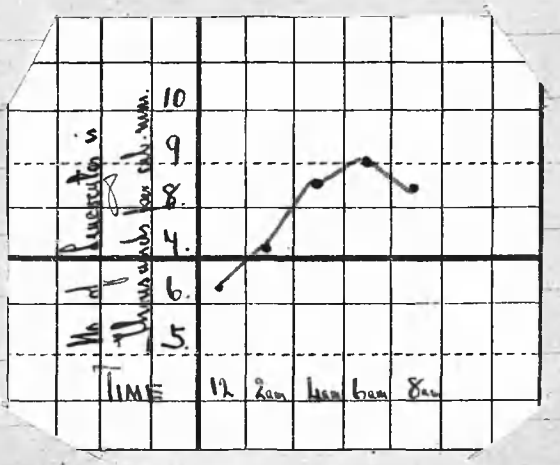
1st Series of Observations

TIME.	No. of LEUCOCYTES per Cub. mm.
12 Midnight.	8,400.
2 a.m.	9,000.
4 a.m.	4,200
6 a.m.	6,400
8 a.m.	4,800



2nd Series of Observations.

TIME.	No. of LEUCOCYTES per cub. mm.
12 midnight.	6,400.
2 a.m.	4,200.
4 a.m.	8,400.
6 a.m.	9,100.
8 am.	8,400.



The counts recorded last show that the number of leucocytes found when a person in health is at perfect rest in bed, and when the digestive processes are working at their minimum, is as low as the lowest count recorded in the daily counts registered in the preceding cases. The parallel to this in patients suffering from pulmonary phthisis will be dealt with later when successive counts from tuberculous patients are being considered. As to the nature of the digestive leucocytosis, I give no opinion at the present juncture, since we are not considering the different cells, but rather the leucocytes as a whole. The remaining point established by the counts in the healthy is that exercise, bathing, and massage all contribute to a temporary leucocytosis. The patients at Crossley Sanatorium are provided with capital douche rooms and adjacent cubicles where sprays and massage can be effectively carried out. The healthy patients from whom the above counts were taken were subjected to a fairly vigorous douching (hot and cold) and massage.

So far, then, there is nothing new to be taken from my findings. Nevertheless, in a process such as enumerating the cells of the blood, the personal factor enters into the process to a moderate extent, and I have deemed it wise to establish the normal before proceeding to the abnormal.

CHAPTER II.

Successive Leucocyte Counts in Pulmonary Tuberculosis.

Having considered somewhat briefly the range within which the leucocytes may vary in health, and the most common exciting factors of this variation, I turn now to consider in greater detail the limits, if there are any, to which the leucocyte may go in pulmonary tuberculosis. By the term "leucocytes" I mean the white cells of the blood without differentiation. Without underestimating the value of a differential blood count, I have adopted the plan of estimating and considering the entire leucocyte content of the blood, simply because the leucocyte count *per se*., has become a recognised clinical procedure, easy of undertaking, and requiring less skill than the differential count. The importance of the differential count, — and more especially the differential count of the nuclei of the polymorphonuclear leucocytes, — is to be discussed later, when the reason for delaying its discussion will be obvious.

In what follows immediately, one point is definitely established, viz: that a distinct "leucocyte swing" is a characteristic feature of certain cases of pulmonary tuberculosis, and that the "swing" bears a certain relation to the morbid processes going on in the system.

Case I. J.A.J. Aet. 22.

Date: 30-X-15.

Physical Signs: On percussion: Impairment of resonance, Rt. upper lobe, anteriorly and posteriorly.

On auscultation: R.M. increased in intensity over Rt. upper lobe, also posteriorly on Rt side at the level of the 4th dorsal vertebra. Crepitations abundant over Rt. upper lobe.

Remarks. Patient was admitted to Crossley Sanatorium on Oct. 16, 191
He was pale and very much emaciated. At first, the temperature was very unsteady, running between 98 and 100° F, but after 6 weeks rest in bed, the morning reading was 94.4 and the evening one 98.8°. The pulse rate did not come below 90 per minute despite the fact that the temperature remained normal.

Several examinations of the sputum were made, and on each occasion Tubercle Bacilli were found. The first examination was made on Nov. 4, 1916 and the last on Jan. 28, 1916. On every slide pus cells were very abundant. At the last examination, Tubercle Bacilli were scarcer than they had been hitherto, but staphylococci, streptococci and pneumococci were present. The patient's general condition improved; on Feb. 26, 1916, - two days after the last series of counts was taken, there was a great improvement noted in the local condition in the chest also.

On Feb. 29, 1916, at 2-15 a.m. there was a dramatic close to the case. Haemoptysis set in and was so profuse that the patient died in five minutes after the onset of the bleeding.

This case illustrates many points to which reference will be made in succeeding chapters.

Case I J.A.J Ht 22.

17-XII-15

Time	Leucocytes.	Remarks
2pm	33,000.	Rest in bed. Temp 99°; 1hr after Lunch
3pm	22,600.	" " " 99·2°
4pm	25,000	" " " 99·4°
5pm	14,800	" " " 99·6°
	Evening Meal at 6 p.m.	
7pm	30,600	" " " 99·4°
8pm	22,400	" " " 99·6°
10pm	25,200	" " " 99·8
11pm	19,200	" " " —

18-XII-15.

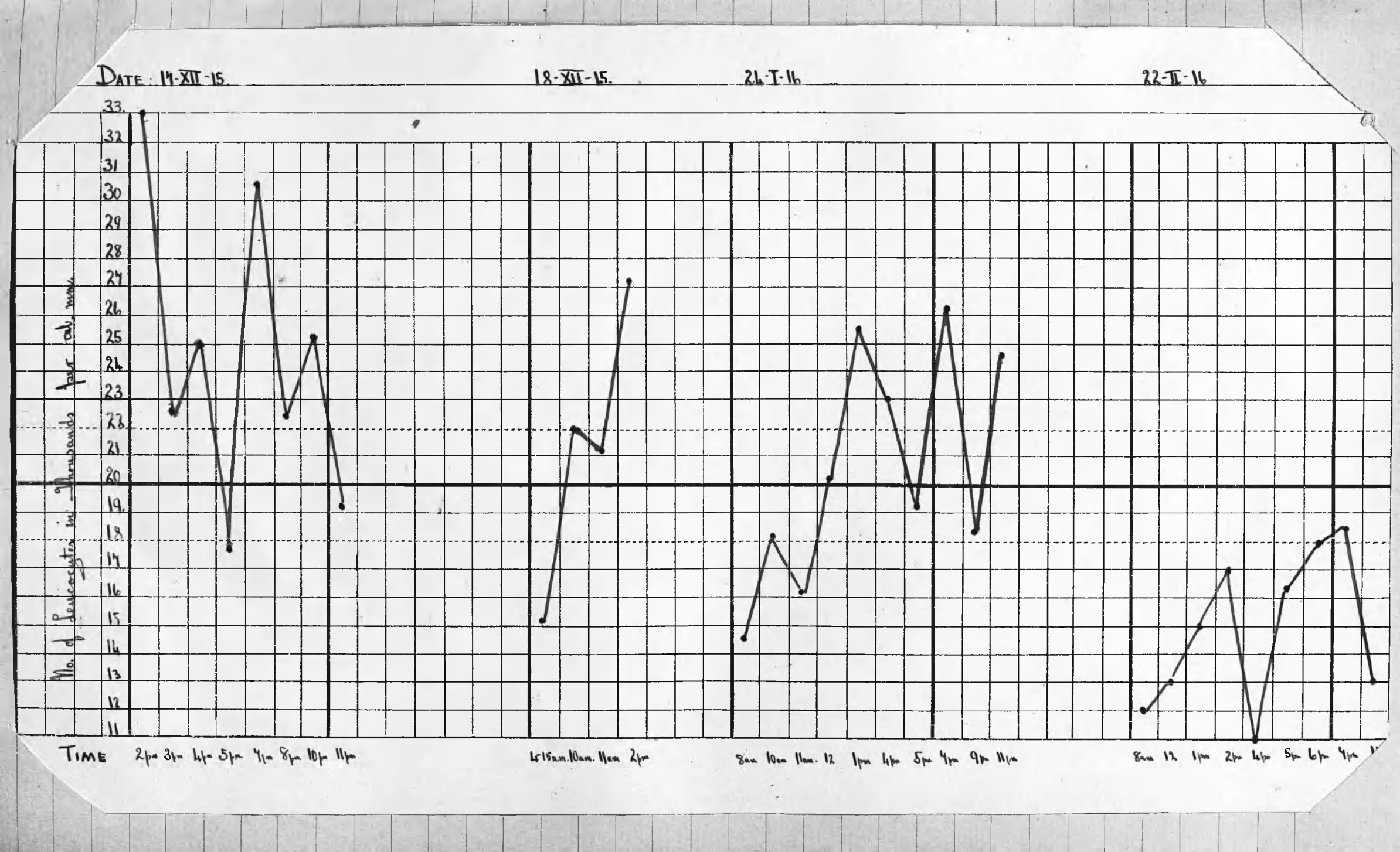
	Asleep for 6 hrs.	
4·15am	15,200	" " " 99·8°
	Breakfast at 9 a.m.	
10am	22,000	" " " 98·2
11am	21,200	" " " 98·4
	Lunch at 1 p.m.	
2pm	27,100	" " " 99·2

24·I·16

Time	Leucocytes	Remarks
8am	14,600	Patient up.
	Breakfast at 9 a.m.	
10am	18,200	Up, but couching.
11am	16,200	" " "
12noon	20,200	" " "
1pm	25,600	" " " (just after lunch)
4pm	23,000	" " "
5pm	19,200	" " "
	Evening Meal at 6 p.m.	
7pm	26,200	" " "
9pm	17,400	In bed ½ hr.
11pm	24,400	" "

22·II·16

Time	Leucocytes	Remarks
8am.	12,000.	Patient up for the day at 8 a.m.
12noon	13,000.	Temperature normal.
1pm.	15,000.	Two hours light
2pm.	14,000	exercise prescribed
4pm.	11,000	viz: 10 a.m – 11 a.m.
5pm.	16,400	2·20 pm – 3·20 pm
6pm	18,000	
7pm	18,500	
11pm	13,000	


DATE : 14-XII-15.
18-XII-15.
24-I-16
22-II-16
No. of Leucocytes in Thousands per cub. mm.
33
32
31
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12
11
TIME
2pm 3pm 4pm 5pm 7pm 8pm 10pm 11pm
5.15am. 10am. 11am 2pm
8am 10am 11am. 12 1pm 4pm 5pm 7pm 9pm 11pm
8am 12 1pm 2pm 4pm 5pm 6pm 7pm

Case II. L. B. Act: 14.

DATE: 9-XII-15.

Physical Signs — On percussion: Rt. upper lobe markedly impaired in resonance; also apex of lower lobe on left side.

On Auscultation: Breath sounds very harsh over whole upper lobe on rt. side. Numerous crepitations heard over rt. apex anteriorly down to the level of the third rib. Moist râles also heard at apex of lower lobe posteriorly on left side.

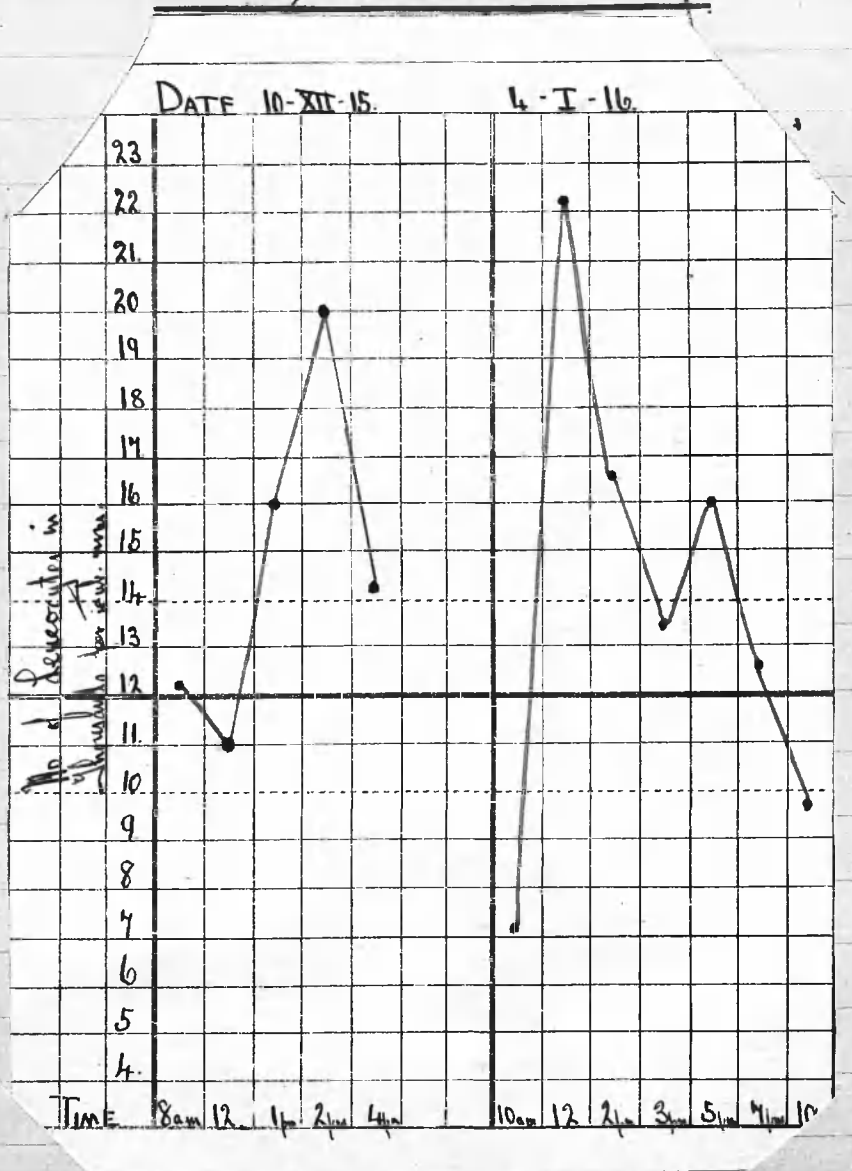
Remarks.

On admission patient was weak and pale. He had a moderately severe cough with a fair amount of expectoration which was found to contain pus cells, elastic tissue fibres, small diplococci and numerous Tubercle Bacilli.
The temperature never rose above 98.8° F. and the pulse rate was never below 90 beats per minute.
Apart from some dyspnoea on exertion patient was fairly well and was able to take a moderate amount of exercise in the shape of walking.
At short periodical examinations of the chest over a period of 3 months, it was noted that the physical signs were extending, although the temperature still remained low (98.8° F).

Case II L.B. Act 14.

10 - XII - 15.

Time	Leucocytes	Remarks.
8 a.m.	12,200.	—
12 noon.	11,000	3 hrs. after breakfast.
1 p.m.	16,000	Just after lunch.
2 p.m.	20,000	—
4 p.m.	14,200.	After walking ½ mile.
4 - I - 16.		
10 a.m.	4,200.	1 hr. after breakfast.
12 noon.	22,200.	3 hrs. " "
2 p.m.	16,600.	1 hr. " lunch.
3 p.m.	13,500.	—
5 p.m.	16,000	—
4 p.m.	12,600.	1 hr. after evening meal.
10 p.m.	9,800	After 2 hrs. rest in bed.



Case III L.D. Ward 23.

DATE. 18-XII-15.

Physical Signs. On Percussion. Both sides of the chest back and front dull to percussion.

On Auscultation. Respiratory murmur very harsh over entire chest especially on left side where whispering pectoriloquy could be heard over the upper lobe. Numerous moist sounds accompanied both inspiration and expiration in both upper lobes.

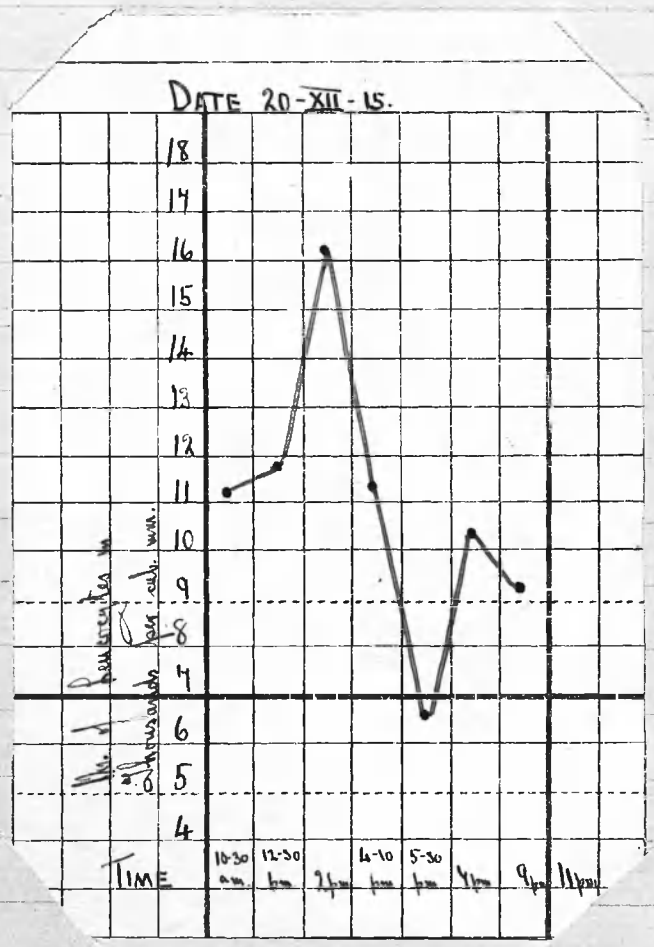
Remarks.

This patient presented an extremely emaciated appearance. The temperature was, on an average, between 99.4 and 100.4° F. She had a moderate cough with a fair amount of expectoration. The latter was examined and found to contain Tubercle Bacilli in large numbers, the average being about fifty to sixty in the field. No secondary organisms of any description could be found either intra- or extracellularly. No elastic tissue fibres were found. The examination of the sputum was made repeatedly with the same results. Pus cells were present but comparatively scarce.

Case III L. D. Act 23.

20-XII-15.

TIME	LEUCOCYTES.	REMARKS.
10-30 a.m.	11, 200	Rest in bed. 1½ hrs. after breakfast.
12-30 p.m.	11, 800	" " " .
2 p.m.	16, 200	" " " ; 1 hr. after lunch.
4-10 p.m.	11, 400	" " " ;
5-30 p.m.	6, 600	" " "
7 p.m.	10, 400	" " " ; 1 hr. after evening meal.
9 p.m.	10, 000	" " "
11 p.m.	9, 400	" " " ; asleep for 1 hr.



Case IV. J. E. Y. Aet. 28.

DATE 6-XII-15.

Physical Signs. On percussion: Marked impairment in resonance over both upper lobes anteriorly. The left side posteriorly also impaired in resonance, while the upper lobe on the rt. side posteriorly was definitely dull.

On Auscultation: Respiratory murmur exceedingly harsh at both apices. On left side anteriorly and posteriorly a few crepitations and numerous rhonchi were heard, while the R.M. amounted to pectoriloquy. The vocal resonance was increased all over the chest.

Remarks.

This patient ran a normal temperature from the time of his admission till the time of his departure from the Sanatorium. There was a small quantity of sputum expectorated daily. Out of six examinations made at fortnightly intervals, tubercle bacilli were found five times in large numbers; pus cells were always numerous, and small diplococci abundant. None of these organisms were noted to be intracellular.

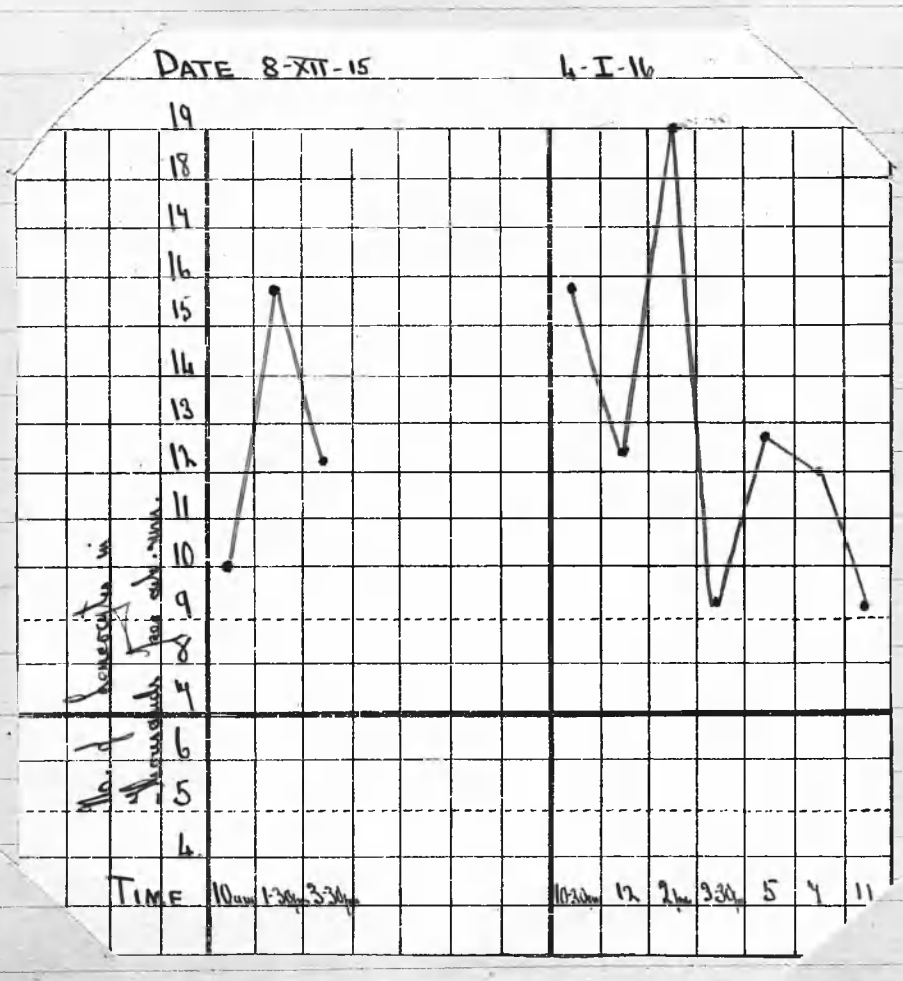
Case IV. J. E. ♀. Act. 28.

8-XII-15.

Time.	Leucocytes.	Remarks.
10 a.m.	10,000.	1 hr. after breakfast.
1-30 p.m.	15,800.	½ hr. " lunch.
3-30 pm	12,200	After 1 hr. light exercise.

4-I-16.

10-30 a.m.	15,800.	1½ hrs. after breakfast.
12 noon.	12,400.	
2 p.m.	19,000.	1 hr. " lunch.
3-30 p.m.	9,400.	After 1 hr. light exercise.
5 p.m.	12,800.	
9 p.m.	12,000.	1 hr. after evening meal.
11 p.m.	9,200.	After 1½ hr. rest in bed.



Case V. T. D. Ad: 22.

DATE: 9-XII-15

Physical Signs On percussion: Rt. apex dull anteriorly and posteriorly.
On auscultation: Breath sounds very harsh over both upper lobes, especially the left. On the rt. side posteriorly towards the base of the lung the B.M. was also distinctly harsh. Numerous crepitations were heard over both upper lobes anteriorly, and over the left upper lobe posteriorly. There was friction in the region of the apex of the lower lobe on the left side.

Remarks. Patient had a severe cough accompanied by a thick viscid expectoration. The temperature swung between 99.8 and 99.4° F. with regularity. The sputum was examined four times in December and each time tubercle bacilli were found as were also many pus cells. Small and larger diplococci were innumerable at the second, third and fourth examinations and small chains of cocci, presumably streptococci were observed, as well as numerous clumps of staphylococci. There were, then, all the evidencies of mixed infection at here.
On Dec. 24, 1915, another examination of the chest was made and the lesion was found to be active and progressive.

Case V. Y. D. Act 22.

11-XII-15.

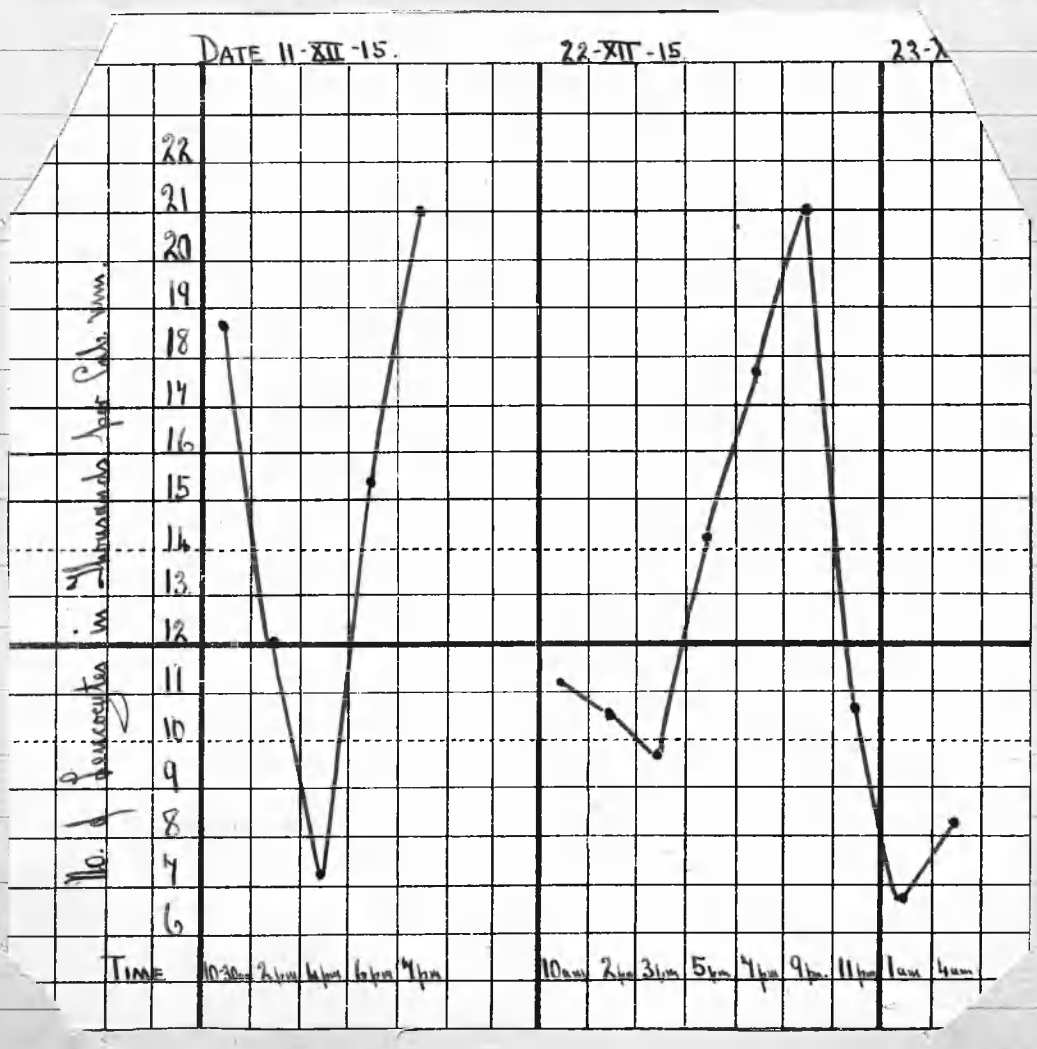
Time	Leucocytes	Remarks.
10-30 a.m.	18,600	Rest in Bed; Temp. 99.8°F. 1½ hrs after breakfast
2 p.m.	12,000	" " "; 1 hr. after lunch.
4 p.m.	4,200.	" " "; Temp. 98°F.
6 p.m.	15,400	" " "; " 99°F.
9 p.m.	21,000	" " "; " 99.4°F.; 1 hr after Evening meal

22-XII-15.

10 a.m.	11,200	Patient up.; 1 hr after breakfast.
2 p.m.	10,600	" " "; 1 hr. " lunch.
3 p.m.	9,800	" " ";
5 p.m.	14,200	Rest in bed;
7 p.m.	14,800	" " "; 1 hr after Evening Meal.
9 p.m.	21,000	" " "
11 p.m.	10,800	" " "

23-XII-15.

1 a.m.	6,800	" " "; after 3 hrs. sleep.
4 a.m.	8,200.	" " "; " 6 " "



Case VI. W.J. Act 19.

DATE. 4-I-16.

Physical signs On percussion: Both apices dull to percussion, more especially the right, anteriorly and posteriorly.

On auscultation: Fine crepitations heard at both apices, but on the rt. side they could be heard as low down as the fourth rib anteriorly, and down to the level of the 4th dorsal vertebra posteriorly. Scattered rhonchi were heard all over the chest At the left base posteriorly there were a few fine crepitations.

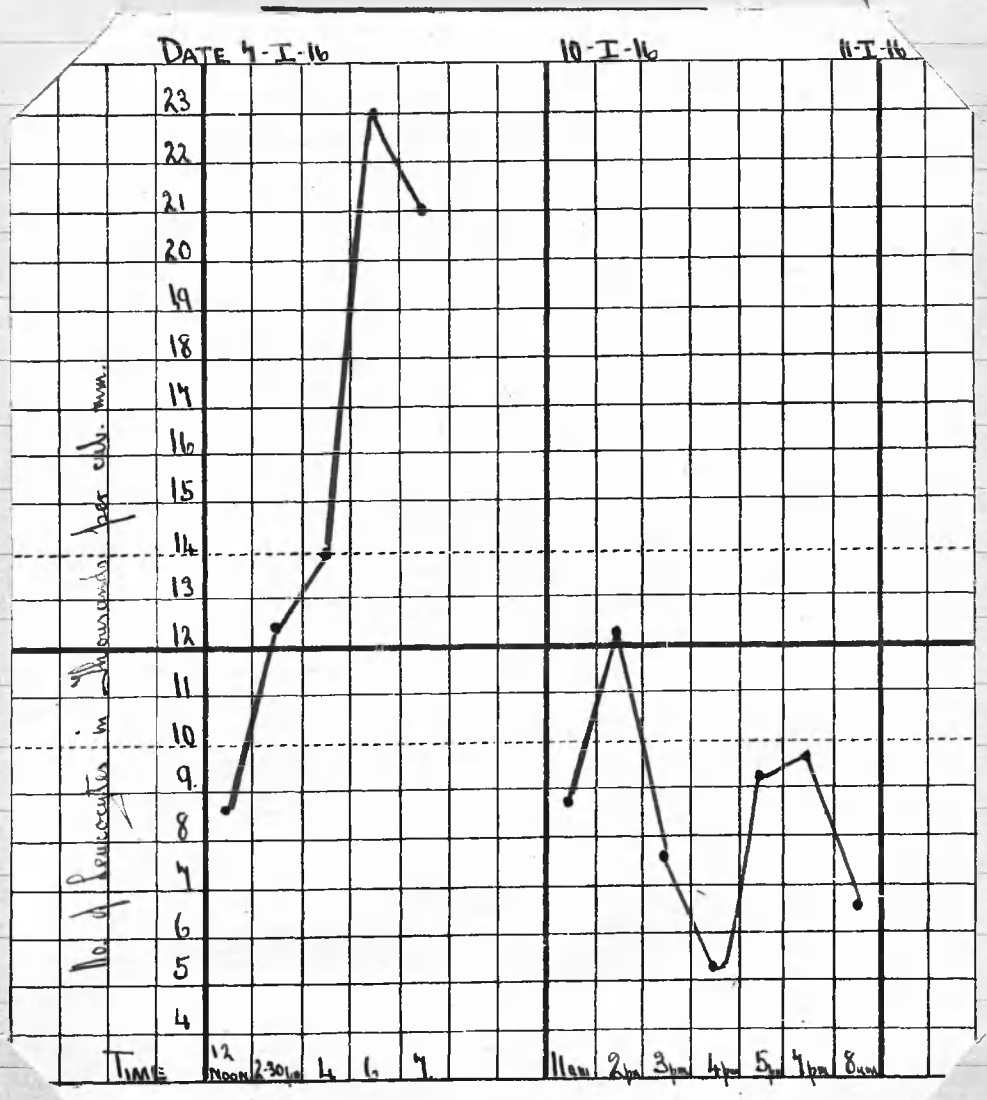
Remarks.

This patient had a normal temperature during the period of his stay in the Sanatorium. He had a violent spasmodic cough with a scanty expectoration. At the first examination of the sputum (Dec. 1st 1915), no tubercle bacilli could be found but pus cells were very numerous. On Dec. 31st, 1915, Tubercle Bacilli were found associated with pus cells, but no other organisms were detected. The pulse rate rarely rose above 84 per. minute.

Case VI. W. J. Ward 19.

4-I-16.

Time	Leucocytes	Remarks.
12 noon.	8,600	Patient up: on light exercise.
2-30 p.m.	12,400	1½ hr. after lunch.
4 p.m.	14,000	—
6 p.m.	23,000	After 6 miles walk and cold douche.
7 p.m.	21,000	1 hr. after evening meal.
10-I-16.		
11 a.m.	8,800	2 hrs. after breakfast.
2 p.m.	12,200	1 hr. " lunch.
3 p.m.	4,600	—
4 p.m.	5,200	—
5 p.m.	9,400	—
7 p.m.	9,800	1 hr. after evening Meal.
11-I-16.		
8 a.m.	6,600	Before rising.



Case VII J. J. Act 18.

DATE 16-XII-15.

Physical Signs: On percussion: There was no impairment in the percussion note in any part of the chest.

On auscultation: The respiratory murmur was normal all over the chest. No adventitious sounds were audible and the air-entry was good.

Remarks.

This boy was sent to the Sanatorium as a suspected case of tuberculosis of the lungs. On one occasion only was I able to get any sputum for examination, and then it was quite negative for Tubercle bacilli; a few pus cells were found, but no organisms of any kind could be detected. The evening temperature never rose above 98·6° F. except on one occasion, after a hot bath, when the thermometer registered 99·6° F.

Case VII. G. J. Act. 18.

14-XII-15.

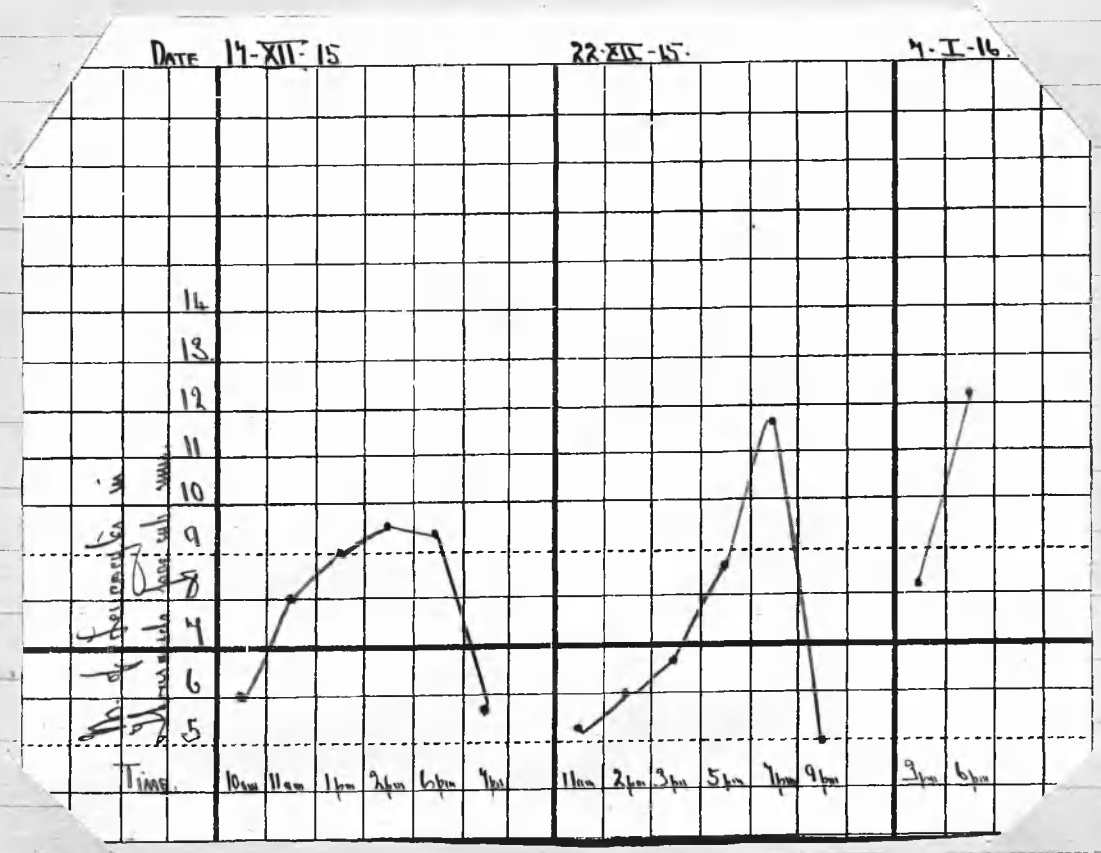
Time.	Leucocytes.	Remarks.
10 a.m.	6,000	1 hr. after breakfast.
11 a.m.	8,000	After 1 hr. light exercise
1 p.m.	9,000	Just before lunch.
2 p.m.	9,600	1 hr. after "
6 p.m.	9,400	Just before Evening Meal.
7 p.m.	5,800	1 hr. after " "

22-XII-15.

11 a.m.	5,400	After 1 hr. light exercise.
2 p.m.	6,000	1 hr. after lunch.
3 p.m.	6,800	
5 p.m.	8,800	After 2 hr. exercise, including golf.
7 p.m.	11,800	1 hr. after Evening Meal.
9 p.m.	5,000	After 1 hr. rest in bed.

4-I-16.

3 p.m.	8,200.	2 hr. after lunch.
6 p.m.	12,200.	After 6 mile walk and cold douche.



Case VIII Y. Den. Ref 18

DATE 16·XII·16

Physical Signs On percussion. No definite dulness to be made out in any part of the chest, but the percussion note was more or less impaired all over.

On auscultation. The breath sound was very harsh over both apices. The outstanding feature of the case was, however, the large numbers of rhonchi which were heard at different times all over the chest.

Remarks.

In this case, the patient's chief symptom was cough. He had no other symptom which might be regarded as pathognomonic of phthisis. The expectoration was examined several times with the same result, - numerous pus cells and small diplococci, but no tubercle bacilli. Under sanatorium regime he improved markedly, and for a few weeks at a time the cough would disappear. During these periods of well-being, the chest was correspondingly clear, but on the slightest provocation, the rhonchi would return and the expectoration become profuse. Coincident with the little bouts of bronchitis, the temperature became slightly elevated, - 99 to 99.4° F.

The counts recorded in connection with this case were taken during one of these attacks from which the patient suffered.

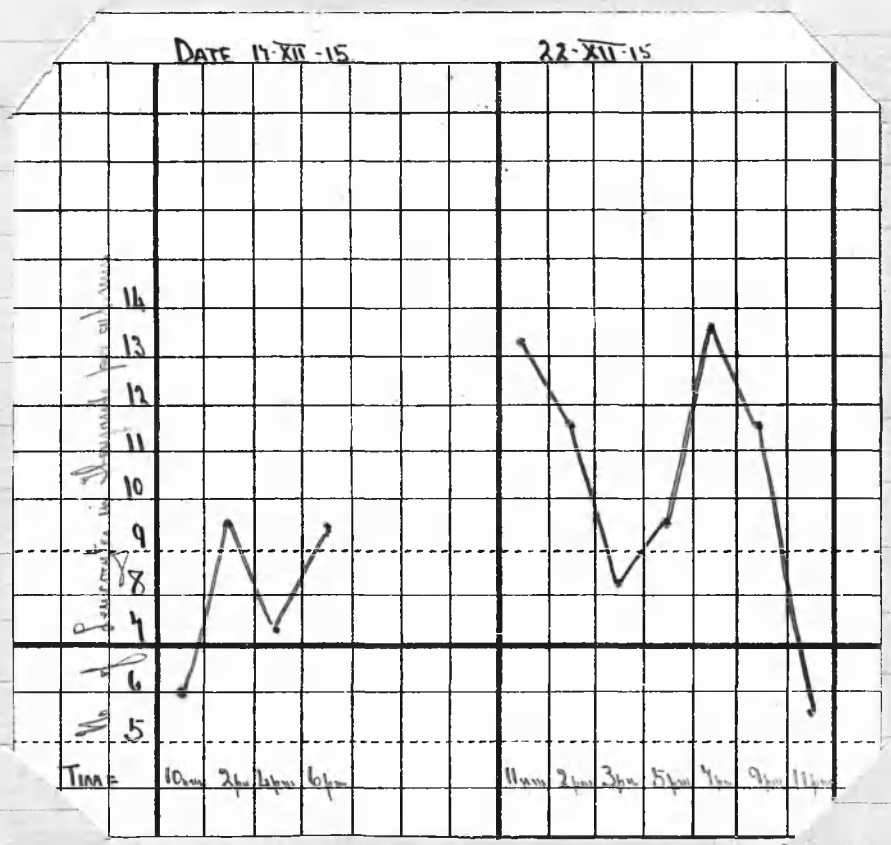
Case VIII J. Den.. Act 18.

14-XII-15.

Time	Leucocytes	Remarks.
10 a.m.	6,000	1 hr.. after breakfast.
2 p.m.	9,600	1 hr. .. lunch.
4 p.m.	4,400	After two hours bouching.
6 p.m.	9,600	Just before Evening Meal.

22-XII-15.

11 a.m.	13,400	2 hr. after breakfast.
2 p.m.	11,600	1 hr. after lunch.
3 p.m	8,200	—
5 p.m.	9,600.	—
4 p.m.	13,600.	1 hr. after Evening Meal.
9 p.m.	11,600.	After 1 hr. in bed.
11 p.m.	5,600.	" 3 .. " "



Case IX. J. W. Aet., 39.

DATE. 18-XII-15.

Physical Signs. Rt. apex dull anteriorly and posteriorly, on percussion. On auscultation. Crepitation heard all over the upper lobe on rt. side anteriorly and posteriorly.

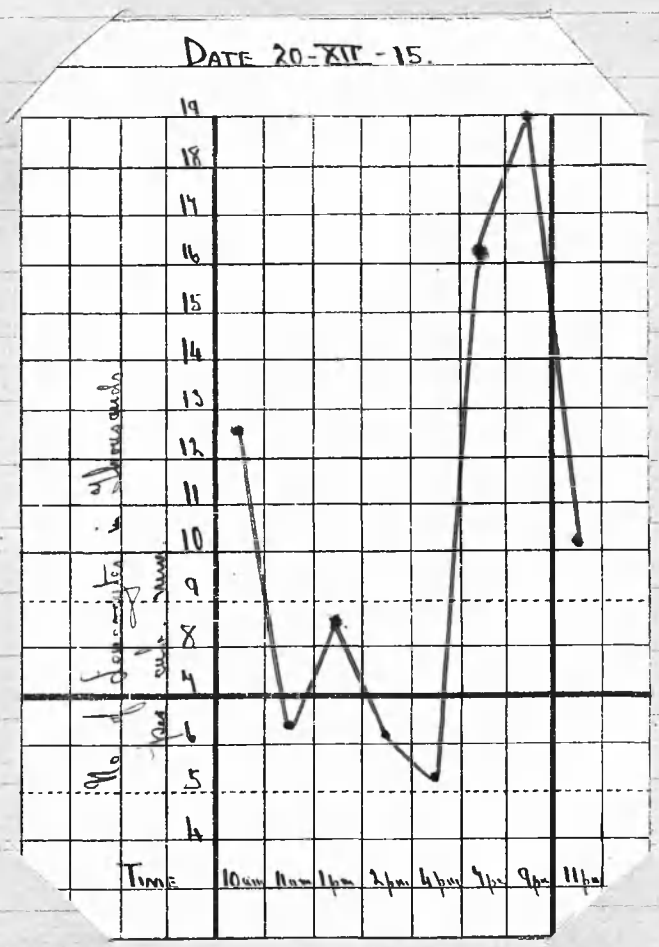
Remarks

The larynx was affected in this case. Both cords were infiltrated, and the left partially fixed by adhesions. There was a troublesome cough, and a moderate amount of expectoration. The sputum contained tubercle bacilli in large numbers, and pus cells were very abundant. A few staphylococci and streptococci were also found. Patient put on weight steadily, and the temperature remained normal throughout, except on one occasion, after a six-mile walk, when it rose to 99° F.

Case IX. J. W. Act 39.

20-XII-15.

Time	Leucocytes	Remarks.
10 a.m.	12,600.	1 hr. after breakfast.
11 a.m.	6,400	—
1 p.m.	8,600	Just before lunch.
2 p.m.	6,200	1 hr. after lunch.
4 p.m.	5,400	After 1 hr. digging.
4 p.m.	14,200	1 hr. after Evening Meal: Temp. 99
9 p.m.	19,000	—
11 p.m.	10,200.	After 2 hr. rest in bed.



Case X A. J. Act 25.

DATE 15-XII-15.

Physical Signs. On percussion. Both apices were dull to percussion, anteriorly and posteriorly. This dulness was, however, more marked posteriorly.

On auscultation. The respiratory murmur was weak all over the chest; at the left apex, one or two fine crepitations were heard at the end of inspiration.

Remarks.

Patient was very emaciated on admission. He complained more of fatigue and general weakness than of cough and expectoration. The general weakness was reflected more particularly on the digestive system where examination of the stomach revealed very audible succussion.

By the month of January, the body generally had regained its lost tone and stomach symptoms, both objective and subjective, subsided.

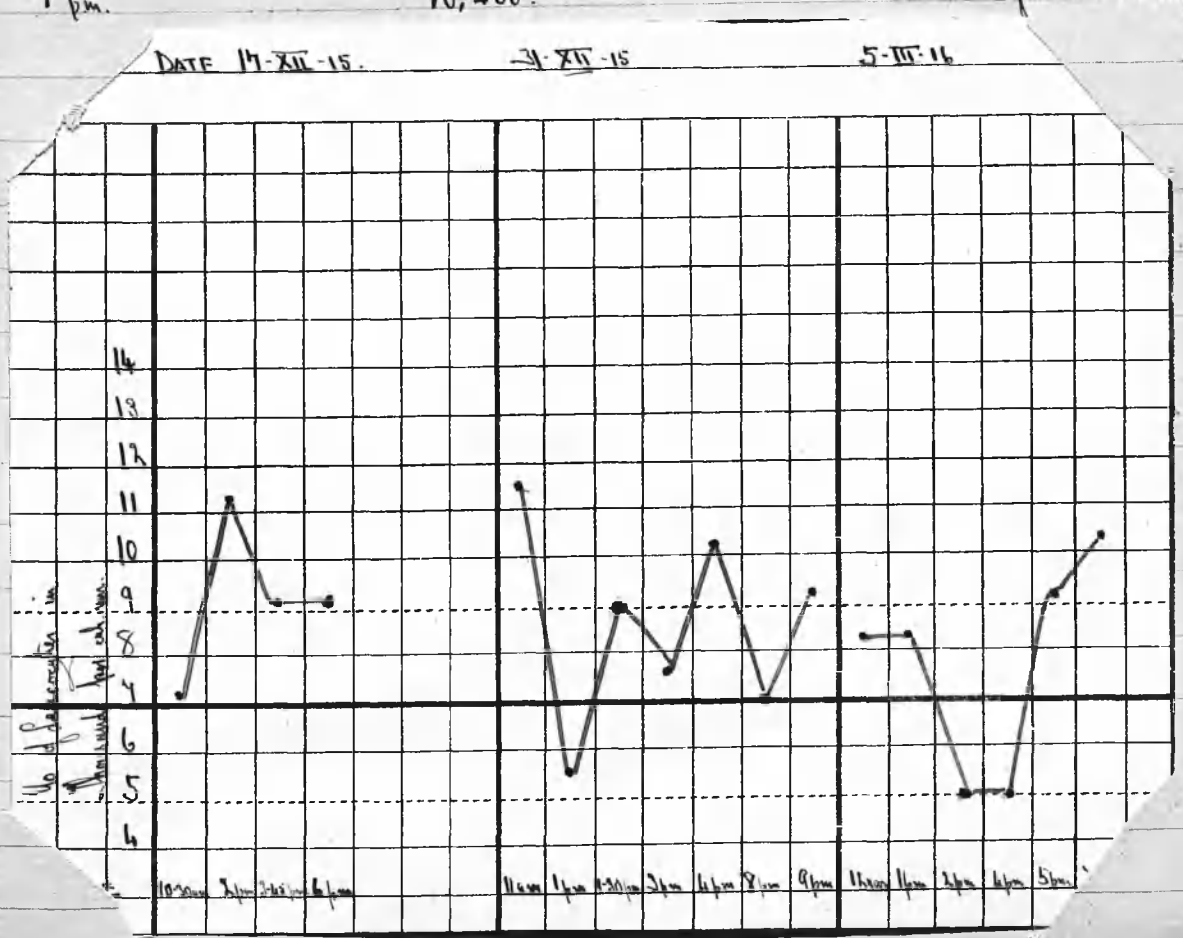
On Dec. 24, 1915 tubercle bacilli were found in the sputum, but I made no further comment on the latter for that date.

On Feb. 8, 1916 pus cells were numerous, no secondary organisms could be detected, and Tub. Bacilli were found again.

The patient was discharged on March 4, 1916., feeling perfectly well, although bacilli were still present in the sputum. The temperature, after the first few days after admission, ran a normal course.

Case X A. Y. Act. 35.

Time	Leucocytes	Remarks.
17-XII-15.		
10-30 a.m.	4,200	1½ hr. after breakfast; up and about.
2 p.m.	11,400	1 hr " lunch.
3-45 p.m.	9,200	After 1 hr. light exercise.
6 p.m.	9,200.	Just before Evening meal.
31-XII-15		
11 a.m.	11,600.	2 hrs. after breakfast.
1 p.m.	5,600	Just before lunch.
1-30 p.m.	9,000	" after "
3 p.m.	4,600	—
4 p.m.	10,200	—
8 p.m.	4,000	2 hrs. after Evening Meal
9 p.m.	9,400.	After 1 hr. rest in bed.
5-III-16.		
12 noon.	8,400	3 hrs after breakfast.
1 p.m.	8,400	Just before lunch.
2 p.m.	5,000	1 hr. after "
4 p.m	5,000	—
6 p.m.	9,200	—
4 p.m.	10,400.	1 hr after Evening Meal.



Case XI. E.J. Ast. 23.

DATE. 22-XII-15.

Physical Signs. On percussion. Both apices lacking in normal resonance anteriorly and posteriorly.

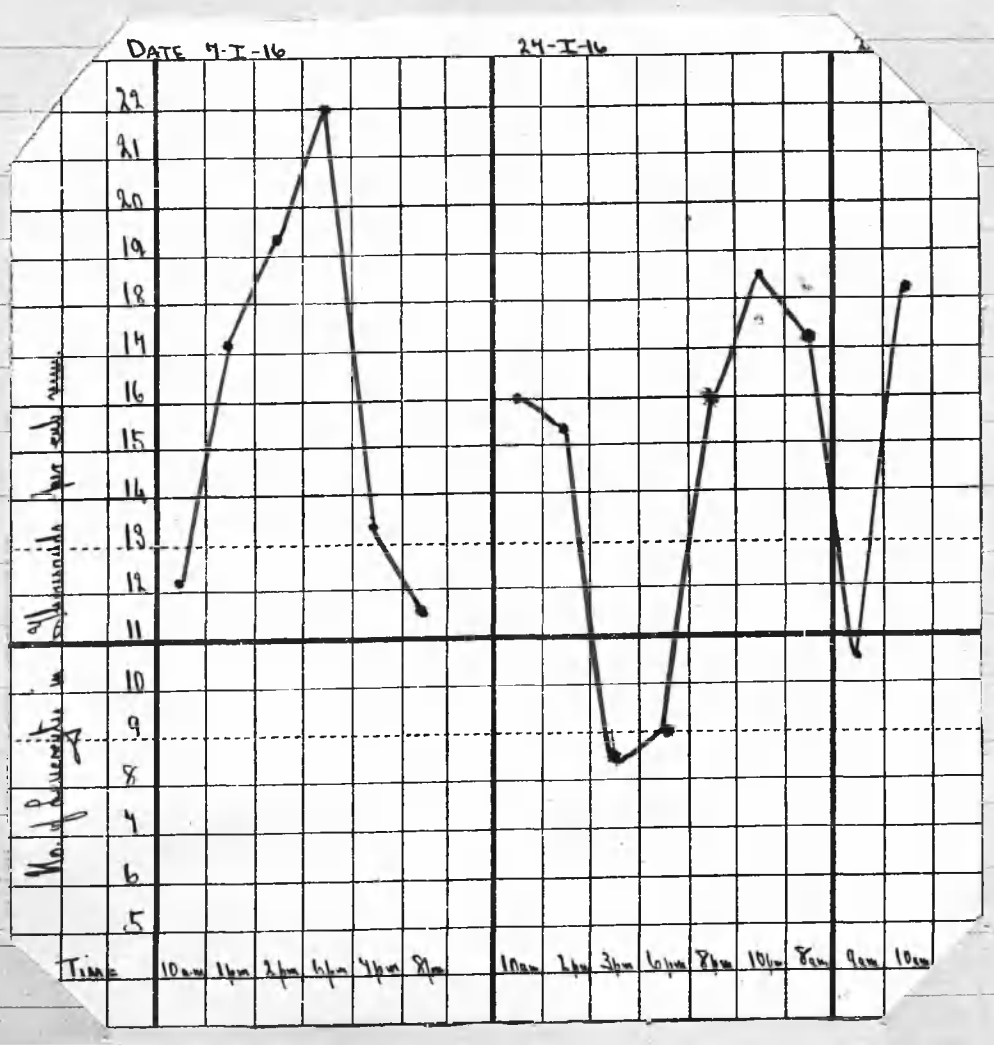
On auscultation. The R.M. at both apices very intense. Numerous moist sounds were present at the rt. apex, and at the left a few scattered crepitations were heard.

Remarks.

Patient had a disturbing cough and a fair amount of expectoration. The temperature rose occasionally to 99° F in the evenings, but no definite subjective symptoms displayed themselves. The temperature settled on Jan. 2nd. 1916, and the patient allowed up. Gradually, he was give some very light exercise. There was nothing to indicate that the patient was retrogressing; in fact, so well did he appear and feel on Jan. 4, that he was given some exercise in the form of walking. On Jan. 20, 1916 he complained of cough and expectoration being more prevalent than usual. The temperature was 99° F. on that occasion.
The sputum was tinged with blood on Jan. 24, and when the patient was thoroughly examined on Feb. 3, it was found that the disease had made startling progress. The left apex was now infiltrated and the pulse rate was 100 to 110 per minute. The temperature did not, however rise above 99.2° F.
Sputum examination showed tubercle bacilli in fair numbers; elastic tissue fibres and pus cells were abundant. Staphylococci and small diplococci were exceedingly abundant at all examinations.
Patient was discharged "Worse" on Feb. 15, 1916.

Case XI E. J. Act. 23.

Time	Leucocytes.	Remarks.
4-I-16		
10 a.m.	12,200.	1 hr. after breakfast.
1 p.m.	14,200.	Just before lunch.
2 p.m.	19,400.	1 hr. after "
6 p.m.	22,000.	After walking 4 miles.
4 p.m.	13,400.	1 hr. after Evening Meal.
8 p.m.	11,600.	
24-I-16.		
10 a.m.	16,000	1 hr. after breakfast.
2 p.m.	15,400	1 hr. " lunch.
3 p.m.	8,600	Patient up, but "Couching."
6 p.m.	9,000	Just before Evening Meal
8 p.m.	16,000	In bed; pulse 120; Temp. 99·2°; perspiring.
10 p.m.	18,600.	" " ; " 116; " 99·4°; "
28-I-16.		
8 a.m.	14,200.	Rest in bed; before breakfast.
9 a.m.	10,600	" " " ; just after "
10 a.m.	18,400	" " " ; 1 hr. " "



Case XII. J. L Aet. 24.

DATE. 6-I-16.

Physical Signs. On percussion: The left side of the chest was dull to percussion anteriorly and posteriorly.

On auscultation: Respiratory murmur was almost inaudible over left side of chest, but no adventitious sounds were heard. The cardiac boundaries were within normal limits and no departure from normal could be made out in the heart sounds.

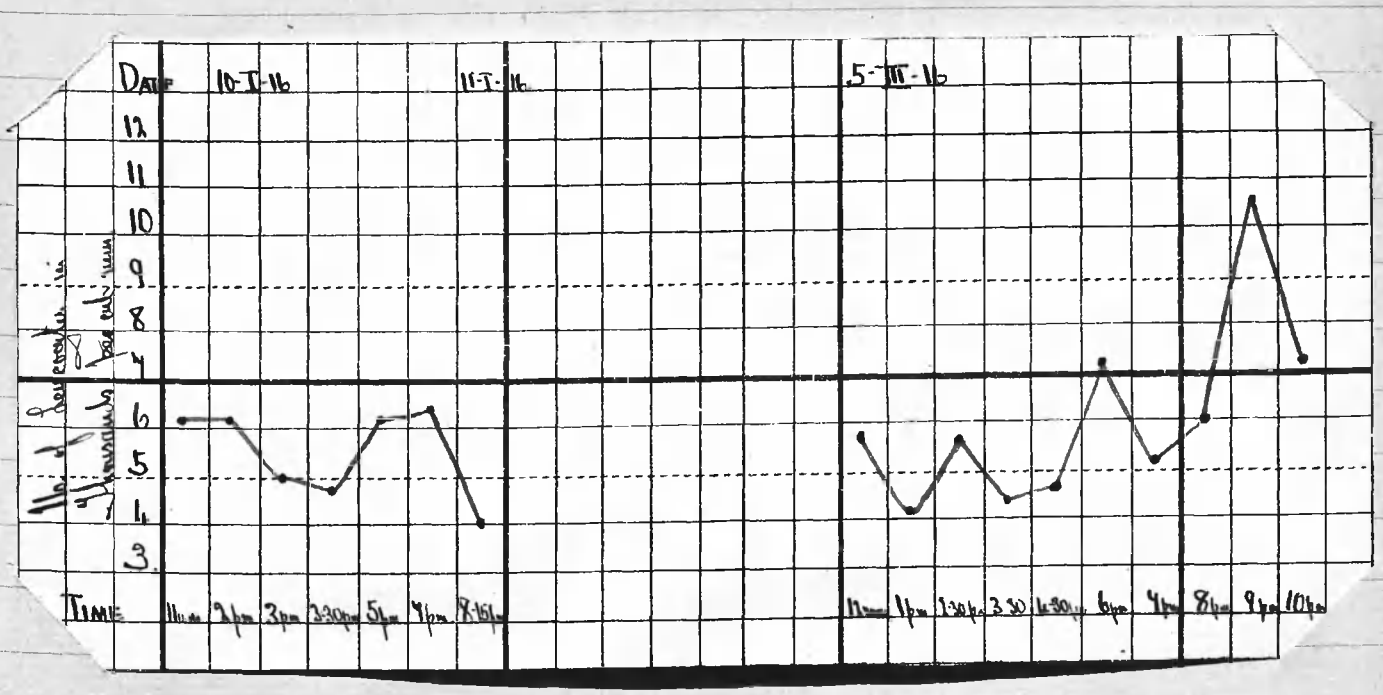
Remarks.

In August 1915 patient had had an empyema, following pleurisy. The chest was opened then, and part of the seventh rib in the posterior (left) axillary line was resected. On admission to Crosby Sanatorium in December 1915, patient complained of no pain in the side and the wound in the chest was quite well. During his stay at Crosby Sanatorium, he had a perfectly normal course in every respect; the heart was in its normal position and the pulse-rate was never above 80 per minute. Patient had no cough or spit, and the temperature remained normal.

Case XII. G. L. Act 24.

10-I-16.

Time	Leucocytes.	Remarks
11 a.m.	6,200.	2 hrs after breakfast.
2 p.m.	6,200	1 hr. " lunch.
3 p.m.	5,000	–
3-30 p.m.	4,800	–
5 p.m.	6,200	After a mile walk.
4 p.m.	6,400	1 hr. after Evening Meal.
11-I-16.		
8-15 a.m.	4,000	Patient up; before breakfast.
5-III-16.		
12 noon.	5,600	–
1 p.m.	4,200	Just before lunch.
2-30 p.m.	5,600	1 hr. after "
3-30 p.m.	4,400	–
4-30 p.m.	4,600	–
6 p.m.	4,200	Just before Evening Meal
4 p.m.	5,200	1 hr. after " "
8 p.m.	6,000	–
9 p.m.	10,600	–
10 p.m.	4,200.	After 1 hr. in bed.



Case XIII. E.R. Act 34.

DATE 4-I-16.

Physical Signs On percussion. Both apices, but especially the right, dull to percussion.

On auscultation. Numerous moist sounds were heard over both apical fronts. Posteriorly, on the rt. side, some sibilant rhonchi were audible. At the apex of the lower lobe on the left side, the breath sounds were very harsh, and a few crepitations were heard.

Remarks. On admission patient was much emaciated, but was able to get up and go about, so long as he was not exerting himself. The temperature remained normal during January, and this was so despite a 6 miles walk on Jan 4. 1916. At the beginning of March there was a change in patients condition for the worse; the physical signs had extended and the temperature registered 99·8 to 100·6 in the evenings.

The sputum was examined four times during January and February. 1916., and each time, tubercle bacilli were present in large numbers. Pus cells were very abundant and of secondary organisms observed, the staphylococcus or streptococcus preponderated.

This patient was discharged "Worse" on March 14. 1916.

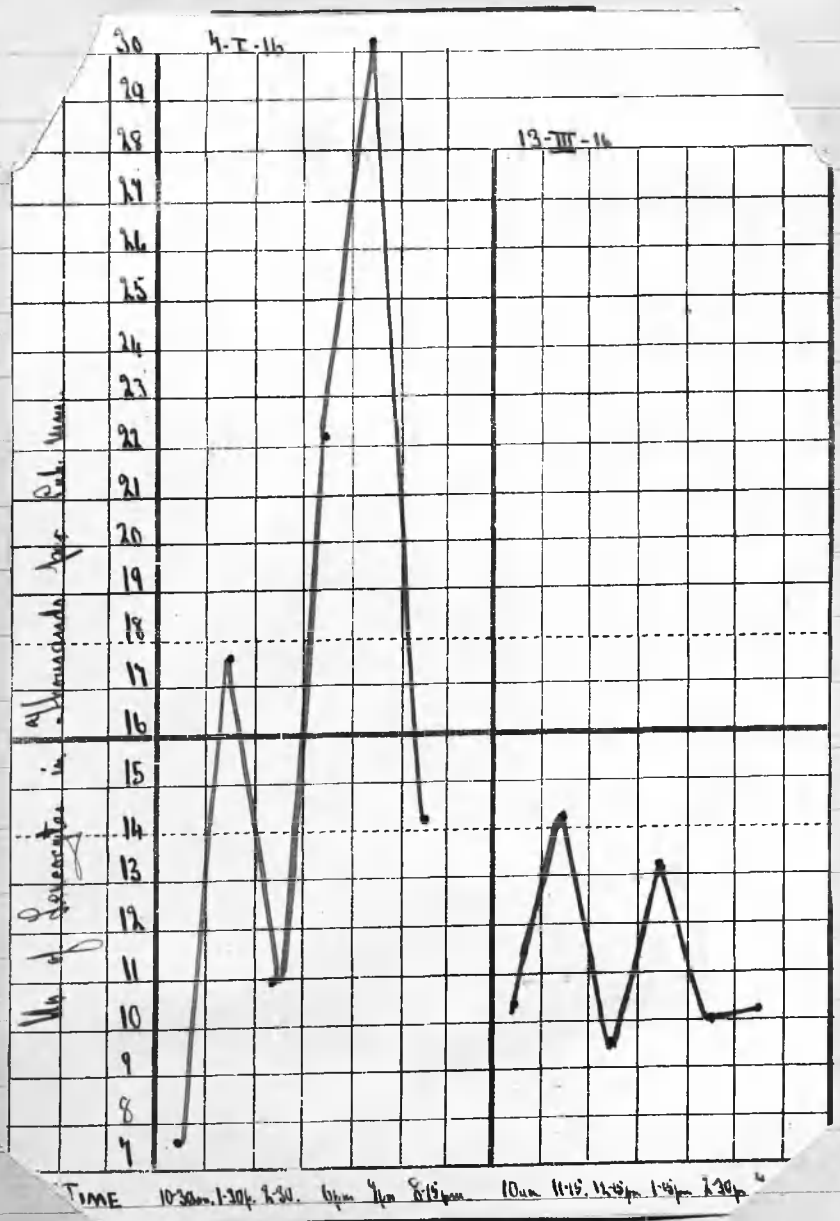
Case XIII E. R.. Act. 34

4-I-16

Time.	Leucocytes	Remarks.
10-30 a.m.	4,600	1½ hr. after breakfast.
1-30 p.m.	14,600	½ hr " lunch.
4-30 p.m.	11,000	
6 p.m.	22,200	After 4 miles walk and douche: Temp. 98.6°
7 p.m.	30,400	1 hr. after evening meal.
8-15 p.m.	14,200	Just in bed.

13-III-16

10 a.m.	10,600.	1 hr. after breakfast; In bed.
11-15 a.m.	14,200	Temp. 98·8° F.; " "
12-15 p.m.	9,600	" 99° " "
1-15 p.m.	13,200.	" 99·6° ; " "
2-30 p.m.	10,000.	1 hr. after lunch.
4 p.m.	10,200	1 " " Evening Meal.



Case XIV. G. L. M. Ref. 10.

DATE. 9-XII-15.

Physical Signs. On percussion: Rt. apex impaired in resonance, anteriorly and posteriorly. Left apex dull posteriorly.

On auscultation: Respiratory murmur harsh over entire Rt. upper lobe. A few crepitations were also heard at this apex. Over the left upper lobe the breath sound was distant, but no adventitious sounds could be heard in this situation.

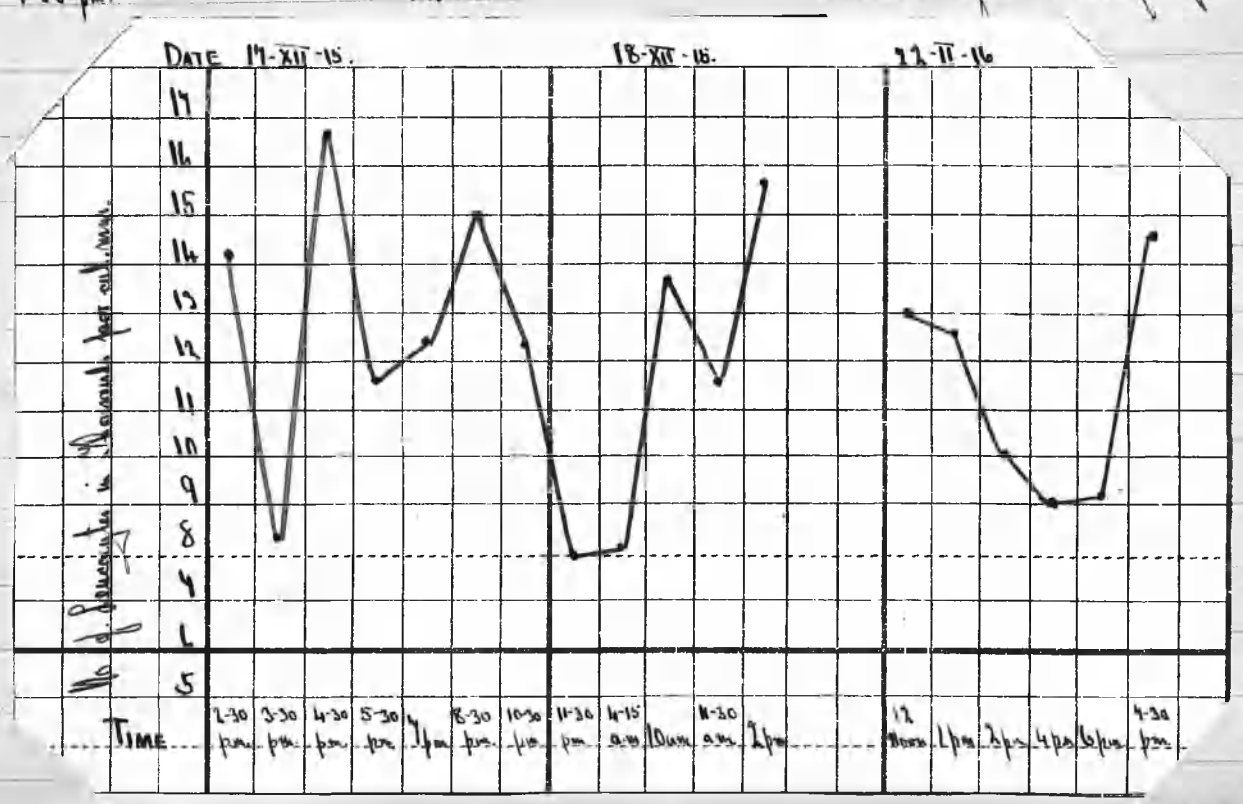
Remarks.

This patient was well-nourished on admission. During his stay in the Sanatorium he put on twelve pounds in weight. His temperature was, however, slightly unsteady, reaching 99° F. on several occasions. Tubercle bacilli were found in the sputum at all examinations; pus cells were abundant and a few secondary organisms were found, including staphylococci and small diplococci. The pulse rate was never below 86 per minute.

Case XIV. J. D. M. Act. 20.

14-XII-15

Time	Leucocytes.	Remarks.
2-30. pm	14,200.	1 hr after lunch. In bed.
3-30. pm.	8,400.	" "
4-30 pm.	16,800.	" "
5-30 pm.	11,600	" "
4 pm.	12,400	1 hr after Evening Meal; " "
8-30 pm.	15,000.	" "
10-30 pm.	12,400.	" "
11-30 pm.	8,000.	" "
18-XII-15.		
4-15 am	8,200.	After 6 hours sleep. " "
10 a.m.	13,800.	1 hr after breakfast. " "
11-30 am.	11,600.	" "
2 pm.	15,800.	1 hr. after lunch.
22-II-16.		
12 noon.	13,000.	Patient up: first bouncing
1 pm.	12,600.	Just before lunch.
2 pm.	10,000.	1 hr. after lunch.
4 pm.	9,000.	
6 pm	9,200.	Just before Evening Meal
7-30 pm.	14,600.	1½ hr after Evening Meal.



Case XV C. W. Act. 32.

DATE 6-XII-15.

Physical Signs. On percussion: Upper lobes on both sides impaired in resonance, anteriorly and posteriorly.

On auscultation. Breath sounds very harsh over both upper lobes. A fair number of rhonchi heard at left upper lobe.

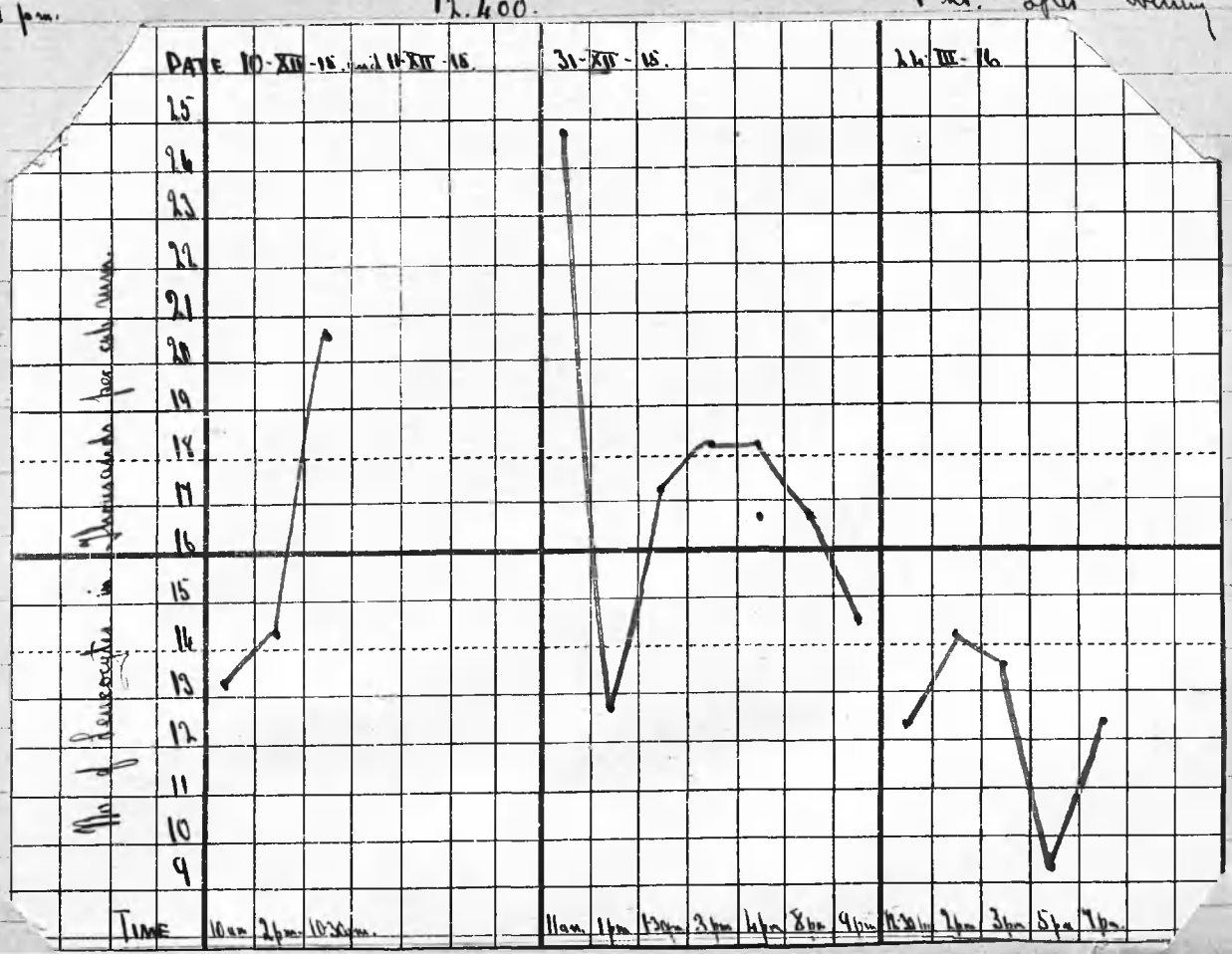
Remarks.

Patient complained mostly of cough and expectoration. The latter was examined several times, and tubercle bacilli, staphylococci, streptococci and numerous diplococci of various sizes were found. Pus cells were always abundant. The temperature at first was moderately elevated, - 99 to 99.8° F. but after a few weeks treatment this subsided and a normal evening temperature was obtained. By the middle of January the patient was feeling very well. The rhonchi had disappeared from the left apex, but a few tubercle bacilli were still found in the sputum.

Patient returned to report himself on March 24, 1916 when it was noted that the bronchitis had returned. A few counts were taken on that date.

Case XV C. W. Act. 32.

Time	Leucocytes	Remarks.
10-XII-15.		
10 a.m.	13,400.	1 hr after breakfast:
2 p.m.	14,400	1 " " lunch.
11-XII-15.		
10-30 a.m.	20,800.	1½ " breakfast.
31-XII-15.		
11 a.m.	24,800	2 hrs. " breakfast. Up and about.
1 p.m.	12,800	Just before lunch.
1·30 p.m.	14,200.	Immediately after lunch.
3 p.m.	18,200.	
4 p.m.	18,200.	
8 p.m.	16,800.	2 hrs after Evening Meal.
9 p.m.	14,600.	After 1 hr. in bed.
24-III-16.		
12·30 p.m.	12,400.	Patient walking about.
2 p.m.	14,200	1 hr. after lunch.
3 p.m.	13,800	
5 p.m.	9,400.	
7 p.m.	12,400.	1 hr. after Evening Meal.



Case XVII J. P. Act 25.

DATE 14-XII-15.

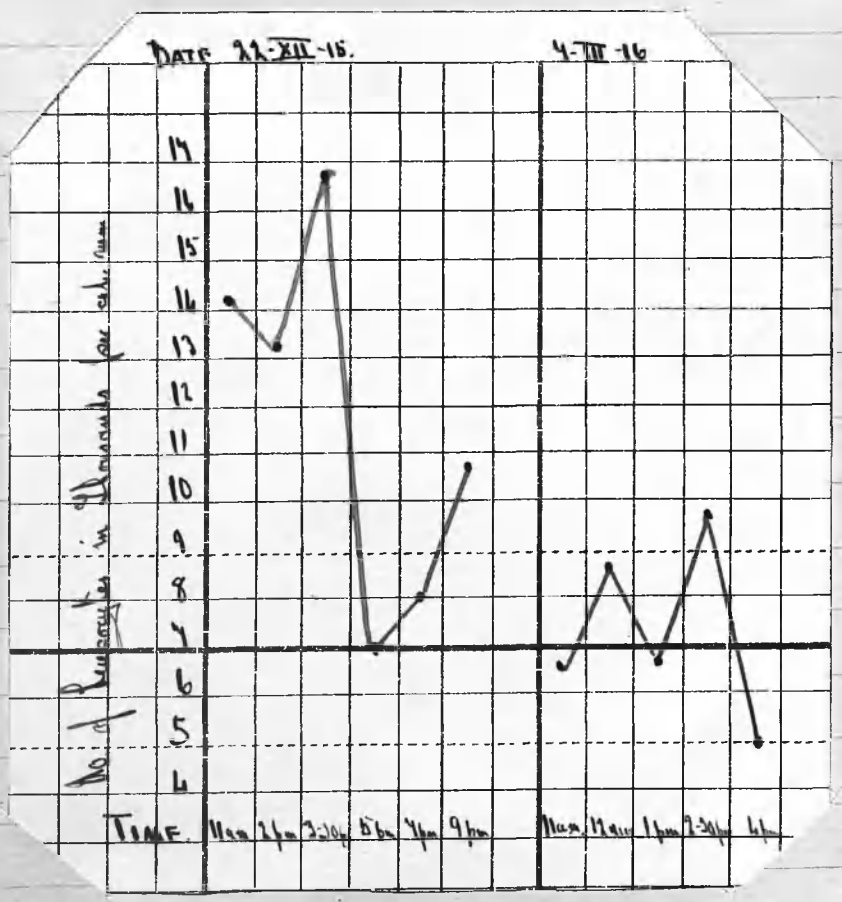
Physical Signs. On percussion. Rt. apex dull to percussion both back and front. Left apex impaired in resonance in front. On Auscultation. The breath sounds at the Rt. apex were tubular in quality; accompanying both inspiration and expiration were numerous crepitations, with a few rhonchi occasionally. The left apex was also the seat of a few moist sounds.

Remarks. On admission the temperature was 102° F. For the first two weeks the temperature remained more or less hectic. After this an abrupt change set in. The temperature became normal and the pulse rate dropped from 100 to 80 beats per minute. At the beginning of February the Rt. apex was almost "dry" and the breath sound was extremely harsh. Since that date patient has had an uninterrupted period of treatment. Tubercle bacilli were present in the sputum on admission; pneumococcal-like organisms were also observed. On an examination of the sputum on March 28, no tubercle bacilli could be found; a few pus cells and small diplococci were the most prominent elements in the field.

Case. XVI. J.P. Act 25.

22-XII-15.

Time	Leucocytes	Remarks.
11 a.m.	14,200	In bed; 2 hr after breakfast.
2 p.m.	13,200	" " 1 " lunch.
3-30 p.m.	16,800	" " —
5 p.m.	4,000	" "
4 p.m.	8,000	" " ; 1 " Evening Meal.
9 p.m.	10,800	" "
4-III-16		
11 a.m.	6,600.	Patient up: on slight Exercise
12 noon.	8,600	"
1 p.m.	6,800	Just before lunch.
2-30 p.m.	9,800	1 hr. after "
4 p.m.	5,000	—



Case XVII. W. R. Act 26.

DATE Jan 10. 1916.

Physical Signs: On percussion Both upper lobes dull to percussion, back and front.

On Auscultation Breath sound very harsh all over the chest. Rt lung riddled with tuberculous disease. Very active lesion at Left apex. No cavity formation

Remarks.

This patient was very much emaciated on admission. The temperature swung for five weeks between 99 and 102°.4. The pulse rate was never below 100.

The patient was discharged on March 14, with a very active lesion in the chest. He has, I am told, since died.

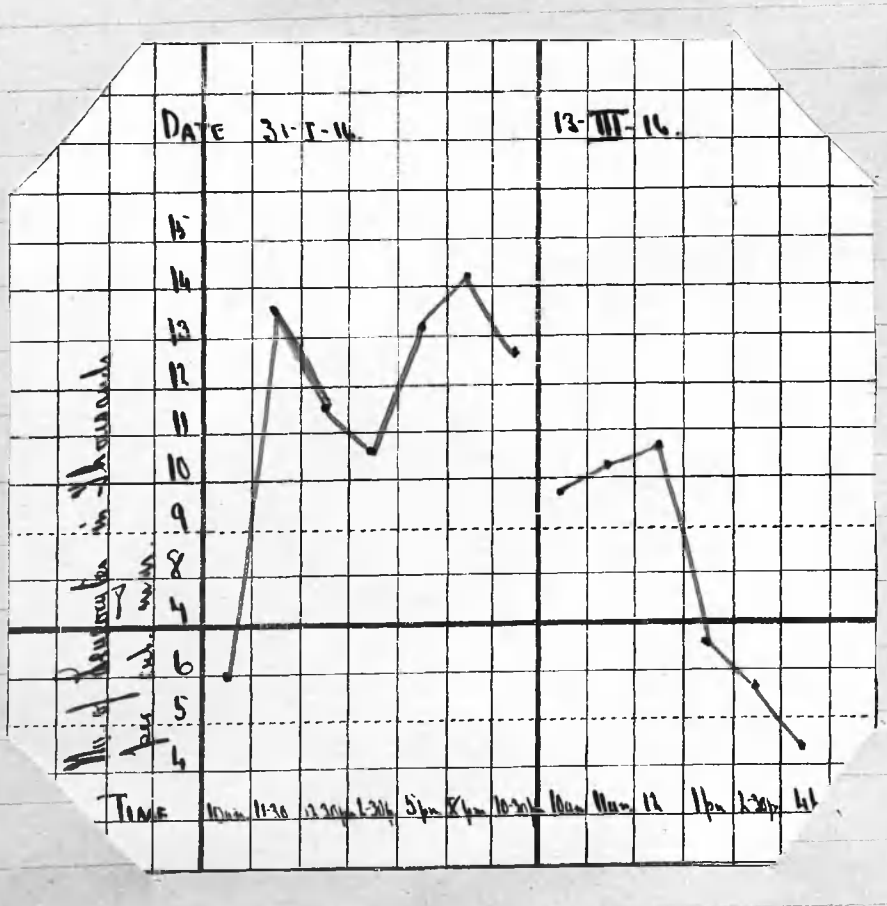
The sputum contained many pus cells at first, but tubercle bacilli and streptococci were much in evidence

The counts here quoted are very interesting.

Case XVII W. R. aet 26.

31-I-16.

Time	Leucocytes.	Remarks.
10 a.m.	6,000	Temp 99. At rest in bed; 1 hr after breakfast.
11-30 a.m.	13,600	" 99·6 " " " " ;
12-30 a.m.	11,600	" " " " "
2-30 a.m.	10,600	" 100·4 " " " " ; 1 hr. after light lunch.
5 p.m.	13,200	" 101 " " " "
8 p.m.	14,200	" 101·8 " " " " ; 2½ hr after Evening Meal.
10-30 p.m.	12,600	" 100 " " " "
13-III-16.		
10 a.m.	9,600	" " " " " ; 1 hr after breakfast.
11 a.m.	10,400	" " " " " —
12 noon.	10,800	" " " " " —
1 p.m.	6,800	" " " " " ; Just before lunch.
2-30 p.m.	5,600	" " " " "
4 p.m.	4,400	" " " " "



Case XVIII. O/P.B. Act 23

DATE 12-XII-15.

Physical Signs. On percussion. Impairment in resonance over both upper lobes, back and front.

On auscultation. Beyond some slight harshness in the breath sounds at both apices, and at the apex of the lower lobe on the rt. side, there was nothing to make out in the chest.

Remarks.

This patient has a normal temperature during his stay at the Sanatorium. The pulse-rate tended to be a little fast occasionally, but it seldom reached more than 86 per minute.

The sputum was examined eight times. Tubercle bacilli were found six times; pus cells were always present in large numbers and staphylococci were isolated from the washed sputum on two occasions.

Beyond having slight troublesome cough, the patient did very well.

15-XII-15.

TIME	LEUCOCYTES.	REMARKS.
10 a.m.	10,000.	1 hr after breakfast.
2 p.m.	9,000.	1 - - lunch.
3 p.m.	10,600	After 1 hr. exercise (golf)

19-XII-15.

10 a.m.	4,000	1 hr. after breakfast.
12 noon.	13,000.	—
2 p.m.	10,800.	1 hr. - lunch.
3 p.m.	12,400.	After 1 hr. exercise.
5 p.m.	12,600.	
7 p.m.	6,000	1 hr. after Evening meal
11 p.m.	12,400.	After 4 hrs in bed.

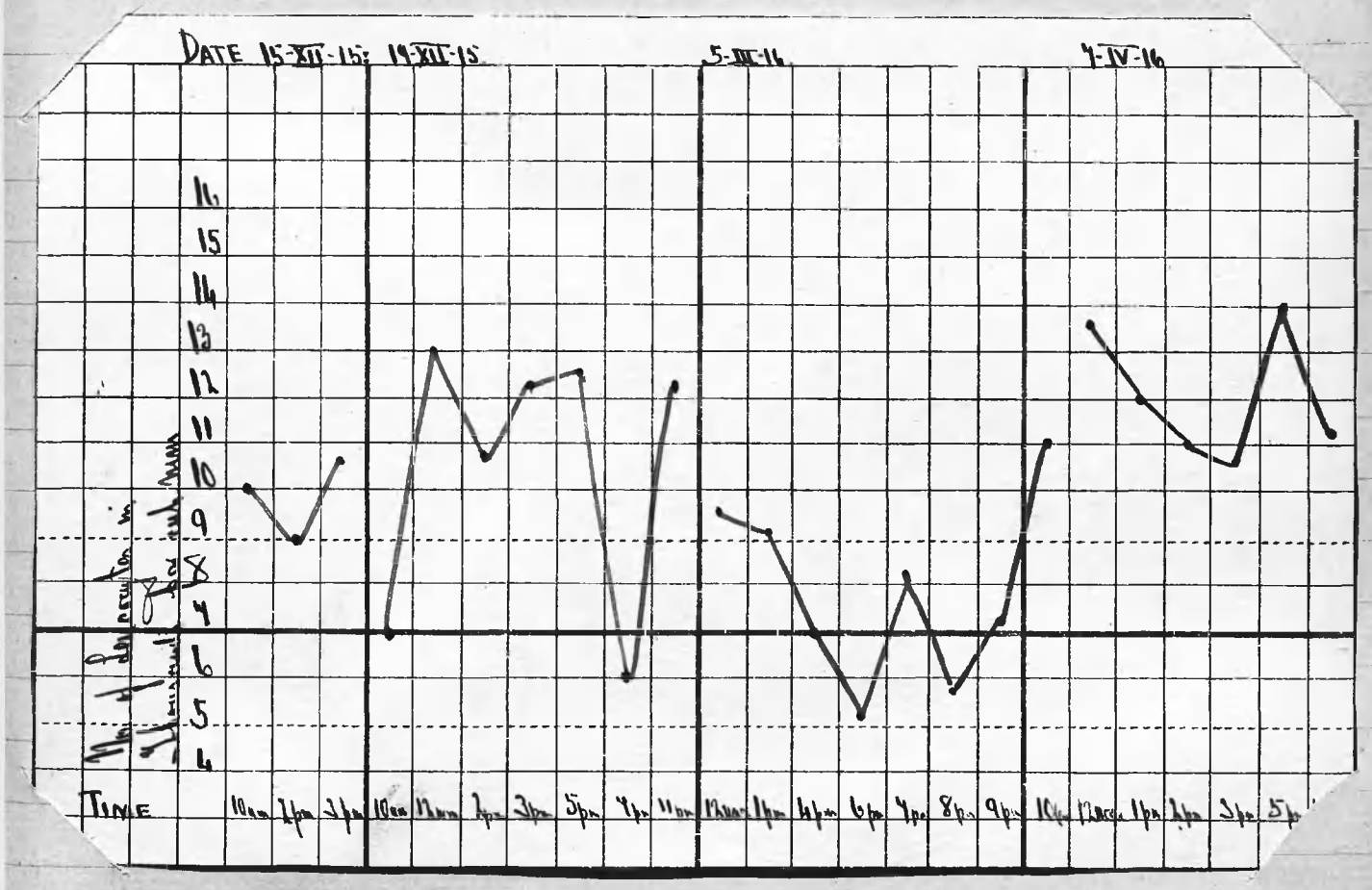
Case XVIII. (cont) J.J.B. Ætat 23.

5-III-16.

Time	Leucocytes	Remarks.
12 noon.	9,600	3 hrs after breakfast.
1 pm.	9,200.	Just before lunch.
4 pm	4,000.	After 2 hrs. exercise (walking and golf)
6 pm.	5,200.	Just before Evening Meal.
4 pm.	8,200.	1 hr after
8 pm	5,800.	—
9 pm.	4,200.	After 1 hr. in bed.
10 pm.	11,000	—

4-IV-16.

12 noon.	13,600	3 hrs after breakfast.
1 pm.	12,000	Just before lunch.
2 pm.	11,000	1 hr. after
3 pm.	10,600	—
5 pm.	14,000.	After 2 hr. exercise (golf)
4 pm.	11,200.	1 hr after Evening Meal.



Case XIX J. W. B. Aet. 44.

DATE 18-XII-15.

Physical Signs: On percussion. Very little alteration from the normal presented itself. The rt. apex was, if anything, slightly impaired in resonance.

On auscultation. The breath sounds at the rt. apex were a trifle harsh. In the left axilla a few crepitations were audible.

Remarks.

The patient's chief complaint was cough, which was almost invariably accompanied by a tough, viscid expectoration. The examination of the sputum by the ordinary Carbol Fuchsin and Methylene Blue method failed to reveal the presence of Tubercle Bacilli at any of the examinations made. The Gram stain showed however, that pus cells were very numerous and that there were many small diplococcal organisms present.

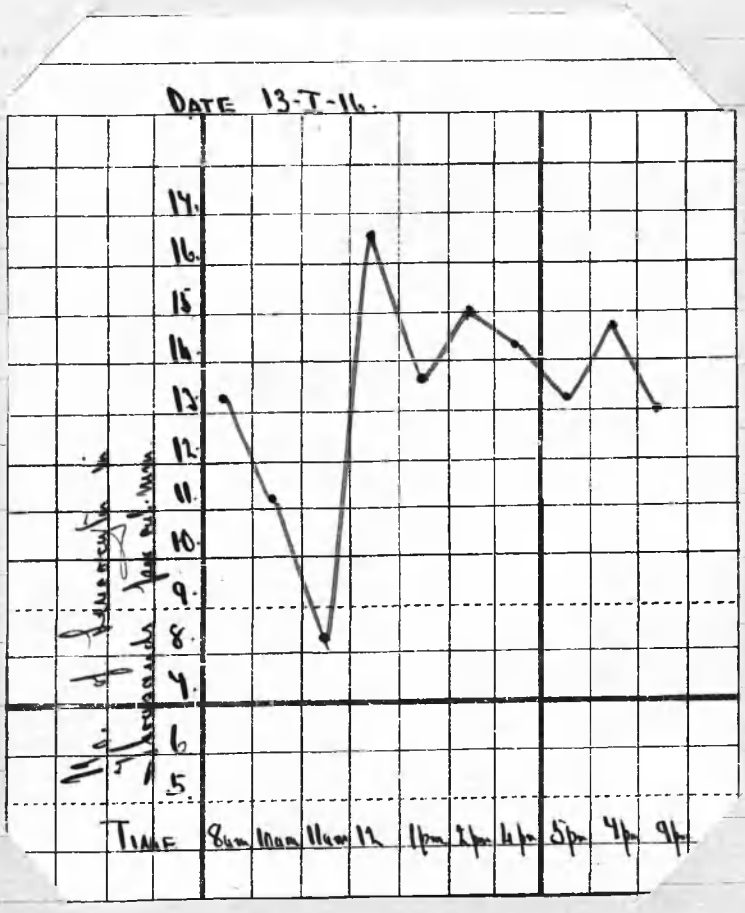
The Antiformin method was ultimately used for the sputum and Tubercle bacilli were found.

The evening temperature was for weeks, 99° F, but no symptoms other than those mentioned, presented themselves.

Case XIX J. W. B. Act 24.

13-T-16.

Time	Leucocytes	Remarks.
8 am.	13,400.	Patient up; before breakfast.
10 am.	11,200.	1 hr. after breakfast.
11 am.	8,400.	—
12 noon.	16,600.	—
1 pm.	17,800	Just before lunch.
2 pm.	15,000	1 hr after.
4 pm.	14,400.	—
5 pm.	12,400.	—
4 pm.	14,800.	1 hr. after Evening Meal.
9 pm.	13,000.	After 1 hr in bed: Temp. 99°7.



Case XX A. M. Ht 14.

DATE 4-I-16.

Physical Signs On percussion. Beyond some slight dulness to percussion over both upper lobes anteriorly there was no abnormality.

On auscultation. The breath sounds were weak and distant over both apices. No adventitious sounds were ever heard in the chest while the patient was in the Sanatorium.

Remarks.

Patient had had pleurisy in Sept. 1915; and in his younger days had been "threatened with tuberculous peritonitis." The patient was in perfect health whilst under treatment and at no time did he complain of cough, expectoration etc..

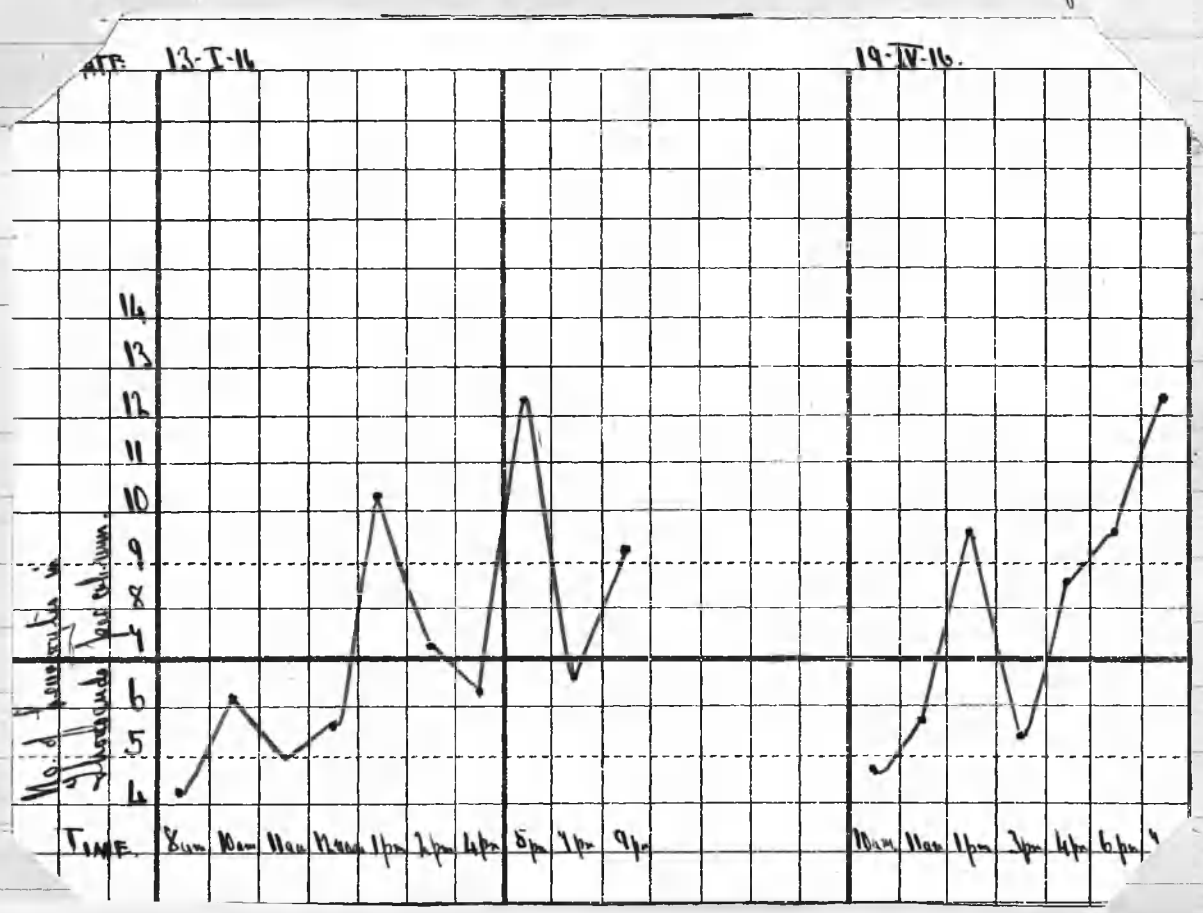
Case XX A. M. Act 14

13-I-16.

Time	Leucocytes.	Remarks.
8 am.	4,200	Before breakfast.
10 am.	6,200	1 hr. after.
11 am.	5,000	—
12 noon.	5,600	—
1 pm.	10,400	Just before lunch.
2 pm.	4,200	1 hr. after "
4 pm.	6,400	—
5 pm.	12,400.	After 4 miles walk and douche.
7 pm.	6,600.	1 hr after Evening Meal.
9 pm.	9,200.	After 1 hr. in bed.

19-IV-16.

10 am.	4,800.	1 hr. after breakfast.
11 am.	5,800	2 " " "
1 pm.	9,600	Just before lunch.
3 pm.	5,400	—
4 pm.	8,800	—
6 pm.	9,600	Just before Evening Meal.
7 pm.	12,400.	1 hr. after " "



Case XXI J. A. Act 34.

DATE. 15-XII-15.

Physical Signs. On percussion: Rt apex and upper lobe impaired in resonance; left upper lobe dull anteriorly and posteriorly.

On auscultation. Tubular breathing heard over left upper lobe. Crepitation abundant over the same area. At left base posteriorly, the number of moist sounds was few, but here too the breath sound was harsh. No adventitious sounds could be heard at the Rt. apex.

Remarks.

Patients chief complaint was shortness of breath on exertion. The amount of cough was small, but on some occasions, especially after exertion, the sputum would be profuse. It contained tubercle bacilli in moderate number, pus cells in large number, and many staphylococci and small diplococci.

The pulse rate was constantly above 90 per minute; the temperature occasionally rose up to 99·6° F.

20·XII·15.

TIME	LEUCOCYTES.	REMARKS.
10 a.m.	8,400	1 hr after breakfast.
12-30 p.m.	16,400.	Patient up but Crouching.
2 p.m.	19,600.	1 hr after lunch.
4 p.m.	24,000.	—
5 p.m.	19,200.	—
7 p.m.	15,600.	Patient in bed.
9 p.m.	19,000.	3 hrs. after Evening Meal.

Case XXI J. A. Ætat 34 (Cont.)

24-III-16.

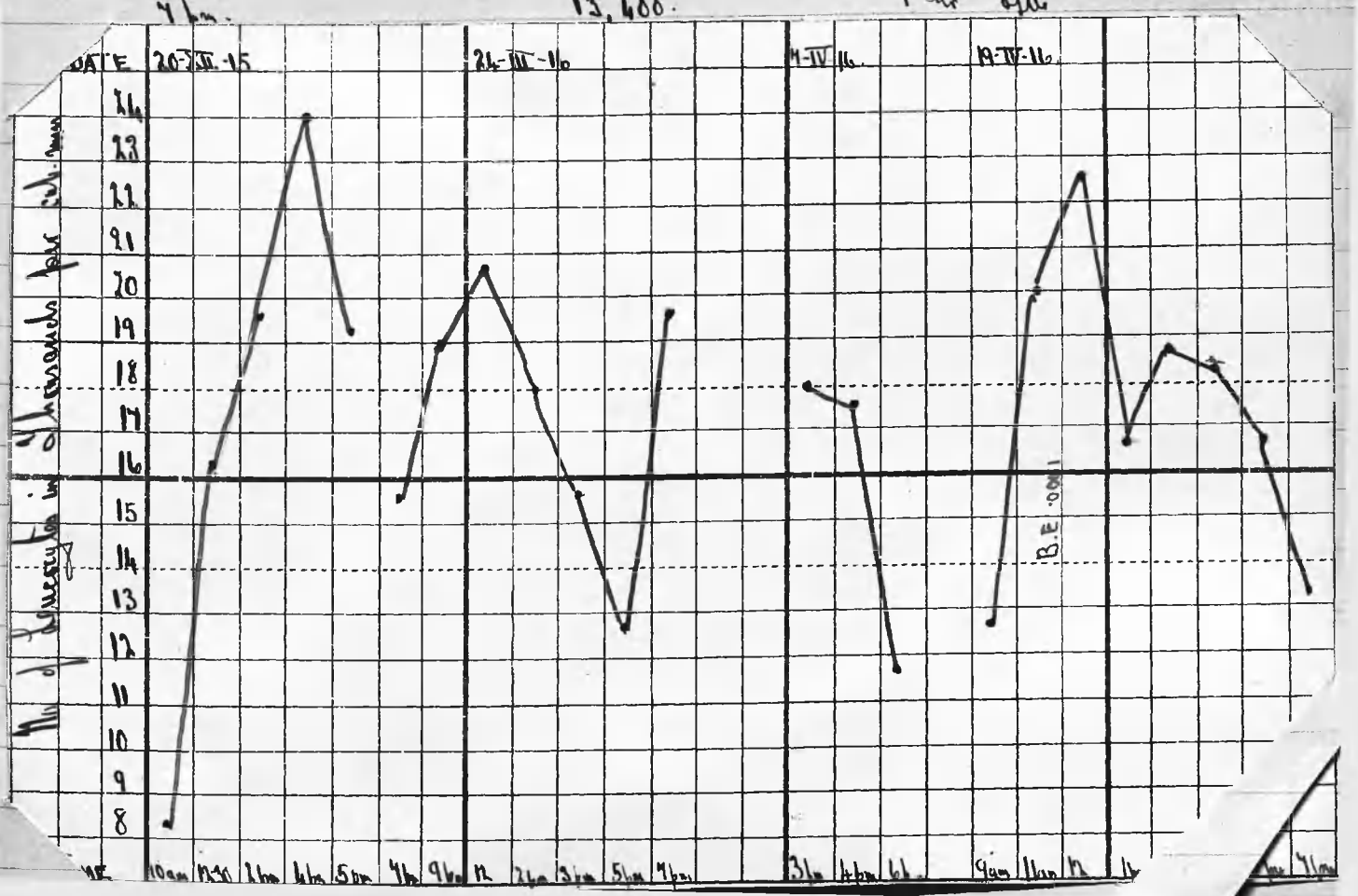
Time	Leucocytes.	Remarks.
12 noon.	20,800	Rest in bed.
1 pm.	18,000.	" " "; 1 hr after lunch.
3 pm.	15,800	" " ";
5 pm.	12,800.	" " "
7 pm.	19,600.	" " "; 1 hr after Evening Meal.

14-IV-16.

3 pm.	18,000.	Patient up: 2 hrs. after lunch.
4 pm.	14,600	" ", but "Coaching"
6 pm.	11,800.	Just before Evening Meal

19-IV-16.

9 am.	12,800.	Just before breakfast.
11 am.	20,000.	Patient up but Coaching.
12 noon.	22,600.	1 hr after Tuberculin .000IBE
1 pm	16,800.	Just before lunch.
2 pm.	18,800	1 hr. after "
4 pm.	18,200.	—
6 pm.	16,600.	Just before Evening meal.
7 pm.	13,400.	1 hr after "



Case XXII P.M. Ret. 39.

DATE 18-I-16.

Physical Signs. On percussion. Chest dull to percussion all over, but more especially on the left side.

On Auscultation. Signs of cavity formation over left upper lobe. Numerous crepitations heard all over left lung; friction in left axillary region. Fine crepitations and sibilant rhonchi at it apex. The respiratory murmur was very harsh over left side of chest, and diminished in volume over it. side.

Remarks.

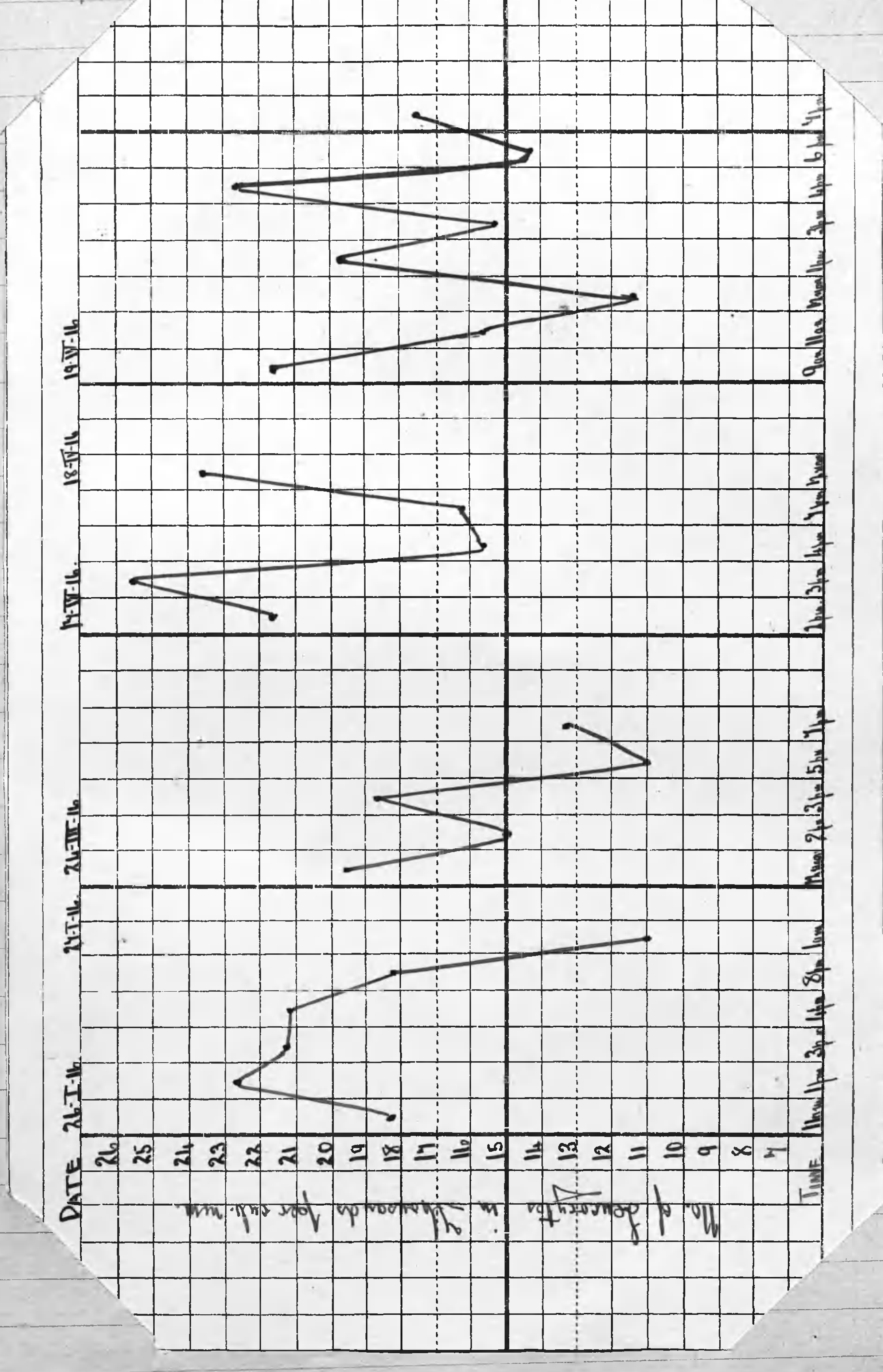
Patient was in bed most of the time during which he was in the Sanatorium. The temperature was very irregular, rising to 99 and 101 in the evenings and falling to 94 at 96 in the mornings. The pulse rate was 90 to 100 per minute.

Sputum examination showed that the infection was a mixed one, tubercle bacilli, elastic tissue fibres, staphylococci, streptococci and various sizes of diplococci being present. Pus cells were always abundant.

Case XXII.

Time	Leucocytes	Remarks.
26-I-16.		
11 am.	18,400	Patient up, but "Couching"
1 pm.	22,800	Just before lunch.
3 pm	21,400	
4 pm.	21,200	
8 pm.	18,200.	After 1 hr. in bed.
27-I-16.		
1 am.	11,000.	Just before lunch.
24-III-16		
12 noon	19,600.	Rest in bed.
2 pm.	15,000.	1 hr after lunch: in Bed.
3 pm.	18,800	" "
5 pm.	11,000.	" "
7 pm.	13,400.	1 hr. after Evening Meal.
14-IV-16.		
2 pm	21,800.	1 hr. after lunch. In Bed
3 pm.	25,600.	— " "
4 pm	15,800.	— " "
7 pm.	16,200	1 hr " Evening Meal.
18-IV-16.		
12 noon.	23,600.	Rest in bed.
19-IV-16.		
9 am	21,600	Just before breakfast; rest in bed.
11 am.	16,600	— " " "
12 noon	11,400	" " "
1 pm.	19,800	Just before lunch. " " "
3 pm.	15,400	" " "
4 pm	22,800	" " "
6 pm	14,400.	Just before Evening Meal; " "
7 pm.	14,600.	1 hr. after " " "

P.M. Act. 39.



Case XXIII J. K. Aet 22.

DATE 20-I-16

Physical Signs. On percussion: Dulness over R^t side of chest from clavicle down to the level of the fourth rib in front and to the spine of the scapula posteriorly.

On auscultation: Respiratory murmur very harsh over the dull area. Crepitations abound ant.

Remarks.

Patient's temperature was very irregular for the first fortnight after admission, reaching 99.6° in the evenings. At the end of that time the pulse rate was 80 per minute and the temperature had subsided to 98.8° F. He complained of much breathlessness on exertion, and had a troublesome cough. The sputum was scanty, but contained tubercle bacilli, and many small micrococci like the diplococcus catarrhalis. No streptococci were visible by microscopic examination.

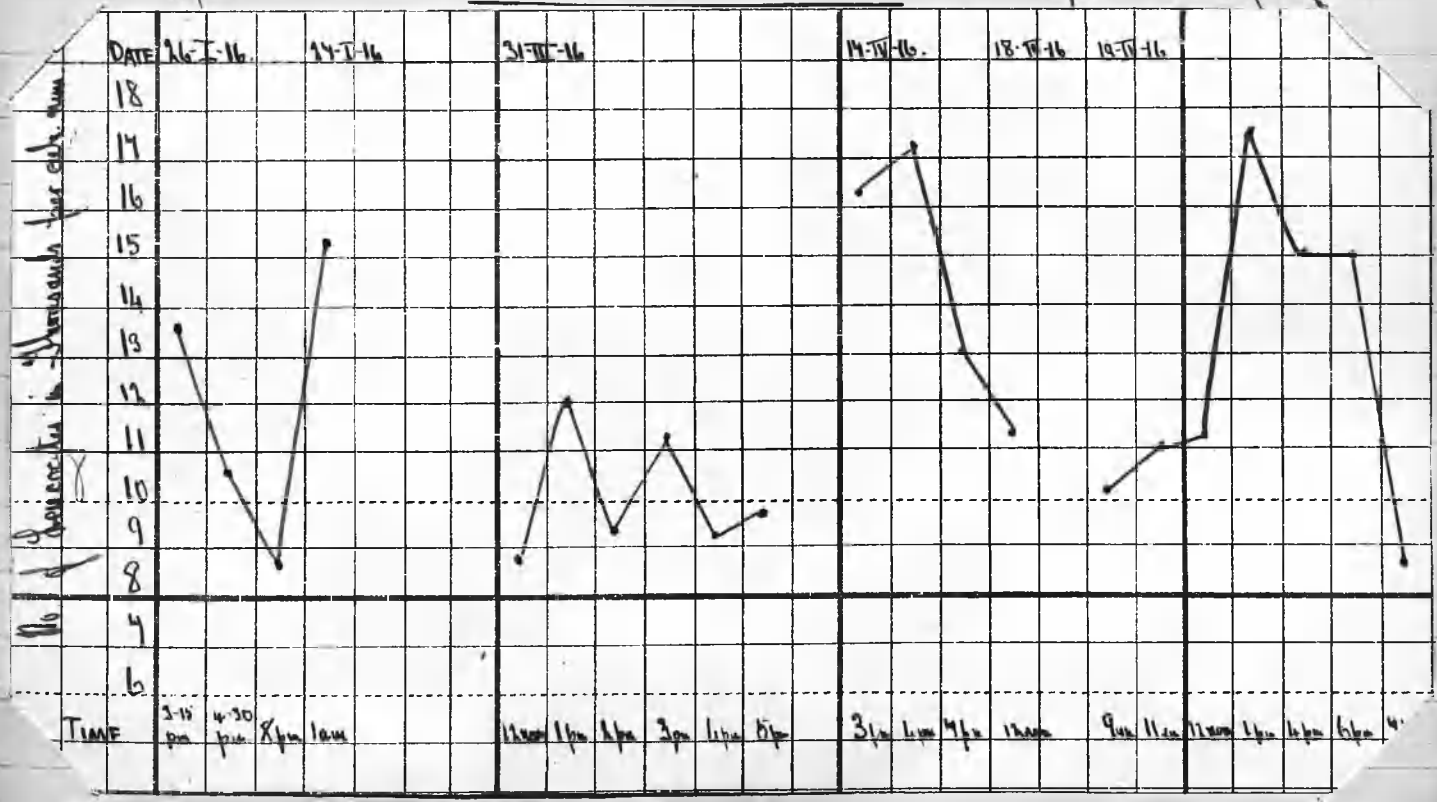
26-I-16.

TIME	LEUCOCYTES.	REMARKS.
3-15 pm.	13, 600.	Patient in bed.
4-30 pm.	10, 600.	—
8 pm.	8, 800.	2 hrs after Evening Meal.
27-I-16.		
1 am.	15, 400.	After 3 hours sleep.

Case XXIII. G. K. Aet 22.

31-III-16.

Time	Leucocytes.	Remarks.
12 noon.	8, 800.	Patient up. but "Coaching"
1 pm.	12, 000.	Just before Lunch.
2 pm	9, 400.	1 hr. after lunch.
3 pm	11, 400.	—
4 pm	9, 200.	—
5 pm.	9, 800.	—
14-IV-16.		
3. pm.	16, 400.	Patient up, but "Coaching"
4. pm	14, 400.	—
4. pm.	13, 000.	1 hr. after Evening Meal.
18-IV-16.		
12 Noon.	11, 400.	—
19-IV-16.		
9 am	10, 200.	Just before breakfast.
11 am.	11, 000.	2 hrs after.
12 noon.	11, 200.	—
1 pm.	14, 600.	Just before lunch.
4 pm.	15, 000.	—
6 pm.	15, 000.	—
7 pm.	8, 600.	1 hr after Evening Meal.



Case ~~XXIV~~ J. N. Act 34.

DATE 20-I-16

Physical Signs On percussion. Both apices looking in normal lung resonance. Numerous crepitations heard all over rt. upper lobe on auscultation. The R.M. was very harsh over rt. upper lobe.

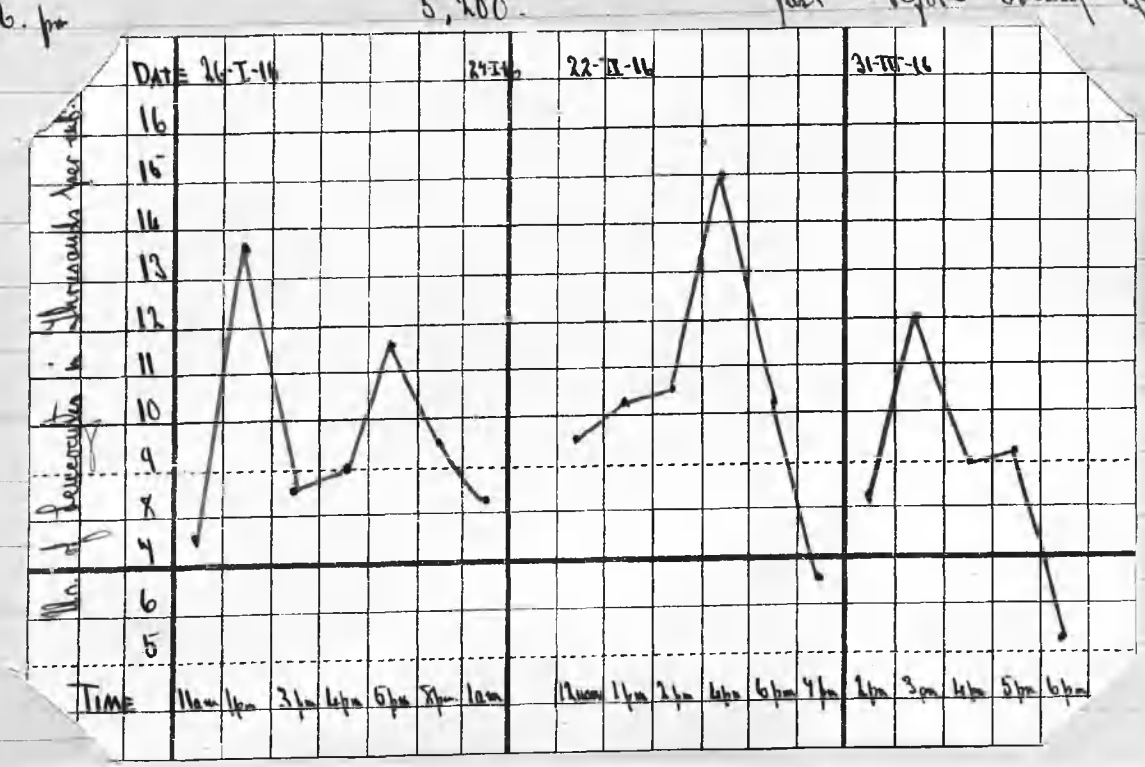
Remarks.

The outstanding symptom was cough which was almost invariably accompanied by expectoration. The latter was examined four times, and tubercle bacilli were found on each occasion. Pus cells were present, but not so prominent at any time as they were in some of the other cases. A few cocci were noted at the third and fourth examinations, - these organisms were almost always arranged in groups, - like staphylococci.
The temperature rose to 100° F. on several occasions; in the intervals between the exacerbations of temperature the patient felt in good health and was able to perform light duties in the grounds.

Case XXIV J. N Æt. 34.

26-I-16

TIME	LEUCOCYTES	REMARKS.
11 a.m.	4,600.	Patient up; but "Touching".
1 p.m.	13,800.	Just before lunch.
3 p.m.	8,600.	—
4 p.m.	9,000	—
5 p.m.	11,600	—
8 p.m.	9,600	2 hrs. after Evening Meal.
24-I-16.		
1 a.m.	8,400.	After 4 hrs. sleep.
22-II-16.		
12 noon.	9,600.	Patient up; on very light exercise.
1 p.m.	10,400.	—
2 p.m.	10,600	1 hr. after lunch.
4 p.m.	15,000.	—
6 p.m.	10,200	
4 p.m.	6,800	1 hr after Evening Meal.
31-III-16.		
2 p.m.	8,400	1 hr after lunch.
3 p.m.	12,000	—
4 p.m.	9,000	—
5 p.m.	9,200	—
6. p.m.	5,200.	Just before Evening Meal.



Case XXV A. M. Aet 31.

DATE 1-II-16.

Physical Signs On percussion: Chest showed normal lung resonance all over. On auscultation: A few moist sound were heard at the end of inspiration when patient was admitted.

Remarks.

Patient was well-developed and able to do plenty of hard manual labour. He was sent to Crosby Sanatorium because he had had an attack of haemoptysis in December 1915. From the time of his admission the temperature did not rise above normal, except on one occasion when the thermometer registered 99.2°F. in the evening. Patient had neither cough nor spit; the pulse rate was normal.

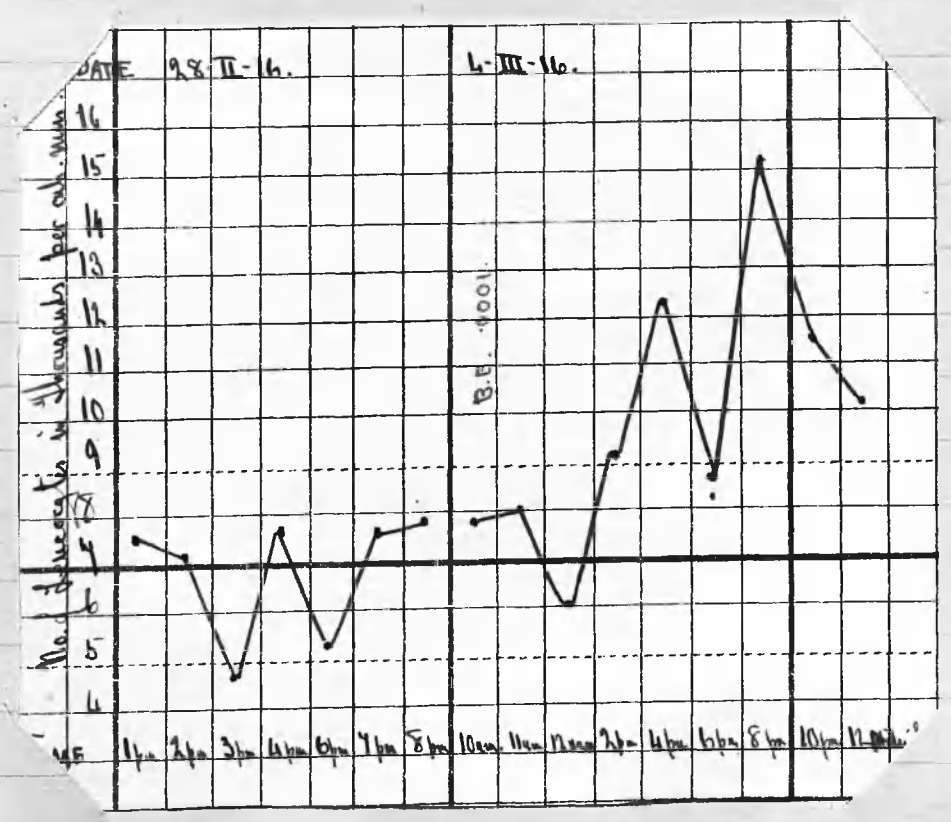
Case XXV A. M. Act 31.

28-II-16.

Time	Leucocytes	Remarks.
1 pm.	4,600.	Patient up and on full exercise.
2 pm.	4,200.	1 hr. after lunch.
3 pm.	4,800.	—
4 pm.	4,800.	After 2 hrs exercise including golf.
6 pm.	5,400	—
4 pm.	4,600.	1 hr. after Evening Meal.
8 pm.	4,800.	—

4-III-16.

10 am.	4,800.	1 hr. after breakfast.; B.E. Tuberculin given .0001 cc.
11 am	8,000.	Patient told to rest on couch.
12. noon	6,000.	Temperature. 99.8°F.
2. pm	9,200	1 hr. after lunch. Temp. 98.2.
4 pm	12,400	—
6 pm	8,800	— Temp. 98.4.
8 pm	15,200	2 hrs. after Evening Meal. Temp 98.4.
10 pm.	11,600	After 2 hrs. in bed.
12. midnight.	10,200.	—



Case XXVI H.C. Art. 26.

DATE. March. 2. 1916.

Physical Signs: On percussion. Rt. apex impaired in resonance. On Auscultation. Breath sounds very weak over whole upper lobe on rt. side. No adventitious sounds heard.

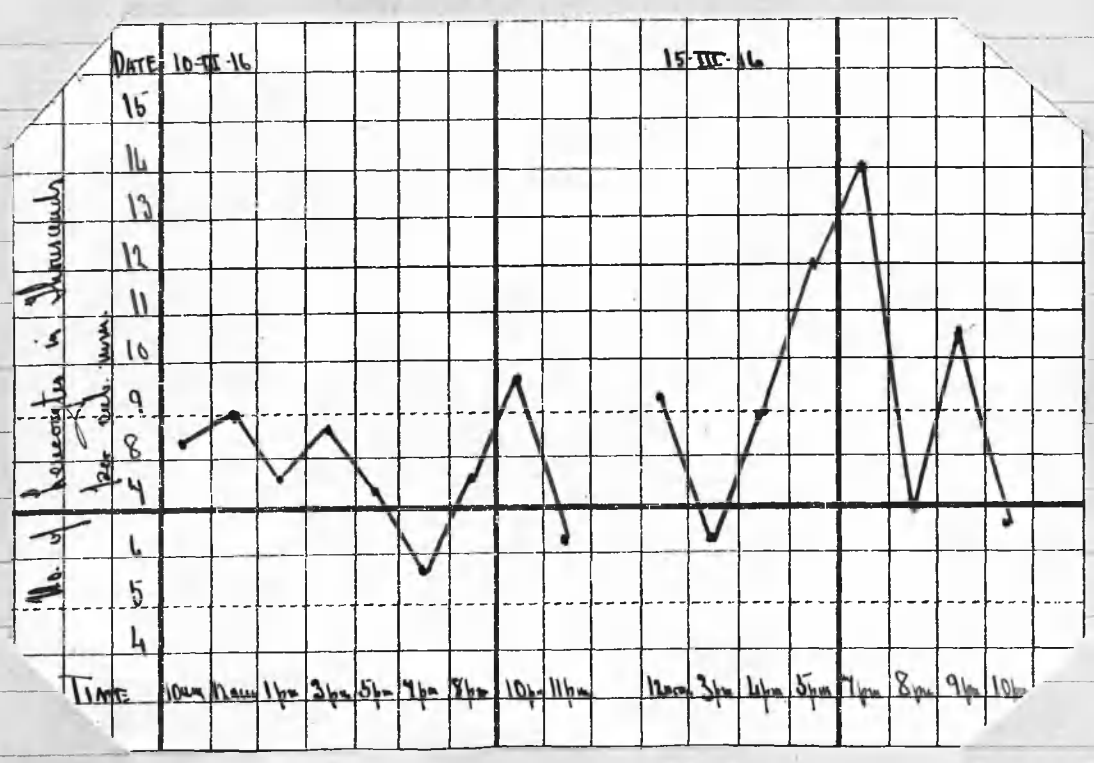
Remarks

Patient had been in Crossley Sanatorium in 1912, when tubercle bacilli were found in the sputum. He was readmitted because he was feeling fatigued and weary; he had no spit on this occasion.
The pulse rate was normal and the temperature never rose above 98.4° F..

Case XXVI H.C. Oct 16.

10-III-16.

Time.	Leucocytes.	Remarks.
10 a.m.	8,400	Patient up and about; 1 hr after breakfast.
12 noon.	9,000	—
1 p.m.	4,600.	—
3 p.m.	8,800.	2 hr after lunch.
5 p.m.	4,400	—
4 p.m.	5,800.	1 hr after Evening Meal.
8 p.m	4,600.	—
10 p.m.	9,800.	after 1 hr. in bed.
11 p.m.	6,200.	
15-III-16.		
12 noon.	9,400.	—
3 p.m.	6,200	1 hr. after B.E. .0001. (Tuberculin)
4 p.m.	9,000.	—
5 p.m.	12,000	—
4 p.m.	14,000.	1 hr. after Evening Meal Temp. 98.4.
8 p.m	4,000.	
9 p.m.	10,600	after 1 hr. in bed.
10 p.m.	6,600.	—



Case XXVII A. C. Art. 24.

DATE 14-II-16.

Physical Signs. On percussion. No definite impairment of the percussion note was to be made out anywhere in the chest. On Auscultation. On admission there were innumerable rhonchi all over the chest. The sounds produced in this way obscured any crepitations which may have been present.

Remarks.

For the first fortnight after admission patient was treated as a case of bronchitis. He responded very well to medicinal measures and by Feb. 28, 1916 he was feeling perfectly well; the cough, which troubled him originally had now disappeared.
The chest condition also showed great improvement. The rhonchi disappeard and nothing but a pure vesicular breath sound became audible.
Patient succeeded in putting on 28 lb in weight in six weeks.
The temperature was never above 98⅘° F, and the pulse rate never above 80 beat per minute.
The diagnosis in this case was open to doubt.
No sputum was examined in this case.

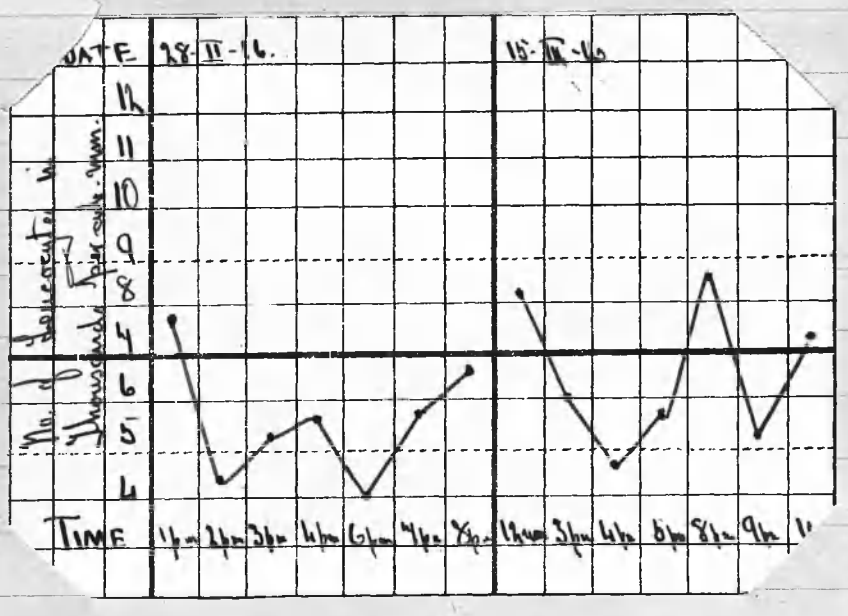
Case XXVII A.C. aet 24.

28-II-16.

TIME	LEUCOCYTES	REMARKS.
1 pm.	4,800.	Just before lunch.
2 pm.	4,400.	1 hr. after "
3 pm.	5,200.	—
4 pm.	5,600.	After "digging" exercise.
6 pm.	4,000.	—
7 pm.	5,800.	1 hr. after Evening Meal.
8 pm.	6,800.	—

15-III-16.

12. noon.	8,200.	—
3. pm.	6,000	1 hr after BE ·002.
4, pm	4,800.	—
5, pm.	5,800.	—
8 pm	8,600.	2 hrs. after Evening Meal.
9 pm	5,200.	—
10. pm.	4,200.	After 2 hrs. rest in bed



Case XXVIII R. Q. Act 41.

DATE 21-II-16.

Physical Signs. On percussion. No dulness was to be made out anywhere in the chest.

On auscultation. Breath sound vesicular and devoid of adventitious sounds.

Remarks. This patient was in apparently perfect health. He had had "pleurisy" on the rt. side in Oct. 1915. Whether the diagnosis was correct or not, it was certain that he had no signs of pleural inflammation during his stay at Crossley Sanatorium.
The temperature and pulse rate were never beyond normal limits. He had no cough and no expectoration.

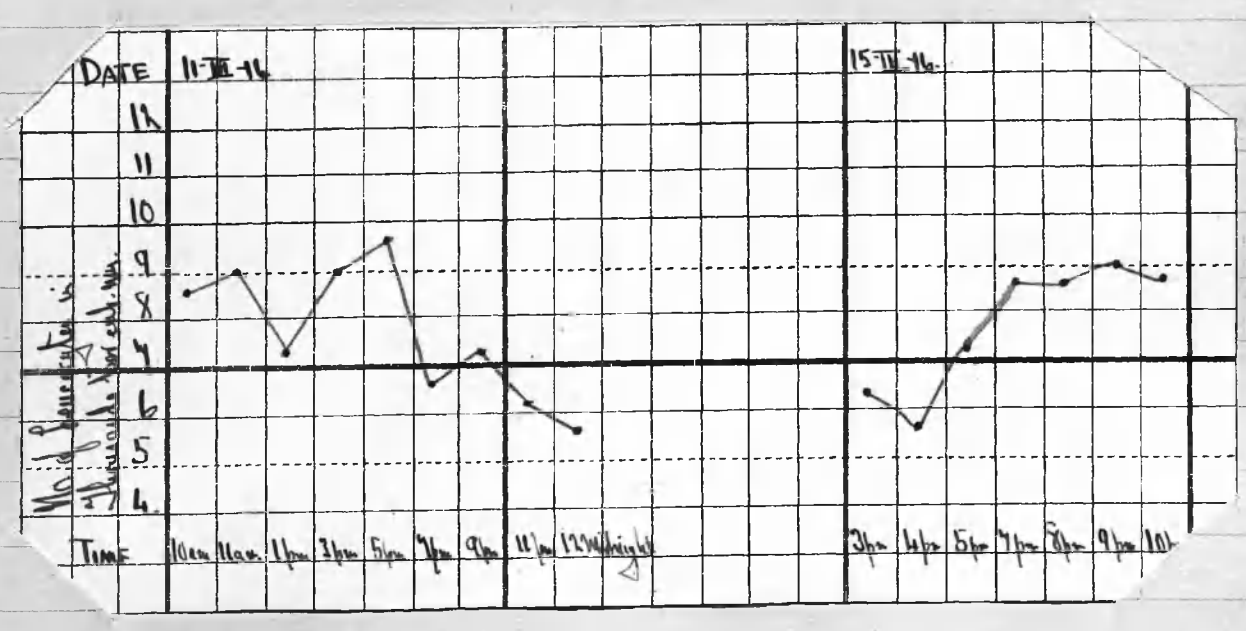
Case XXVIII R. Q. aet 41.

11-III-16.

Time	Leucocytes	Remarks.
10 a.m.	8,600	1 hr. after breakfast.
11 a.m.	9,000	Patient up and on full exercise.
1 p.m.	7,400	—
2 p.m.	9,000	2 hrs. after lunch.
5 p.m.	9,800	After 2 hrs. exercise.
7 p.m.	6,800.	1 hr. after Evening Meal.
9 p.m.	7,400.	—
11 p.m.	6,200.	After 2 hrs. in bed.
12 midnight	5,600.	—

15-III-16.

3 p.m.	6,400	1 hr after Tuberculin BE. ·0003 c.c.
4 p.m.	5,800	—
5 p.m.	7,200	—
7 p.m.	8,600	1 hr after Evening Meal.
8 p.m.	8,600	—
9 p.m.	9,000	—
10 p.m.	8,800	After 2 hrs. in bed.



Case XXIX W.H. Act 34.

DATE 3-I-16.

Physical Signs: On percussion: Both upper lobes impaired in resonance, anteriorly and posteriorly.

On auscultation: Breath sound very weak all over the chest, especially posteriorly towards the bases.

Remarks

Patient's general condition was very poor. On admission the temperature remained normal, and remained so for three weeks. Then there was some slight fever, 99 at 99.6 being registered in the evenings. The pulse rate was always raised proportionately to the amount of fever. During March '16, patient improved markedly and began to put on weight, having gained 16 lbs. in twelve weeks.

The sputum contained tubercle bacilli. No secondary organisms were discoverable, and pus cells were only moderately numerous.

13-I-16.

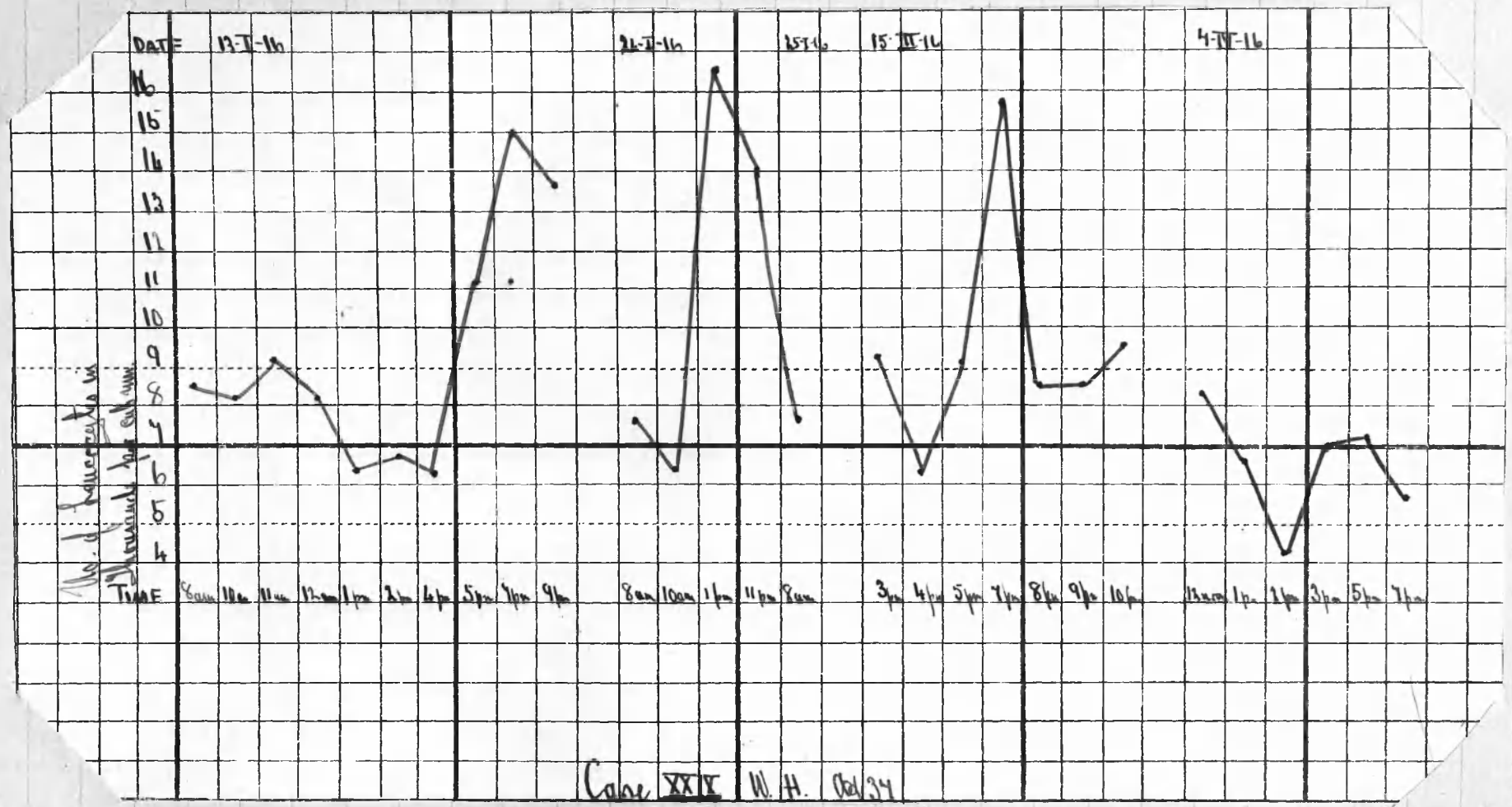
TIME	LEUCOCYTES.	REMARKS.
8 a.m.	8,600	Rest in bed; just before breakfast.
10 am	8,200	" " "; 1½ hrs after "
11 am	9,200	—
12 noon.	8,200	—
1 pm	6,400	—
2 pm	6,800	1 hr after lunch.
4 pm	6,400.	—
5 pm	11,200.	—
7 pm	15,000.	—
9 pm.	13,800.	—

Case XXIX W. H. Ast. 34.

24-I-16.

Time	Leucocytes	Remarks.
8. a.m.	4,600.	Patient up: just before breakfast.
10 a.m.	6,400	" "; 1 hr. after "
1 p.m.	16,600.	" "; just finishing.
11. p.m.	14,000.	After 2 hrs rest in bed.
25-I-16.		
8 a.m.	4,800.	Before rising.
15-III-16.		
3 p.m.	9,400.	Patient up: 1 hr. after. B.E. 0004 (Tubercular)
4 p.m.	6,400.	—
5 p.m.	9,200.	—
7 p.m.	15,800.	1 hr after Evening Meal.
8 p.m.	8,600	—
9 p.m.	8,600	After 1 hr in bed.
10 p.m.	9,600	
4-IV-16.		
12 noon.	8,400	Patient up: on light exercises.
1 p.m.	6,600	—
2 p.m.	4,200	1 hr after lunch.
3 p.m.	4,000	—
5 p.m.	7,200	—
7 p.m.	5800.	1 hr after Evening Meal.

[For Chart, see over]


DATE
13-I-16
24-I-16
15-I-16
15-III-16
4-IV-16
16
15
14
13
12
11
10
9
8
7
6
5
4
TIME
8am 10am 11am 12noon 1pm 2pm 4pm 5pm 7pm 9pm
8am 10am 1pm 11pm 8am
3pm 4pm 5pm 7pm 8pm 9pm 10pm
12noon 1pm 2pm 3pm 5pm 7pm
Case XXIX W. H. Oct/34

Case XXX. H.R. Ad. 39.

DATE. 30 XI - 15.

Physical Signs. On percussion: Rt. apex dull to percussion, back and front. Whole of left lung impaired in resonance, anteriorly and posteriorly.

On auscultation. The breath sounds were very harsh over both lungs posteriorly. Crepitations were numerous over the posterior aspect of left lung and Rt. upper lobe. In front, a few moist sounds were audible at Rt. apex.

Remarks.

For disease so extensive patient displayed remarkably few symptoms. He had a slight cough and a little expectoration, which contained Tubercle bacilli in all of seven examinations. Many small diplococci were found and on two occasions, clumps of staphylococci were also noted. Pus cells were moderately plentiful. The temperature remained normal throughout, and the pulse rate was constantly between 80 and 90 per minute.

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6 - XII - 15.

TIME	LEUCOCYTES.	REMARKS.
10 am.	10,600	patient up: 1 hr after breakfast.
3 pm.	12,000	" "
4 pm.	9,400.	" "
31 - XII - 15		
11 am.	10,200.	Patient on light exercise.
1 pm.	14,400.	-
2 pm.	8,800.	1 hr. after lunch.
3 pm	16,200.	-
4 pm.	12,600.	After 1 hr. exercise Golf
8 pm.	10,200.	2 hrs. after Evening Meal.
9 pm	11,200.	After 1 hr. in bed.

Case XXX HR. Adm. 31. (Cont)

24-I-16.

Time.	Leucocytes.	Remarks.
8 a.m.	6,800.	Just before breakfast.
10 a.m.	10,000.	1 hr after "
1 p.m.	12,600.	—
11 p.m.	10,800.	After 2 hrs. rest in bed.

28-II-16.

1 p.m.	9,600.	—
2 p.m.	12,400.	1 hr after lunch.
3 p.m.	8,400.	—
6 p.m.	6,000.	—
8 p.m.	4,800.	—
9 p.m.	8,800.	1 hr after Evening Meal.
8 p.m.	15,800.	After 1 hr. walk.

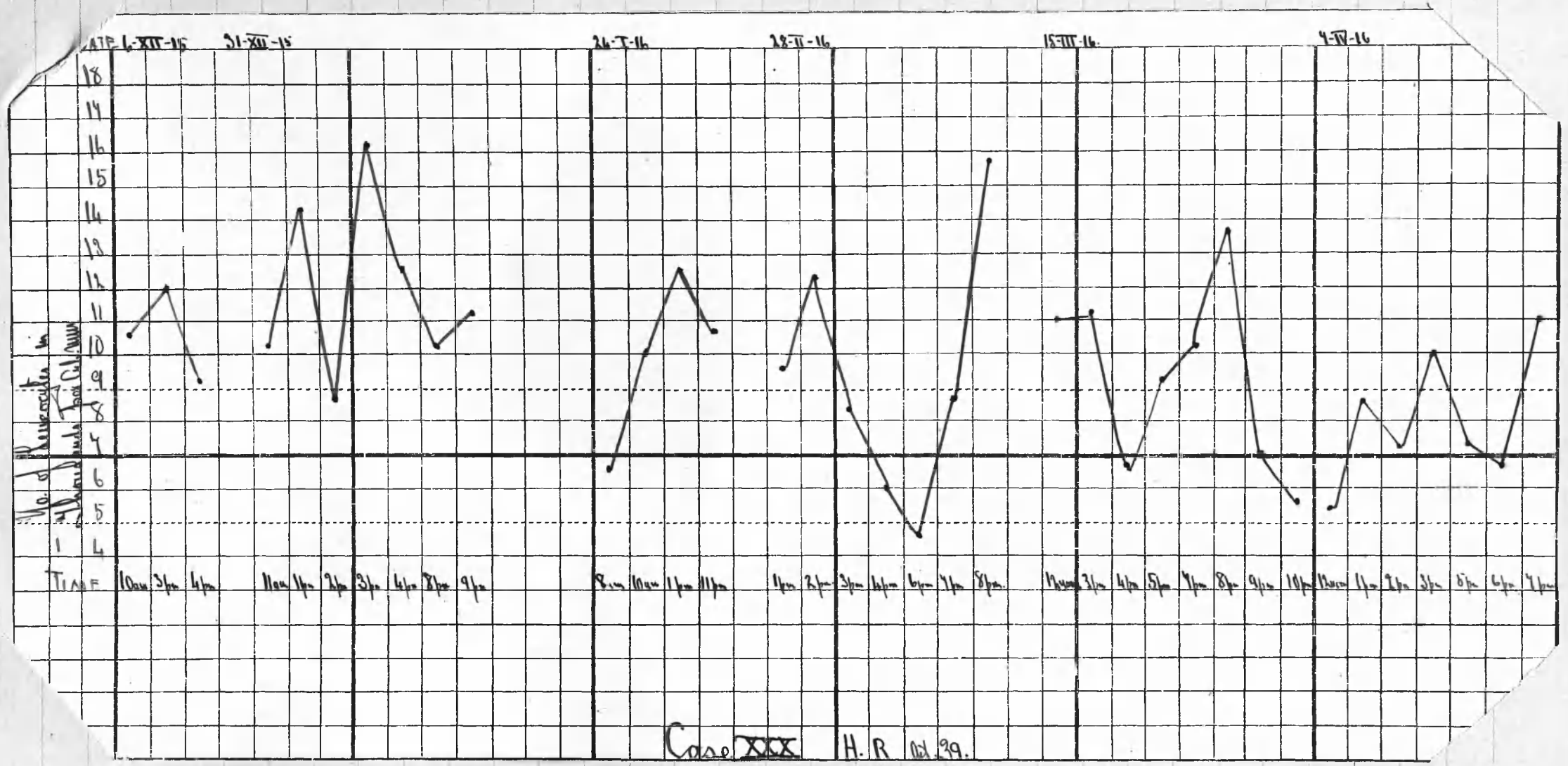
15-III-16.

12 noon.	11,000.	—
3 p.m.	11,200.	1 hr after Intravenin BE. 0.006 cc.
4 p.m.	6,800.	Patient up. but Coaching
5 p.m.	9,400.	Patient " " "
4 p.m.	10,200.	" " " " 1 hr after Evening Meal
8 p.m.	13,200.	—
9 p.m.	4,000.	After 1 hr. in bed.
10 p.m.	5,600.	—

4-IV-16.

12 noon.	5,400	Patient up and on full exercise.
1 p.m.	8,800.	" " " " "
2 p.m.	4,200	1 hr after lunch. " "
3 p.m.	10,000.	" " "
5 p.m.	4,400.	After 2 hrs. Golf.
6 p.m.	6,800.	—
9 p.m.	11,000	1 hr after Evening Meal.

[For Chart, see back]


DATE 6-XII-15
31-XII-15
24-I-16
28-II-16
15-III-16
4-IV-16
No. of Pulmonary Tubercle Bacilli per Cubic mm
TIME
10am 3pm 4pm
11am 1pm 2pm 3pm 4pm 8pm 9pm
8am 10am 1pm 11pm
1pm 3pm 3pm 4pm 6pm 7pm 8pm
12noon 3pm 4pm 5pm 7pm 8pm 9pm 10pm
12noon 1pm 2pm 3pm 5pm 6pm 7pm
Case XXX H.R Pat. 29.

Chapter III

The Significance of the Successive Leucocyte Count in Pulmonary Tuberculosis.

"It has been said that a leucocyte count per se is of very little practical value unless it has also been determined which cells participate in the bringing the count up to the given value. Such a dictum may be very sound in theory, but one must recognise that, once it has been established that a certain cell is the predominating one in any particular disease, then a total white cell count must be relied upon to give some clue to the content of that cell in the blood. Take, for instance, the ordinary septic infection. From clinical experience we know that the polymorphonuclear leucocytes are the cells which are present in largest number and which constitute, in effect, the leucocytosis. Similarly, in lymphocythaemia, the lymphocytes constitute the bulk of the cells upon which the high counts of that disease depend. It is far from me to minimise the importance of a differential blood count. As I hope to show later on, the differential leucocyte count in phthisis is of extreme importance as an aid to diagnosis, but from some observations I have made I can show that in cases commonly known as cases of "mixed infection", the predominating cell is the polymorphonuclear leucocyte. This is, in fact, the common opinion. Klebs agrees that the leucocytosis of tuberculosis, when present, is usually of the polymorphonuclear variety. Holmes, Da Costa, Emery, Einhorn, Herbert and Bandelier and Roepke are also of the same opinion, while

Galland and Goodall state that the polymorphonuclear leucocytosis in advanced cases of tuberculosis is the result of the septic rather than the tuberculous infection. With these writers I am in absolute agreement, for in all cases in which I have found a leucocytosis, I have found the neutrophile polymorph to be the cell concerned in the production of the leucocytosis, amounting sometimes to as much as 90% of the total number of the white cells. In early cases of phthisis showing a leucocyte count within normal limits, the polymorph does not have the same numerical value. In fact, in these early cases, the neutrophile leucocytes are frequently decreased in number at the cost of an increase in number of the lymphocytes. Further discussion of the differential leucocyte count would, however, take me beyond the scope of my thesis, so I shall return to the consideration of the consecutive leucocyte counts enumerated in Chapter II, bearing in mind the role of the polymorphonuclear leucocyte in the leucocytosis of tuberculosis.

A careful study of the thirty cases on which consecutive leucocyte counts were done brings up several points for our consideration.

In many of the cases examined, it will be noticed that the daily variation in the number of leucocytes found in the blood was undoubtedly a most outstanding feature. Such a daily variation has been noted to occur in other diseases, and in Martin's work, to which I have already referred, this variation was observed in phthisis. By the term variation, I mean, variation in excess of that occurring normally. In the healthy patients whom I examined I found that a count of 13,000 leucocytes per cub. mm., after

slight exercise may be compatible with health. The comparatively low counts secured from the healthy patients when the observations were made during the night show also that, normally, there is a tendency to a low E. count in health during the late evening and early morning hours. It requires only a cursory glance through the charts I have made (Chapt II) to convince one that there is a remarkable tendency for the total leucocyte count in pulmonary tuberculosis to vary enormously in some cases. This variation does not occur in all, but I propose now to consider one or two circumstances which, in my opinion, are responsible for such a phenomenon.

The Influence of the Diseased Lung.

Remembering that pulmonary tuberculosis is a disease of chronic tendencies, involving the respiratory organs, it becomes obvious that not only must the diseased tissue be exposed at some time or other to contamination with organisms other than the tubercle bacilles, but the chronicity of the disease also renders it possible for other organisms to postpone their attacks, as it were, to a more favourable time.

In some cases, — in fact, in all cases at first, — the tuberculous lesion is a closed one, and if the process of encapsulation of the bacilli be complete there may be no symptoms or signs whatever to justify the diagnosis of tubercle. In these cases the tubercle bacillus is the only organism concerned in the pathological process. Sooner or later, however, the lesion becomes "open", and the clinical manifestations are tubercle bacilli in the sputum, some slight bronchitis localised to one apex, and, perhaps, a slight elevation of temperature. The presence of

tubercle bacilli in the sputum can be easily understood. Their appearance represents an advancement in the pathology of the disease, but there is another element which strikes me as being of undoubted value when found in any quantity in the sputum. I refer to pus cells. By the ordinary method of counterstaining with Methylene Blue or Malachite Green, these pus cells can be found in every sputum examined. But I doubt very much whether sufficient importance has been attached to their presence. I know of no method whereby it is possible to count the number of pus cells in any given sputum, but their presence in enormous number in some cases is paramount evidence that they play an important part in the reaction of the body to invading organisms in the lungs and bronchi. Both Lowenstein and Wolff have in the past directed attention to the significance of pus cells in the sputum, but altogether, considering their relative abundance, they have attracted comparatively little notice. In the cases which I have enumerated in the previous chapter I have made a short note on the examination of the sputum from each case where possible, and when I have noted pus cells in any quantity I have always made a special note of the fact.

The rôle of the pus cell in ordinary pyogenic infection is no longer a subject of contention. We know that the pus cell represents a piece of dead protoplasm, the victim of direct organismal attack, or indirect, by means of toxins. The presence of the pus cell in any quantity signifies the presence of pus forming organisms, and when the tubercle bacillus is found in association with large numbers of pus cells, one must reflect on the term "non-pyogenic" as applied to the Koch-bacillus.

From microscopical examination of pathological tissues, we have seen that the polymorphonuclear leucocyte plays a very inferior part in the construction of the tubercle in its earliest conception. If, however, the tubercle erodes its way into a bronchus, or even if it becomes into communication with the inspired air through the means of alveolar tissue, the result will be the same, - namely, contamination with other organisms. The discharge from even a very small tuberculous lesion will excite a local inflammatory process by virtue of the irritation which it, as foreign matter, produces. Incidentally, this will lead to a weakening of the tissue, - a bronchiole it may be, - and a bronchiolitis is thus produced, which may manifest itself clinically in slight cough and expectoration, even when no physical signs in the chest are to be observed on examination. One might conclude, à priori, that an advancing lesion of this nature which includes alveolitis, bronchiolitis, and bronchitis, according to the situation of the lesion, would evidence itself in ways other than by physical signs in the chest alone. In those cases where an elevation of temperature complicates the tuberculous process, we have been in the habit of ascribing the former, vaguely, to "mixed infection", even when it has been impossible to find the organism or organisms other than the tubercle bacillus, responsible for the damage. The researches of Inman have proved conclusively that it is impossible by methods at present at our disposal to tell when a mixed infection is absent. He has found that in all "Resting Febrile" cases examined by him, there was evidence of secondary infection, and in the "Ambulant Afebrile" group such infection could not be excluded. The temperature chart alone, he concludes,

cannot determine the presence or absence of a secondary infection.

It is true that in many cases we can say definitely that it is present, but I agree with Inman in saying that a normal temperature, — and, I would add; a normal pulse-rate, are not sufficient to exclude a mixed infection. With this view many writers, including Ortner, agree. Ortner lays particular stress on the distinction between the tuberculous and the pneumonic processes going on in the pulmonary tissue; they are different histologically as well as etiologically. The pneumonic processes so common in pulmonary tuberculosis are the result of the activity of the Micrococcus pneumoniae; the tubercles, of that of the tubercle bacillus.

The term "mixed infection" is an unfortunate one inasmuch as it includes a great many definitions, being first used by Brieger and Ehrlich in 1884 when recording a case of enteric fever which was complicated by the onset of malignant oedema. Nowadays, we should not term such an occurrence a mixed infection; as a matter of fact, the the term "mixed infection" has been so extensively used in connection with phthisis that we are now inclined to consider it as alluding solely to phthisis. Spengler would not consider phthisis developing in a person with bronchitis, a mixed infection; he would term that an attendant infection.

Riviere and Morland define a mixed infection as follows: "For a mixed infection in phthisis, the two germs must be present, not merely at the same time, but also in the same place, and a mixed infection in phthisis is one in which the tubercular tissue becomes secondarily the settling ground of other organisms." As these authors themselves say, it is a matter of it

considerable difficulty to accept this definition, for an organism does not necessarily require to be in the tubercular tissues in order to make its presence felt. The definition is, therefore, open to argument, and cannot be said to represent the case. Bearing in mind the frequency with which phthisis follows chronic, or even acute bronchitis, pneumonia and influenza, the association of other organisms with the tubercle bacillus is not to be wondered at; the relative frequency with which these organisms are found will be discussed immediately. Of course, it does not follow that the secondary invaders are always virulent, but my thesis is that they do make their presence felt much more commonly than is observed, and in taking consecutive leucocyte counts I believe we have one possible means of estimating their virulency.
We are all familiar with the havoc played by other organisms, — the staphylococcus or the streptococcus particularly, — in lupus, and in "cold" abscesses which have been opened and left unheeded.
What holds true of lupus, mutatis mutandis, is true of every tuberculous affection to which microbes can gain access. (A. E. Wright)
Besides, it does not follow that an organism like the Micrococcus Catarrhalis remains lowly pathogenic when in symbiosis with other organisms. Prudden's experiments show conclusively that the concurrent action of two distinct pathogenic organisms may result in a considerable modification of the lesions which either could produce alone. Von Korczynski has gone further and proved that the poisons of the tubercle bacilli increase the virulence of some organisms. (bacillus coli, streptococcus and staphylococcus).
The question arises then, "What is the significance of

pus cells in the sputum?" As I have said, one seldom examines a sputum without finding pus cells in fair numbers permeating the mucus on the slide.

If, in the case of pulmonary tuberculosis, we start with the assumption that the tubercle bacillus is not a pus producing organism in the proper sense of the term pyogenic, we must find another explanation for their presence in such large number in so many cases of phthisical sputa examined.

It has been shown by numerous observers that many different organisms may be present in conjuction or in association with the tubercle bacillus. Their relative frequency is, for the purposes of our argument, of little value, but the undermentioned authorities have made the following observations.

J. W. Hastings, quoted by Webb, found that in 345 cases of nontubercular pulmonary conditions, (tuberculosis suspected but tubercle bacilli not found) the frequency of secondary organisms was as follows.

1, Micrococcus Catarrhalis.
2, Pneumococcus.
3, Streptococcus pyogenes
4, Staphylococcus pyogenes (aureus, albus or citreus)
5, Friedlander's bacillus (Bac. mucosus capsulatus).
6, Micrococcus tetragenus
4 Bac. Influenza
8, Bac. Pyocyaneus.

In 105 of the 345 cases, cultures were taken and the same order of frequency was observed except that staphylococci were first instead of fourth.

Webb himself examined 156 cases of pulmonary tuberculosis where tubercle bacilli were present in the sputum and made cultures in 20 cases, with the following results:

1 Streptococcus pyogenes.
2, Micrococcus catarrhalis.
3, Pneumococcus (Fraenkel).
4, Staphylococcus (aureus, albus or citreus)
5, Bac. Pyocyaneus.
6, Friedländer's Bac.
7, Mic. Tetragenus.

Ortner's results may be tabulated thus:

Group I.

Tuberculosis and pneumonic foci.

Cases examined = 24.; Tub. Bac. found in 24.; M. Pneumoniae found in 23.

Group II

Tuberculosis without signs of inflammation round the tuberculous foci.

Cases examined = 15.; Tub. Bac found in 15; M. pneumoniae found in 5;
No secondary organisms in 10.

Group. III.

Acute or Subacute Miliary Tuberculosis.

Cases examined 9.; Tub. Bac found in 8; M. Pneumoniae found in 8
Staphylococcus found in 1.

Petroff examined 44 cases and the following organisms were found.

Staphylococcus in 23 cases. Streptococcus in 18 cases. Pseudo-diphtheria bac. in 8 cases.
Bac. Pyocyaneus in 4 cases. Mic. Tetragenus in 4 cases. Bac. Coli Comm. in 1 case.
None in 3 cases.

One of the best contributions to the literature of mixed infection is by Ravenel and Irwin. Twenty-two cases were investigated and the following bacteria were isolated from the sputum, which was, of course, washed after the method suggested by Kitasato:

Streptococcus 22 times : Staphylococcus 18 times; Bac. Coli Communis 4 times.; Bac. Diphtheriae 2 times : Bac. Subtilis 3 times; Pneumococcus 9 times; Sarcinae 14 times : Others 8 times.

My own observations may now be recorded. Altogether, I have, for the purposes of this investigation, examined 238 sputa microscopically. The order of frequency of organisms met with were as follows.

1, Micrococcus Catarrhalis.
2, Tubercle Bacillus.
3, Staphylococcus.
4, Streptococcus
5, Pneumococcus.
6, Diphtheroid - bacilli.
7, Micrococcus Tetragenus.

In fifty of the above cases, - all "first stage" cases according to the Turban - Gerhardt classification, I made cultures on blood-agar after washing the sputum in relays of water, as Webb has done, with the following results:

Staphylococcus. 31 times. Streptococcus 26 times.
Micrococcus Catarrhalis. 24 times. Pneumococcus 16 times.
Diphtheroid bacilli 4 times. Other organisms: 12 times.

So far, then, from the clinical side, the evidence in favour of the presence of secondary organisms is conclusive.

From the pathological side of the question there are the experiments of Sata and Ophüls who have examined the lungs post-mortem in cases which died from tuberculosis of the lungs. The former observer found bacteria in the walls of cavities or in the interior of bronchi-pneumonic foci either alone or in conjunction with tubercle bacilli, in 12 out of 21 cases examined, the streptococcus predominating. Ophüls examined 26 cavities and found tubercle bacilli alone in 4; in all the others there were mixtures of bacteria, which included Streptococcus, Pneumococcus, and pseudo-diphtheria bacilli. The incidence of secondary organisms in phthisical cavities is given by Ravenel and Irwin as follows:

36 Cavities were examined.

The Streptococcus	was found	23 times.
Staphylococcus	" "	30 "
Pneumococcus	"	4 "
Bac. Pyocyaneus	" "	1 "
Bac. Col. Comm.	"	20 "
Bac. Lactis Aerogenes	"	3 "
Bac. Diphtheriæ	"	5 "
Yeasts.	were "	9
Sarcinæ	" "	4 "

The power of many of the above-mentioned organisms to produce pus is undisputed, and it is a very significant fact that those which head the lists belong to the class of true pyogenic organisms.

Remembering for a moment that in a case of advanced phthisis, with cavity formation, and an open lesion discharging tubercle bacilli, elastic fibres and connective-tissue fibres, and running a typical hectic fever, we are in possession of a case of mixed infection, we must enquire into the blood picture to see if any help

can be obtained therefrom, or if any parallel can be drawn between the nature of the case in question and the leucocyte count. Reference to Cases I, V, XI, XIII, XXII etc will show that the amount of "leucocyte swing" is considerable, reaching as high as 33,000 and falling as low as 11,000 in Case I. On the other hand, in Case III, where there was cavity formation and a temperature of 100.4° F. on the day of examination the highest leucocyte count obtainable was only 16,200; all the other counts were well within normal limits. In Case III also, although tubercle bacilli were found repeatedly, no other organisms were ever noted, which of course does not signify that they were absent; I have noted particularly that pus cells were comparatively scarce. From my experience of cases like this one I can endorse the views of those who dissent from Stein and Ortmann, who have maintained that the absence of leucocytosis excludes cases with cavity formation. Undoubtedly, the beginning of cavity formation is the beginning of a pneumonic process with ultimate expectoration of the necrotic tissues. The leucocytosis which accompanies such a case is certainly associated with the presence of other organisms. Once the cavity is established, however, repair may be complete, and very few secondary organisms found, provided the case show any signs of arrest. It is in cases such as these that a leucocytosis need not necessarily accompany cavity formation.

This theory is in perfect harmony, I have noted, with that set forth by Kjer-Petersen in 1906.

In Case I, which is in many ways the most interesting in the series, the daily variation in the leucocyte count is very marked. The maximum count on Dec. 14. viz 33,000 caused me to repeat the examination four times, with results not differing by more

than 3 per cent. The temperature on that occasion was 99° F.. I showed my findings in this particular case, to Dr Heathcote, my predecessor at Crosby Sanatorium, and informed Dr M. C. Haring to whom the patient belonged. We regarded the condition as a clinical curiosity and I resolved to repeat my observations on this case, which I did on Jan 24, 1916 and Feb. 22, 1916.. The patients general condition was improving meanwhile as was also the local condition in the chest, as evidenced by the decrease in the number of moist sounds, a normal temperature and a diminished pulse rate. The latter, however, was at times somewhat rapid; 90 to 100 per minute; even when the temperature was normal. The sputum was never free from tubercle bacilli, and pus cells were always abundant. From my experience with another case, I felt justified in regarding the disease as still being active and, accordingly, I postponed giving this patient the benefit of exercise until after I had examined him again on Feb. 24. 1916.. The subsequent history of the case more than justified my conclusions, for the patient died suddenly from haemoptysis on Feb. 29, 1916. I dwell at length on this case because,-

1st. The temperature was not hectic; it never rose above 99.8° F.

2nd, The patients general condition was, to all appearances, improving.

3rd, There was also an improvement, apparently, in the physical signs in the chest

4th, There was no cavity formation.

The only points which suggested themselves to me that the patient was not altogether free from danger were.-

1st, The accelerated pulse-rate.

2nd, The presence of pus cells and tubercle bacilli etc. in the sputum (See Case I Chapt II)

3, The results of the successive leucocyte counts.

Here, then, are cases which vary widely in respect of physical

signs in the chest and which present blood-pictures of more than usual interest. Is it possible to reconcile the blood findings with the physical signs in the chest? Briefly put, it appears as if the leucocyte count has a definite relationship to the acuteness of the process, and that the acuteness of the process has, in turn, a more or less intimate connection with the presence of organisms other than the tubercle bacillus. So far as leucocytosis is concerned, the consensus of opinion is in favour of this view when strictly analysed. Thus Gravitz maintains that in Stage I the number of leucocytes is unaltered; in Stage II they are moderately increased, and in Stage III, with fever, the leucocytes are much increased. Allom and Craig found them to average 10,286 in the first stage, 14,442 in the second, and 14,041 in the third.

In several of my cases eg. Cases ~~X~~ XVIII, XXV. there was no reason to suppose that the patients in question had any active disease in the chest as judged by the physical signs revealed, by the pulse rate or by the temperature, and in those same cases one can hardly doubt the fact that phthisis did exist. The diagnosis in those cases was that of chronic phthisis or early phthisis in the process of arrest. One can conclude justly that although the tuberculous process was still present, the pulse rate, temperature and physical signs all pointed to quiescence of the disease. The leucocyte count in these cases was not far short of being within normal limits and the sputum examination was either negative for Tubercle bacilli or else it showed very few pus cells and other organisms with tubercle bacilli. We may state, therefore, that in these cases, — cases of apparently uncomplicated tuberculous infection, — the leucocyte count is normal.

But when we come to examine many of the cases, we find

that not only is there a leucocytosis, but that this leucocytosis is not constant in the sense that the leucocytosis of pneumonia or of a moderately severe septic infection is constant. It is in those cases that there is what I have termed a "leucocyte swing", which is a distinct departure from normal.

In the extreme cases of mixed infection as exemplified by Case XXII, there is an infection not only by the tubercle bacillus, but also by other organisms. Now, all the organisms present in the diseased focus are in a vascular area, so to speak. The usual explanation given for an abrupt rise in temperature occurring in a tuberculous individual running a hitherto normal temperature, is that it is caused by an autoinoculation. The physiology of an autoinoculation is, briefly, a carrying away from the tuberculous area of the patient's own tuberculin, the agent being the blood stream. (The importance of the blood stream as a conveyance of toxicity must not be underestimated, for we know that it is a feature of the tubercle bacilli to establish themselves, primarily at least, in vascular organs, eg. the face in lupus, the lungs in phthisis and the epiphyseal line in bones.) If, however, there are products of other organisms to be carried into the blood-stream as well, it follows that the autoinoculation must be a compound one, composed of the toxins of the organisms present in the diseased tissue. The staphylococcus, streptococcus and the pneumococcus we know to be capable of producing pus, and incidentally, a leucocytosis. The advanced phthisical case, then, with the lung tissue swarming with staphylococci, streptococci, tubercle bacilli etc is merely containing in his chest an incubator for these organisms. The wonder is that he survives so long. No doubt,

part of the defence of the body in this state is by means of the leucocytes, acting as phagocytic agents, or as carriers of complement; - an interesting point for discussion which I will deal with later. This explanation of the leucocytosis of advanced phthisis is so far in keeping with the explanation of the leucocytosis of ordinary septic infection. What is the explanation of the extreme variation in the count which occurs in many cases?

As I have shown from the charts in Chapt. II and as Martin has also pointed out, there is very little definite about the count except that it tends to reach its minimum in the late evening and in the early morning hours. After all, this is to be expected. When the patients were examined in the very early morning or in the late evening it was found almost without exception that the count was at the lowest point it could attain in 24 hours. I agree further with Martin in saying that, ~~even~~ even although the count is high during the late evening and early morning hours, yet one can surmise with considerable justification that a count taken from the same person in the afternoon would be much higher. I have shown (Chap. I) that in a healthy individual, when counts are taken during the night, the number of white cells tends to be smaller than during the day. The most important factor producing such a result in a healthy person is undoubtedly the state of rest, - rest of muscles and rest of digestive processes, - which accompanies the late evening and early morning hours in most people. The influence of rest on the number of leucocytes has been established for all ages. Wernstedt and Schkurina quoted by Brauner, have found that in the normal infant the white cells are fewer during rest and sleep, and are increased with crying and during the waking state.

I maintain that in the case of a tuberculous person with a well advanced lesion which is the seat of secondary infection, rest certainly plays an important part in the regulation of the leucocyte content of the blood. During rest, the cardiac, respiratory, muscular and digestive systems are working at their minimum. In Case I (Chap. II) the first series of counts was made when the patient was at rest in bed. It will be noticed that in this case, the counts taken during the day time are very high despite the fact that the patient was in bed. But one must consider that all the body functions are working at a higher pressure during the day than during the night, the most outstanding example being the digestive functions. This patient was not, moreover, at absolute rest. He was allowed to sit up, read, and write letters; — efforts which, although apparently trivial in themselves, suffice to show that the difference between the wide-awake and the sleeping condition is to be reckoned with as an excitor of leucocyte formation.

It is difficult to explain why a count of 21,000 leucocytes per cub. mm. should be followed, two hours later, by a count of 10,800 leucocytes, as is the case in Case V Chap. II. Several of the other cases quoted in Chap. II exhibit a similar phenomenon. One can do no more than suggest a possible explanation for such a thing.

The function of the polymorphonuclear leucocyte, despite what is known of its structure and life-history, is far from clear. If we regard it as a weapon of defence, then we must specify whether it defends by direct or by indirect methods. There are, in other words, two main views as to the function of the polymorphonuclear leucocyte; firstly, that it is phagocytic; secondly, that it is an important element in the process of immunity. The first view is the one which was held.

previous to the formation of the hypothesis of immunity elaborated by Ehrlich. In order to fit in with Ehrlich's theory it was necessary to ascribe to the leucocyte a rôle in the production of immunity; and so, according to Metchnikoff, the complement of Ehrlich is represented by the Alexins, certain chemical substances of the nature of an unstable nucleo-proteid.

So far as the phagocytic function of the polymorph is concerned, there is no doubt that the cell possesses this power in a marked degree; — to some organisms more than to others. It is in relation to the immunising properties of the polymorphonuclear leucocyte that special interest centres. So intimately, however, is the question of immunity bound up with that of phagocytosis, that it is convenient to give several possible causes for the remarkable low counts which interpolate themselves with such regularity in certain cases of tuberculosis of the lungs.

For these periodical remissions in the consecutive leucocyte counts, we may offer several explanations.

1st. That they are due to Rest.

This, obviously, is not the case, for although the counts tend to be lower during the usual resting hours, yet one can find a very low count during the day time, when patients are up and going about. It is the very existence of this diminished count in the day time that gives the successive counts their characteristic "swing" when recorded in series. Absolute rest, does, however, tend to reduce the total number of cells in the manner explained above i.e. by reducing the working of all the body processes, of which the heart's action is the most important, to a minimum.

2nd That they are due to Bone-marrow exhaustion.

If this were the case, one would expect that one low count would be followed by another. So far as the total number of cells is concerned, this is not the case. At present, we are considering the quantitative, rather than the qualitative changes in the cells, and from the observations on the cases in Chap. II we are not entitled to say that a temporary diminution in the total white cell counts is indicative of marrow exhaustion. But an interesting point presents itself here. Suppose, for example, that we reconsider Case I. The counts taken on Dec. 14, 1915 represent internal acute processes which are being responded to by leucocytosis. The counts taken on Feb. 22, 1916 may represent one of two things, either that the lung disease was becoming less acute, and that a smaller leucocyte response was necessary, or that the bone-marrow was becoming exhausted. One is hardly in a position to say that a leucocyte count of 18,500 denotes marrow exhaustion. (vide Case II Feb. 22, 1916; 4 pm); it certainly does not indicate marrow exhaustion from a quantitative point of view. As I hope to show later, it is not at all uncommon to find a leucocyte count of 12, to 20,000 per cub. mm. in an advanced case of phthisis with, however, a very poor qualitative picture. By the latter term I mean a differential leucocyte count, not only of the white cells en masse, but of the polymorphonuclear cells in particular, as has been estimated by the methods of Arneth and Schilling. By making use of these combined methods of estimating the value of the polymorphonuclear leucocytes, one is enabled to say definitely whether a given leucocytosis represents a healthy reaction on the part of the bone-marrow to the infection, or whether the apparently satisfactory quantitative reaction is in reality a poor qualitative one and indicating, therefore, a

failure on the part of the bone-marrow to satisfy the demands of the body. It has been definitely proved by Andrewes and Cadbury that in cases of wasting diseases such as tuberculosis, the bone marrow itself was in a condition of mucoid transformation, very poor in cellular elements when the leucocyte count was as high as 100,000 per cub. mm.
The outcome of this argument is, therefore, that the low counts which present themselves in some cases do not per se represent an exhaustion of the resources of the bone marrow, but, when the cells are examined qualitatively, much important information may be evolved. (vide post).
In all my investigation on the leucocyte counts in patients suffering from pulmonary tuberculosis, I have not had a case showing constant leucopenia. In some respects I have been surprised at this, for in many cases, the daily output of polymorphonuclear leucocytes is three, four, and sometimes five times greater than that occurring in health, and this output has been kept up for weeks at a time (see Case XXII Chap. II)
It is not fair to assume that the haemopoietic organs can keep up the necessary quality as well as the requisite quantity of cells; the former certainly suffer, as I shall show when considering the differential counting of the cells.

3rd <u>That they are due to periodical intermissions of substances acting on them by a process of negative chemiotaxis</u>

It is only by supposing that some such substance exists that the periodical remissions of the leucocytes can be explained with any degree of satisfaction. In the light of our present knowledge, we can state two facts with certainty, firstly, - pyogenic organisms have the power of producing a leucocytosis when present in the body in the requisite number,

or when sufficiently virulent; secondly, tubercle bacilli do not possess this property. Muir was among the first to show that a leucocytosis of inflammatory origin was synonymous with a leucoblastic reaction in the bone-marrow. Andrewes, on the other hand failed to get any leucoblastic response after infection with the Tubercle bacilli, the bone-marrow appearing normal in all respects.

In the extreme case of Miliary tuberculosis, where the body tissues are inundated with tubercle bacilli, or their toxins, the existing condition in the blood is one of leucopaenia, a point of special significance in virtue of the fact that in such a case we are dealing with an overwhelming dose of bacilli and toxins.

Now, in these cases of miliary tuberculosis, one cannot say that the bone-marrow is exhausted in the sense that it has produced so many polymorphs that it cannot produce more. We must, as in the case of Typhoid infection, suppose that there exists in the circulation a substance inhibiting the production of leucocytes.

The tubercle-toxin is, then, an Aggressin, but what the exact nature of the Aggressin is, we do not know. Bail, it is true, regarded his Aggressins as non-toxic substances, but it is only fair to state that others e.g. Lauerbeck, dissent from this view, and regard negative chemiotaxis as a minor manifestation of toxicity.

Andrewes, from whom I have quoted before, supports my contention in the following: "I do not find it illogical to conceive that certain inherent products of the natural bacterial body may have become positively chemiotactic to the leucocytes, - thus explaining the facts of spontaneous phagocytosis, while believing that the more highly specialised parasites have secondarily acquired the power of producing another chemical substance which may keep phagocytosis in abeyance."

In the advanced cases of phthisis, – typical cases of mixed infection, – the tuberculo-toxin or Aggressin is also present, but only in conjunction with the toxins of staphylococci, streptococci etc., which are essentially stimulators of leucocyte production. The balance between the various toxins is never equal; one or other predominates at different times and in this way the "leucocyte swing" is maintained, being high when the bone-marrow is suitably stimulated, and being low when the tubercule-toxin is acting.

From such a hypothesis it is easy to explain why the extent of the lesion may be of negligible value in giving a prognosis. (See Case IV where the lesion was extensive and the "leucocyte swing" small; and Case I where the converse was equally true)

It may be pertinently asked at this juncture, 'What happens to the surplus of leucocytes when the low counts are found between high ones?'

Experiments done by Ellermann and Erlandsen, of Copenhagen show that in health, the assumption of the erect posture, or the sudden change to the recumbent position from the erect attitude may be associated with an equally sudden change in the number of leucocytes in the peripheral blood, a change which they distinguish as a static leucocyte reaction. The explanation which they offer for this is that the increased rapidity of the heart's action and the greater velocity of the blood stream produced in consequence, force the leucocytes from the deeper vessels into the superficial capillaries. In phthisis, and more particularly in advanced phthisis, the heart action is extremely irregular as regards rate. The intoxication of the system by the offending organisms and their toxins is the cause of the accelerated pulse-rate; and those same toxins are carried throughout the body at an increased velocity to act on the leucopoietic organs. The stimulation of leucocyte

formation is known to take place at the bone-marrow, but whether the inhibition of leucocyte production is worked from the bone-marrow as a centre is extremely problematical.
The researches of Goldscheider and Jacob., and of Bence and of Andrewes go to show that in cases of rapid decrease in the leucocyte content of the blood, the cells are "held up in the lung, screened off, as it were, by the pulmonary capillaries." Why the leucocytes should go to the pulmonary capillaries is again a matter for speculation. To me, there appear to be two possible explanations; firstly, for oxygenation, the view supported by Andrewes; and secondly, for the combined purposes of phagocytosis and distribution of complement. In connection with the second theory I submit that so long as the leucocyte count remains normal in every respect, - and by that, I mean quantitatively as well as qualitatively, then the leucocytes are carrying sufficient complement for the reaction between Antigen and Antibody to take place. The disease may progress in the lung, and yet the balance between Antigen and Antibody may be quite good, the only departure from normal being a qualitative change in the leucocytes as estimated by Arneth's method. With the onset of any complication such as pneumonia bronchitis or secondary infection, which are sure to come at some time in the progress of the disease, there is a demand for complement of another sort, according to the nature of the infection. In such cases, the bone-marrow may or may not be able to supply the demand then made upon it, and degeneration sets in, - a degeneration which is reflected in the polymorphs in the peripheral blood as I shall show. If, in spite of the intensity of the infection, the leucocytes respond, the patient will overcome his infection simply because his immunity has been sufficient in virtue of his successful qualitative polymorph

response, — qualitative, because an increased leucocyte count per se is not constantly associated with increase of complement. In some cases, a successful outcome will result from a leucocytosis of, say 14,000 per cub. mm., and in other cases it may require 30,000. It is Nature that determines the extent of the leucocytosis. The ebb of the "leucocyte swing" means that the leucocytes are required on ~~that~~ another front, namely, the lung, in order to carry out the two processes on which life depends, viz. immunity and phagocytosis.

4th That they are due to Anaphylactic Phenomena.

There has been a considerable amount of work done recently on the relation of anaphylaxis to tuberculosis. By some it has been said that the reaction which sometimes follows the injection of tuberculin is an anaphylactic phenomenon. Certain it is that the clinical symptoms of anaphylactic shock in no way resemble the clinical symptoms following tuberculin injection. In the former the temperature is markedly lowered, some dyspnoea results, and the end may be in convulsions; in the latter, the temperature is raised, and there is no choking or severe dyspnoea such as is observed in the former. Again, while anaphylaxis can be passively transferred from one animal to another, no such claim can be brought forward for tuberculous sensitiveness. (Friedemann, Koepke etc.) The researches of Rosenau and Anderson, quoted by Hiss and Zinsser, have demonstrated also that anaphylaxis may be inherited, another claim which cannot be extended as yet to tuberculous sensitiveness. On the other hand, it has been found that the condition of anaphylaxis is associated with a disappearance of complement from the serum, and if, as has been taught by Metchnikoff and others, complement is derived from the leucocytes, then one would expect that anaphylaxis would be accompanied by

a diminution in the number of leucocytes.
Andrewes has actually observed the initial ~~the~~ leucopenia in animals suffering from anaphylaxis, and concludes that leucopoenia is an integral part of anaphylaxis. Da Costa divides the blood phenomena resulting after the injection of bacteria, toxins, albumoses, etc, into hypoleucocytosis and hyperleucocytosis. The former, - hypoleucocytosis, is the first result of the foreign matter introduced, and is represented by a diminution in the number of leucocytes in the peripheral blood. The latter, - hyperleucocytosis, is manifested by an increase in the number of white cells, and follows the hypoleucocytosis. Both the hypo- and the hyperleucocytosis are dependent upon the intensity of the irritant acting. To quote Da Costa, "If the irritant is slight, the repellent influence is feeble, and the consequent cellular increase is inconspicuous..... If the effects of the irritant are severe, both the repellent and the attractive stages are promptly excited and markedly developed, and a general increase in the number of leucocytes through the whole circulatory system promptly results..... It sometimes happens that the attractive influence of the chemotactic principle predominates over its repellent action, in which case the stage of hyperleucocytosis may develop without the initial stage of hypoleucocytosis. Clinically, the preliminary decrease is practically never observed, perhaps partly for the reason last given, but also in a large measure, because the repellent action of the irritant has passed off by the time the disease has developed into a clinical picture."
The parallel between the Hypo- and Hyperleucocytosis, and the negative and positive phases of Wright, which follow tuberculinisation, is apparent.
Applying what has gone before to the findings in the cases of pulmonary tuberculosis in Chap. II., the low counts

would represent the stage of hypoleucocytosis, and the high ones, the stage of hyperleucocytosis. It is impossible for one to dogmatise further than this. Whether this phenomenon is anaphylactic or not matters very little; the symptoms displayed by patients with low counts certainly do not correspond to the symptoms shown by patients suffering from anaphylaxis, and one would be bound to say that every autoinoculation is an anaphylactic phenomenon, if one were to adopt such an explanation for the "leucocytic swing". Indeed, so far as I have been able to make out, the patient's condition is absolutely no indication to the leucocyte count.

Taking everything into consideration, there appears to be very little evidence that the response to inoculation, active or passive, in the tuberculous subject, and anaphylaxis are identical. The fact that one phase in the clinical pathology of the one resembles a similar phase in the clinical pathology of the other is no reason for considering them one and the same thing. As we have seen, there are many points of dissimilarity between the two.

Chapter IV.

The Relation of Tuberculin to the Total Leucocyte Count

Most writers agree that leucocytosis follows the injection of tuberculin. The truth of this statement must, however, be accepted with reservation. To begin with, one must analyze the action of tuberculin.
The tuberculin reaction is a three-fold phenomenon, comprising a local reaction at the site of injection, a focal reaction at the focus of disease, and a general reaction consequent on the focal reaction, and signalised by a rise of body temperature, malaise and other symptoms depending for their severity upon the amount of tuberculin given. It is with the focal reaction that I am particularly concerned at present. This reaction is due to an increased supply of blood and lymph to the diseased part. When this supply has been in excess of that anticipated prior to giving the dose of tuberculin, a general reaction follows due to the toxins from the seat of the disease having been carried into the tissues by the blood stream. Provided the dose of the toxins liberated is large enough, or in potent enough then the heat centre is activated and a rise of temperature results with its usual train of symptoms, headache, nausea malaise, increased pulse rate etc.. If the focal reaction be but slight then the general reaction is also slight. In some cases, one can make out from the physical signs alone, as evidenced by the number of râles being increased, cough etc., that a focal reaction is going on, but this is not by any means always the case. As Rivière and Morland remark, the diagnosis of a focal reaction in the chest depends to a great extent on the

powers of observation of the physician in charge of the case. Similarly, with a general reaction, a rise of temperature and malaise need not be present even when an immunity reaction is taking place. Turban, Spengler, Philipsi and others grant that a focal reaction always precedes a general reaction, and Turban specifies distinctly that a focal reaction may occur without any apparent general reaction. Is there, then, any means whereby we can tell whether there is a reaction going on when the ordinary subjective and objective symptoms fail us?

Just as in some cases in which I have examined the leucocyte counts, and where I have found a fair amount of leucocyte swing without any other indication that there was any systemic disturbance, so also I believe that the leucocyte count gives one an indication of the intensity of the focal reaction, and is therefore a guide to the dosage of the Tuberculin to be given.

More work has been done in connection with the leucocyte count resulting from the injection of tuberculin than in any other branch of haematology in tuberculosis. Despite this fact, however, there does not appear to be any unanimity of opinion on the subject. Fulpton and Brown, for instance, conclude that although 10,000 cells per cub. mm is exceptional, yet an essential increase is often present. They failed to find evidences of preliminary decrease or of preliminary leucopoenia such as Andrewes has described as occurring in animals with symptoms of anaphylaxis. It is, however, noteworthy in this connection, that Kinghorn was able to observe this preliminary decrease following tuberculin, in experiments on rabbits. Amongst other observers in this field may be mentioned Tschistowitsch, and Bischoff who, working independently found leucocytosis following tuberculin. The latter puts

little diagnostic value on the sign, because, he says, leucocytosis often happens without Tuberculin. Hamilton Black also found the number of leucocytes to be increased after the injection of tuberculin.

References to Cases. XXV XXVI, XXVII, XXVIII, XXIX and XXX, Chap. II, all patients who have had tuberculin treatment, will demonstrate the fact that in some cases there is a leucocytosis and in other cases this is absent. The explanation of the phenomenon can only, in my opinion, be that which I have advanced in support of the leucocytosis of tuberculous patients who are not having tuberculin.

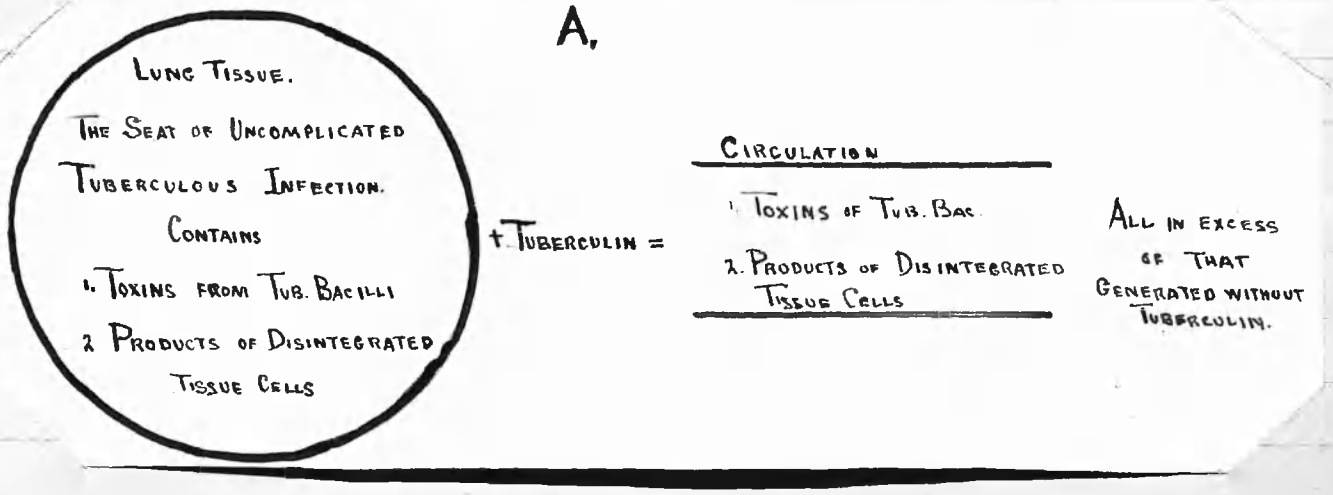
The leucocyte reaction depends entirely on the focal reaction, and upon the nature of the substances, - toxins or otherwise, - sent into the blood stream from the diseased tissue.

The presence of the focal reaction is undoubted; it is the mechanism by which it is produced that is the disputed point. However much we may desire information on the latter question, we must rest satisfied at present with the knowledge that when a reaction occurs, the cause of this is absorption of products from the tuberculous area, and, it may be presumed, from the area in the immediate neighbourhood of the latter. It is apparent, therefore, that the diseased tissue must be counted upon as a source of the reaction apart altogether from the tuberculin administered. But when we come to consider the effect of the tuberculin on the diseased part or parts, we are confronted with a greater difficulty. There is no single tuberculous extract called Tuberculin which can be taken as a standard, either in its chemical aspect or from the point of view of its chemical effects. Some preparations are undoubtedly more potent than others; T, for instance is generally regarded, and is certainly, stronger than B.E. Similarly P.T.O is probably about 40 times weaker than

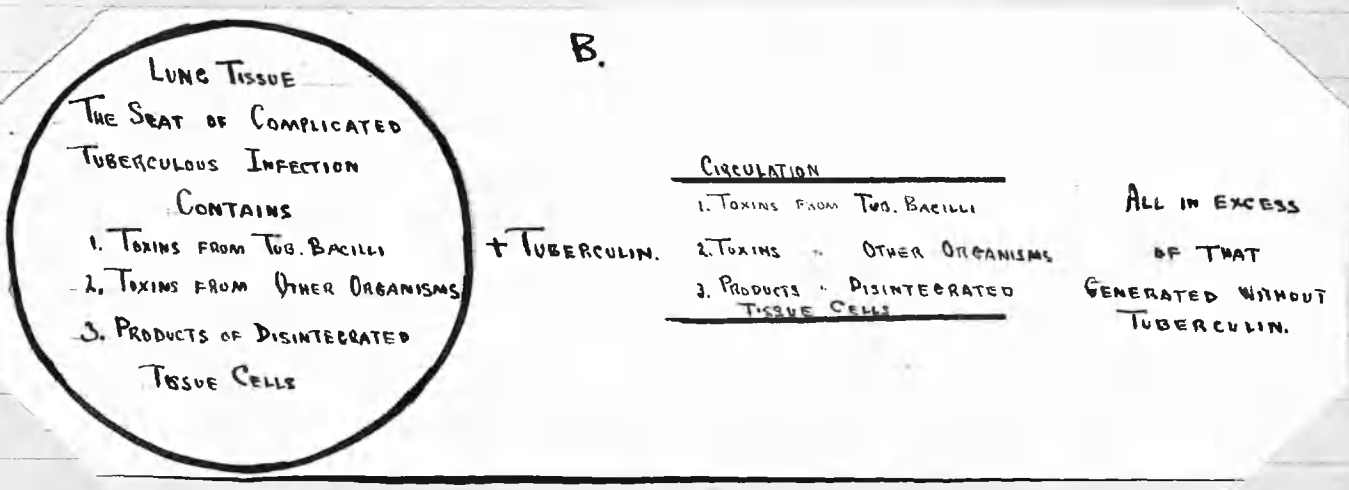
P.T.. The variation in the strengths, rates of absorption, etc., of the different forms of tuberculin must surely be an important point in governing the clinical manifestations of tuberculin treatment. It is an appreciation of this fact which has led to the treatment of tuberculosis by the sequence system, - P.T.O., P.T. T.O. etc..
Besides the "specific" substance or extract in the various tuberculins, there is still another factor of importance. In making "tuberculin" it is found necessary to prepare them in solution with glycerin or water under different forms of precipitation, mixed more or less with other albumoses. (Maragliano.) It is evident, therefore, that the substance which we inject, known as "tuberculin", is not, in its entirety at least, the products of the tubercle bacillus. Ruppel, Levene, and others have done much work in endeavouring to prepare a toxin, much more virulent than the ordinary tuberculin, but, so far, without success. Watsutow agrees with many others in saying that tuberculin, as we know it, is not the toxin of the tubercle bacillus. Marmorek's serum was an outcome of this view, and although it has been proved definitely by Roux and others at the Pasteur Institute, to be very inadequate, yet its very existence is a point in favour of the opinion that tuberculin is not considered even by good authorities, to be the necessary antisubstance for tuberculous infection. Similarly, although the work of Menzer, and Aronsohn on the value of antistreptococcic serum in phthisis is not finding favour because of the poor results following its administration, I call notice to the existence of such sera, not so much for the advances which they signify in the therapeutics of pulmonary tuberculosis, as for demonstrating that clinicians have as yet a very open mind on the nature of a "tuberculous

infection. It appears to me to be a case of extremists being wrong. Below I have made a diagramatic representation of the condition in the lung, as it appears to me. The diagrams represent different phases of tuberculous infection.

A.



B.



In the case of A,- an uncomplicated tuberculous infection,- the toxins of the tubercle bacilli, and the products of the disintegrated tissue cells are responsible for the symptoms and signs of the disease. The extreme example of an uncomplicated tuberculous infection is to be found in Acute miliary tuberculosis, where the numbers of tubercles are countless, and where, to use the words of Weigert, a large amount of tuberculous poison has entered the blood at once. In this condition, any secondary organisms that may be present are overwhelmed in point

of numbers, as well as in the amount of toxin they may produce. The blood picture in miliary tuberculosis has been the subject of considerable discussion, and consequently a reference to one or two opinions may not be out of place. Osler expresses no definite opinion on the leucocyte count, but suggestively remarks that, "leucocytosis is more common in miliary tuberculosis than in typhoid fever, in which leucopenia is the rule." Bolles maintains that there is not only no increase in the number of white cells, but, on the contrary, often a diminution. American writers, and particularly Da Costa, go so far as to say that absence of leucocyte increase is the rule in uncomplicated miliary tuberculosis, tuberculous adenitis, pleurisy and pericarditis. That there is a "marked diminution" in the number of leucocytes in acute miliary tuberculosis has been pointed out also by Gilland and Goodall. The most interesting communication to be found in the literature in connection with the leucocytes in the disease in question is from Matthes' clinic, where Wacks has given some details which are very pertinent to the whole discussion. Nine cases of miliary tuberculosis were examined, and in all but one of these cases, the diagnosis was confirmed in the end by post mortem examination. The average number of leucocytes found by Wacks was 6,400 per cub. mm. The important point brought out by Wacks from the series of cases is that there follows not only a diminution in the number of leucocytes, but also a very noticeable alteration in the differential count as the disease progresses. Van Limbeck, Cornet and Ewing are of the same opinion, but go further and say that in all acute tuberculous infections, without secondary infection, polynuclear leucocytosis is absent, and that a leucocytosis developing in the course of pulmonary tuberculosis speaks for the development of some complication such as pneumonia.

or for softening, or cavity formation, events which are recognised to be caused by secondary invaders.

The series of leucocyte counts quoted from Pabst in Chap. I is further proof of the existence of a low leucocyte count in miliary tuberculosis, his lowest reading being 2,500 and his highest 5,625 cells per cub. mm.

It would not be discreet to put any interpretation on the significance of this low count in this form of tuberculosis; some theories have been discussed in the previous chapter. Suffice it to say at present that in acute miliary tuberculosis, we have an example of extreme tuberculous intoxication, and that the consensus of opinion is that there is not only no leucocytosis, but either a normal count or a leucopoenia accompanying it.

Now, in pulmonary tuberculosis, a pure, intense tuberculous infection limited to the lungs, may not be out of the bounds of possibility. I have no case to record where an acute tuberculous process, confined to the chest, was accompanied by a normal or yet by a diminished leucocyte count. It is not in the nature of things for the tubercle bacillus to be alone in causing an overwhelming systemic infection of pulmonary origin. Nor can I point to any case in the literature as an example of an acute lung disease of tuberculous origin being associated with a normal or with a diminished blood count. But in Cases X, XX, XXV Chap. II, we have examples of an undoubted tuberculous infection of a chronic nature, being accompanied by leucocyte counts which are all well within normal limits. One cannot but conclude from these cases, that, either the tuberculous toxin liberated from the foci in the lungs is an antagoniser of leucocyte formation, or else that it has not any effect whatever on the leucocyte count. Pick, Rieder, Warthin, von Jaksch,

Galbraith, Gramitz and others agree that in cases of pure tuberculosis the leucocyte counts are normal. The effect of tuberculin in these uncomplicated cases of pulmonary tuberculosis is variable; sometimes a leucocytosis develops and at other times there is no sign of such a phenomenon (see Cases XXV and XXVIII; Chap. II)

The explanation of the leucocytosis developing in some of the cases may be that there are, unknown to us, certain secondary organisms lying latent in the chest and that they are forced, by the increased blood supply to the affected area in the lung, to grow and produce toxins which are positively chemiotactic to the leucocytes, or else that the products of the disintegrated tissue cells are swept into the circulation and, acting as foreign proteins, exert an influence on the leucopoietic organs similar to that shown by the toxins of the pyogenic groups. In support of the former view is all the material to hand which confirms the opinion that a "secondary infection" cannot, in any given case, be proved to be absent; and in corroboration of the latter theory is the fact that Undrowes and others have shown that there is a leucocyte response to the presence in the circulation of foreign albuminous extracts. It is pertinent to add that Bullock, in his minority report to the National Association for the Study and Prevention of Tuberculosis, gives it as his opinion that the phenomena often ascribed to mixed infection are really due to toxaemia from absorption of the dead tissue products accompanying phthisis.

In pursuance of this same theory, one can readily understand what the effect of tuberculin would be on the leucocytes of a person suffering from an advanced lesion of the lung associated with an undoubted mixed

infection. To this person, who is already inoculating himself with toxins of several kinds, - tuberculous toxins, toxins from staphylococci, streptococci, pneumococci etc.. and the products of cells which have been necrosed by the action of these organisms and their toxins, - to this person, tuberculin would act like fuel to a fire. The increased hyperaemia induced in the diseased foci must necessarily wash more and more of the poison into the circulation and so intoxicate the patient ultimately to death itself. I have had neither the inclination or the heroism to experiment with tuberculin on advanced and febrile cases of phthisis, but in Case Chapt. II, where, from consecutive counts I had made previously, I had suspected the presence of other organisms, I administered a small dose of tuberculin and found an increase in the "leucocyte swing", showing that at different intervals the various toxins were manifesting their presence, the leucocyte count being high when, (according to the above theory), the leucocytic stimulating toxins were being washed into the blood stream, and low when the toxins of the tubercle bacilli were acting as "repellents" to the white cells. It is worth noting in this connection that C. Spengler believes the increase in sputum following the injection of tuberculin is due to the fact that tuberculin produces about the tubercle a "sero-plastic" inflammation, the number of leucocytes in the sputum being consequently increased. Denys also agrees with Spengler. Between the two extremes, the case of acute miliary tuberculosis, and the typical case of mixed infection, there is the great majority of cases when the leucocytes respond to the toxins sent out in the manner demanded by the toxins which may be acting for the time being. By a careful study of the leucocytes in these cases, one is, I believe, able

to judge the amount of intoxication from which the patient is suffering at the time. The greater the swing the more potent or virulent the toxins.

The conclusions at which we arrive from the study of a series of leucocyte counts in a person said said to be suffering from tuberculosis are: 1st. A sustained leucocyte count represents a septic infection, and negatives the diagnosis of active tuberculous mischief. In some of the cases recorded in Chap. II eg. Nos. XI, XIV, XV, it will be seen that there is a fairly high and moderately well sustained leucocyte count. The explanation of this will that the "septic" element predominates. The existence of one or two comparatively low counts in these cases signifies the tuberculous nature of the infection. Further proof exists in the presence of tubercle bacilli in the sputum.

2nd A leucopoenia represents intense tuberculous intoxication

3rd A normal count, on the other hand, may be explained in one of four ways, viz:

(a) It may be part of an acute miliary tuberculosis. The possibility of this has been discussed already. (b) It may occur in a case of phthisis which is uncomplicated by any secondary infection.

(c) It may occur ~~at~~ in a case of mixed infection, at the ebb of the leucocyte swing.

(d) It may occur, but seldom, and be more or less constant, in a case of progressive tuberculous disease complicated by mixed infection, and its explanation then may be exhaustion of the bone-marrow resources.

The question to be asked now is: "By what method can we tell whether the leucocyte response is favourable or not?" In other words, if a normal or more or less normal

leucocyte count is to be found constantly in cases of phthisis uncomplicated by secondary infection, as well as in cases of progressive "mixed-infection" cases, what means have we for determining, apart from the ordinary bedside signs, to which class the case belongs.

In the succeeding chapter I shall endeavour to bring forward evidence to show that by a further study of the leucocytes one can form some opinion on the subject.

Chapter V.

The Morphological Variations in the Polymorphonuclear Neutrophile Leucocyte Nuclei in Pulmonary Tuberculosis

The adult mature polymorphonuclear leucocyte measures 10-12 μ in diameter. Its shape is variable, being round or spherical when resting, and when moving, polymorphous. In reaction the cell body is cytophile, and the cell itself is filled with granules of various kinds, which are scarce in the immediate vicinity of the nucleus, whilst towards the periphery of the cell they are more abundant.

The nucleus, with which we are specially concerned in this chapter, is polymorphous rather than multipartite, and stains dark blue with Leishman's stain, owing to its richness in chromatin. The latter may be arranged in almost any shape or form depending on circumstances which are at present not very well defined. As Da Costa remarks, the nucleus may be "elongated, wreathed, lobulated, horse-shoe-shaped, or twisted into designs resembling various letters of the alphabet, such as S, Z, U or E." By the use of any of the double stains formed by mixing methylene blue and eosin, the nuclear configuration may be made out with clearness and a fair amount of accuracy. The nuclear outline in the normal polymorph is well-defined in well stained specimens, and the nuclear substance presents a somewhat mottled appearance, due to the chromatin being condensed at various parts of the nucleus.

In order to decide in any given case whether a nucleus is polymorphous or polynuclear, one must give special attention not only to the preparation of the film, but also to the staining of the cells. The usual disposition of the chromatic network is in clumps connected by bridges of chromatin of varying degrees of breadth and thickness. In

some cases, the clumps can be made out with clearness when the bridge or bridges joining them cannot, and careful focussing will frequently reveal bridges shining through the cytoplasm when they were hidden from microscopic view at the time of examining the clumps. In other cases, it is quite impossible to ascertain whether a connecting bridge is present or not, even when the cells are focussed most carefully. In such cases, one is forced to conclude that the nucleus is composed of two or more distinct parts, as the case may be. In the latter case, the term "polynuclear" is an apt one, although it is the exception for the nuclei to be composed of apparently distinct and separate masses of chromatin, unconnected by means of any filament of nuclear substance. In order to obviate this difficulty of deciding when a nucleus is or is not divided, Cooke has made the following definition: "If there is any band of nuclear tissue except this chromatin filament connecting the different parts of a nucleus, the nucleus cannot, for the purposes of Arneth's count, be said to be divided." Such a definition depends for its universal application, upon what one understands by the term "chromatin filament." It is obvious that the staining of the specimen, apart altogether from the powers of observation of the examiner, might convert filaments into bridges and vice versa. It appears, however, that the definition given by Cooke is quite unnecessary, because, for the purposes of the Arneth count, which depends for its accuracy on the nuclear configuration of the neutrophils polymorphs, it matters very little whether a nucleus is divided into distinct and separate parts or not. In 1904, Arneth put the morphology of the polymorphonuclear leucocytes on a more firm basis than it had been hitherto. His work has served as a stimulant of many researches

on the haematology of tuberculosis and other conditions, and in Germany and America particularly, the so-called Arneth count may be said to have established itself in the realm of clinical pathology. Arneth's work has been reviewed by Klebs and others in America. The neutrophile leucocytes are, according to Arneth, divided into five classes according to whether the nuclei are composed of one, two, three, four or five parts. In Class I, the nucleus may be round or may have an indentation in it. Classes II, III, IV, and V contain cells which have separate chromatin parts; round parts or loops as the case may be. Below is a diagramatic representation of the disposition of the chromatin network which determines whether a particular cell belongs to a special class. It will be noticed that it is not necessary for the pieces of chromatin to be separate in order to place a particular cell in Class IV, for example, - a point which Cooke and others in this country have, I believe unduly emphasised. Cells with more than five pieces of chromatin composing their nuclei are placed in Class V.

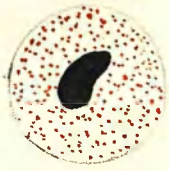
Arneth's method of counting the polymorphs, and the deductions he derives therefrom, have been subjected to strong criticism by Paulicek, Bourmoff and Brugsch Kagan, Schilling and others. (vide post.)

Paulicek asserts that the count is of no value either in diagnosis or in prognosis, and with this the other mentioned observers agree. Briefly stated, Arneth's belief is that, in its change from the myelocytic form, the nucleus of the polymorph is, firstly, indented, then bent, and at last, lobulated, the cells with a single nucleus thereby representing cells of a more youthful age, and the multinucleated cells those of an older type

Graphic Representation of Arneth's System (after Gruner)

Class I


M.


W. 0·2%


T. 5%.

M = Myelocyte W = Wenig = Slight T = Tief = Deep 5%

Class II


2K. 0·27%


2S 23·46%


1K1S 11·69%

K = Runder Kerntiel = Round Nuclear Particles S = Schlinge = Loops 35%.

Class III


3K. 2·27%


3S 5·6%


2K1S 16·6%


1K2S 16·4%

41%

Class IV


4K 3·8%


4S 0·07%


3K1S 6·4%


3S1K 1·6%


2K2S 4·23%

14%

Class V.


5K 1%


4K1S 0·4%


3K2S 0·4%


4K2S 0·07%


3K3S 0·07%

2%

The granules, he says, are more numerous in the older types. It is certainly the case that the cells with three, four and five nuclear segments are rich in granules, but whether the presence of granules determines the polynuclearity, as Blumenthal suggests, is doubtful. As a result of researches on the opsonic index in acute leukaemia, Parvu and Foy suggest that young forms of leucocytes, such as the mononucleated polymorphs, do not possess any phagocytic power and are therefore less effective cells in the body defence.

Bruguch and Schilling declare that the degree of segmentation of the nucleus bears no relation whatsoever to the age of the cell. Pfeiffer believes that the nucleus of a polymorphonuclear leucocyte becomes simpler in form when the cell ceases amoeboid movement, a point in agreement with Abercrombie, who found that if polymorphs are allowed to quiet down before they are killed, their nuclei usually return to a spherical form.

Turner maintains that the age of the cell in question may be deduced by noticing the actual bulk of nuclear matter, the young cells showing thick nuclei, while the older ones have small lobes and long filamentous connections, or are more slender than the first named. In many of the cases of advanced phthisis from which I have taken blood films, I have noted that the nuclei with one or two segments tend to stain very deeply and that their outline is not nearly so distinct as in the case of the cells with three or more nuclear lobes.

Moreover there is, as Cooke has remarked, a tendency for the chromatin to jut out into the cytoplasm in a most irregular fashion, as if polynuclearity were being attempted, but yet impossible.

Whatever be the significance of the lobulation of the

nuclei, it does not appear to alter appreciably during the active movements of the cells. In other words, knobs or round particles do not become bridges or loops, and the converse is equally true. In proof of this statement may be mentioned the experiments of Bruggeh and Schilling, and of Miller and Reed. On three occasions I have repeated Miller and Reeds method of procedure with the same results. The method employed was to scratch the slide with sand-paper, and then to clean it prior to making the blood-film. The blood was then firmly but slowly drawn across the scratched slide in order to ensure that the neutrophile cells would catch on the scratches. The phenomena resulting corresponded exactly with the findings of Miller and Reed; many of the cells were elongated, but the resulting differential count of the nuclei was the same as that obtained from films taken from the same patient, but made and stained in the usual way. It is obvious, therefore, that there is little foundation in the statement made by some, e.g. Klebs, that undue pressure in spreading the ~~film~~ blood on a rough glass can lead directly or indirectly to a distortion of the cells, and so change the picture.

During the past decade, numerous observers of repute have verified Arneth's work, and one and all agree that the counting of the nuclear segments of the polymorphonuclear leucocytes serves as a guide to diagnosis and prognosis in certain diseased conditions, and particularly in pulmonary tuberculosis. Amongst those who have placed reliance on Arneth's method may be mentioned,

1, Kohl and Kothe, — in Appendicitis.
2. Sonnenberg and Kothe, — in peritonitis.
3, Esser in Intestinal Diseases of Children.
4, Levinson in various diseases.

5. Klebs, Sabrazès, Dluski and Rospedishowski, Pottenger, Minor and Ringer, in pulmonary tuberculosis.

All the above mentioned, and more could be named, agree that the work of Arneth is worthy of clinical trial. In the case of tuberculosis, where the opsonic index is now unpopular as a means of diagnosis, the Arneth count furnishes a clinical criterion of the condition of the patient.

Arneth's estimation of a normal nuclear count is as given:

Class I.	Class II.	Class III.	Class IV.	Class V.
5%.	35%.	41%.	17%.	2%.

Below are the estimates of normal counts as given by other observers.

	Class I.	Class II.	Class III.	Class IV.	Class V.
Cooke.	12%.	25%.	46%.	15%.	2%.
Miller and Reed.	5%.	26%.	36%.	28%.	5%.
Hamilton Bleek.	8%	28%.	42%.	22%.	
Minor and Ringer.	2.8%.	16.2%.	55.6%.	18.6%.	5%.

I have mentioned above the importance of careful staining and examination of the film. The personal factor is bound to creep into work like this, and for this reason alone, it would be advisable for every clinician who pretends to make use of the Arneth count in medicine, to get his own "normal" count by examining at least a dozen films taken from persons who are known to be in good health. I have adopted this procedure myself and find that my "normal" count works out at:-

Class I	Class II	Class III	Class IV	Class V.
9%.	31%.	43%.	15%.	2%.

which is the average of twelve observations on individuals who were found healthy in all respects. (These healthy persons were taken from the staff of Standfield Sanatorium, Ryalem.)

Each film was examined three times and an average struck for each person. Having attained proficiency in the art of counting the nuclear segments of a healthy individual's polymorphs according to Arneth's method, one is able to proceed to the examination of the cells in films taken from persons suffering from various diseased conditions.

Before passing on to the discussion of the variation which takes place in the Arneth count in pulmonary tuberculosis it is only fair to call attention to one or two other methods which have been suggested by different observers for recording the nuclear arrangement in the polymorphonuclear leucocytes. Most of the so-called improved methods are merely modifications of Arneth's method. One of the most common procedures adopted is to take the sum of Classes I and II, and one half of Class III, and record this as an index. This plan was first adopted by Bushnell and Trenholtz, and has found considerable support. It has the undoubted value, as Miller and Reed suggest, of being a convenient way of recording Arneth's count without materially altering the value of the same as a clinical entity.

Below I have given the normal index value according to the various observers named.

Authority.	Index.	Remarks.
Arneth.	60·5	In Normal Person.
Bushnell and Trenholtz.	64	" " "
Webb and Williams.	65.	" " "
Minor and Ringer	48·6.	" " "
M° Dowall.	54.	" " "
Miller and Reed.	54	" " "
Cooke.	60.	" " "

Wolff and Von Bonsdorff count the round segments as one, and the bent or loop forms as one-and-a-half, and in this way

only two types of nuclei are counted. The totals are then counted and the result given as so many of "One", and so many of "One-and-a-half". The convenience of this method is undoubted; the accuracy leaves much to be desired. Pappenheim counts the total number of segments in 100 polymorphs, and considers that sufficient. The objection to such a method, however, is the obvious one that we gain no information as to which particular Class is increased. Gallard and Woodall suggest that "since the presence of a moderately high percentage of neutrophiles with rounded, kidney-shaped, or horse-shoe shaped nuclei, indicate a severe infection, the observer very soon learns to recognise that an unusual number of these cells is present without making a special differential count of the neutrophiles."

Next to Arneth's method, the most elaborate description of the nuclei of the polymorphs comes from Schilling, who, using Pappenheim's method of combined May-Grünwald and Giemsa, (see footnote) classifies the polymorphs as on the following page.

FOOTNOTE.

The technique for the use of this stain is given by Grüner as below:

1. Fix the air dried film with May-Grünwald Stain - 3 minutes.
2. Pour on an equal quantity of distilled water, - leave one minute.
3. Rinse briefly.
4. Pour on diluted Giemsa and leave 15 minutes more.
5. Rinse in distilled water.
6. Blot and dry.

Schilling's System of Counting Leucocytes Differentially.

Class I — **Segmented-nucleate polynuclears**, - cells which have two or more separate clumps of nuclear chromatin, united or not by threads. Per Cent in Normal Blood. 63.

Class II — **Rod-nucleate forms**, - cells which have a ribbon like nucleus, without any clumps of nuclear chromatin. Per Cent in Normal Blood. 4.

Class III — **Juvenile polynuclears**, - cells which have an S-shaped nucleus, with the ends of the S marked by clumps of chromatin. Cornelli's T-cells are also included in this class. Per Cent in Normal Blood. 0

Class IV — **Myelocytes**, - cells which are larger than III but which have a slightly indented nucleus. Per Cent in Normal Blood. 0

Class V. — **Large Mononuclears.** Per Cent in Normal Blood. 6.

Class VI — **Lymphocytes.** Per Cent in Normal Blood. 23.

Class VII — **Basophile Cells** (Mast Cells) Per Cent in Normal Blood. 1

Class VIII — **Eosinophile Cells.** Per Cent in Normal Blood. 3.

Schillings "count" for a normal healthy individual reads, therefore;-

No. of White Cells per Cub. mm.	Basophiles.	Eosinophiles.	NEUTROPHILES: Myelocytes	Juveniles	Rod-Nucleate	Segmented-Nucleate	Lymphocyte	Large Mononuclear
6,000.	1	3	0	0	4	63	23.	6

Schilling maintains that a count made in the above fashion serves all the purpose for which Arneth's classification was intended. It will be noticed that Schilling finds the normal number of neutrophiles to be 64% of the total count. Of this, 63 or 96% of the total number of polymorphs are of the segmented-nucleate type, and similarly 6% of the total number of polymorphs are of the rod-nucleate type. According to Schilling's own definition of segmented-nucleate polymorphs, i.e. cells which have two or more separate clumps of nuclear matter, united or not by threads, he must include the following cells under that term.

3K2S	=	0·4% (Arneth)	4K	=	3·8% (Arneth)
4K1S	=	0·4% "	2K1S	=	16·66% "
5K	=	1·0% "	3K	=	2·24% "
2K2S	=	4·43% "	2K	=	0·24% "
3S1K	=	1·6% "	4K2S	=	0·04% "
3K1S	=	6·6% "	3K3S	=	0·04% "

TOTAL = 34·64%.

In the same way, under the term rod-nucleate forms must (according to the definition of that cell) be included.

2S	=	23·46% (Arneth)
3S	=	5·6% "
4S	=	0·04% "

TOTAL = 29·13%.

And since the juvenile polynuclears include cells with a reniform nucleus, where the indentation is "conspicuously deep", they must include Arneth's T cell which amount to 5% of the polymorphs.

Adding together, then, the cells which may be grouped under the term segmented-nucleate forms, rod-nucleate forms, and juvenile polynuclears, we get a total of 41·8%.

Reference once more to Schilling's definition will make it clear that it is impossible under this system of counting the segments of the polymorphs, to include 1K1S (Arneth) or 1K2S (Arneth), which together form no less than 28.09% of the polymorphonuclear leucocytes of normal blood. The sum of 71.8 and 28.09 is 99.89, or approximately 100. It is quite possible, also, to imagine that cell 2K2S could, under certain modification of its morphology, be grouped as a member of Schilling's Class III (Juvenile polynuclears), but, according to the definition of Segmented-nucleate polynuclear, it must be placed in Class I.

So far as I am aware, this discrepancy in Schillings work has not been pointed out before, and were it not for the importance which some American writers e.g. Grüner give it in text books, I should not have laboured the question as I have done. It was not until I endeavoured to make some counts by means of Schilling's method that I became conscious of the difficulty of classifying cells like 1K1S and 1K2S.

Arneth's system of dividing the polymorphs into twenty different divisions is indeed much too cumbersome for general use and I agree with those who say that, for ordinary clinical work, the primary division into five classes, according to the number of nuclear segments, is sufficient for ordinary haematological work.

In diseased conditions there is a tendency for the nuclei of the polymorphonuclear leucocyte to revert to a more or less common type according to the severity of the infecting agent at work. This is, in essence, the opinion of Arneth and others who have worked on the subject. The common type is represented by cells with one or two nuclear segments, cells which are believed to be approaching the myelocyte form, and which consequently indicate that there

is a special call being made on the leucopoietic organs. In leukaemic condition we are accustomed to the presence in the peripheral blood of cells which are found normally in the bone-marrow only. The most important of these is undoubtedly the neutrophile myelocyte, a cell which is included by Arneth in his Class I, but which is not, of course, considered as composing a fraction of the normal blood count. It seems awkward, however, that the myelocyte should figure at all in a differential count of neutrophile polymorphs when, strictly speaking, the myelocyte is not a polymorphonuclear leucocyte in any sense whatever.

In all the recorded counts done by Arneth's method, I have not been able to ascertain how many cells in Class I are really myelocytes. A priori, one might expect to find a fair percentage of myelocytes in a count which showed a great increase from normal in the number of Class I polymorphs. Practically, the nucleus of the myelocyte does not take up the stain (amblychromatic) with the same intensity as do the nuclei of the ordinary polymorphs, which are in this respect trachychromatic. Although I have pointed this difference out, I have not in my counts met with any cells which I could justly term myelocytes. Wark and Kast, working independently, have found myelocytes in tuberculous condition.

The presence of myelocytes in certain cases strongly supports the view that the increase in the polymorphs of Classes I and II in patients suffering from diseased condition, is the result of marrow supply being unable to cope with body-demands and the qualitative output suffers accordingly.

The various counts done by different observers agree fairly constantly inasmuch as they go to show that the more severe the infection, the greater is the "deviation to the left", a phrase which means that the cells of Classes I and II are increased in number at the expense

of cells of Classes III, IV and V.

As has been mentioned, several writers, including Pollitzer have dissented from Arneth. In addition, Busse, Hangemeister and Lang, Flesch and Schossberger, Bournoff and Loken and Strickler all either disapprove of Arneth's count, or accept it with reservation. More recent writers, and especially workers in tuberculosis, have found the count a useful means for diagnosis, and for controlling treatment.

Below I append a few counts taken from the writings of various authorities

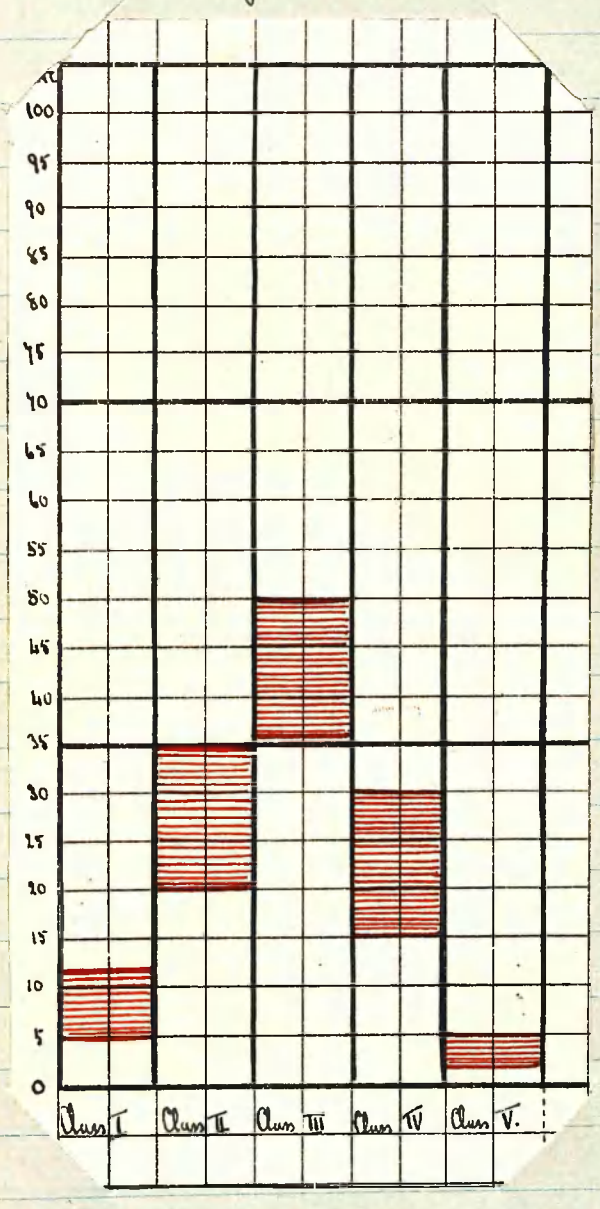
Authority	Disease	Polymorphs Class I	II	III	IV	V	Index (i.e. I + II + III/2)	Remarks.
Arneth	Health.	5.	35.	41.	14.	2.	60·5.	Average of 15 persons
"	Acute Pneumonia Feb.	36	56	8	0	0	96.	Died 9 days later
"	Active Phthisis	14	56·5	24·5	4·5	·5	82·4	Leucocyte Count = 4,600
"	Advanced Phthisis	55	38·5	5·5	·5	·5	96·2	" " = 8,400
"	" "	29·5	60	9	1·5	0	94	" " = 27,080
"	Phthisis	51	46	2	1	0	98	" " = 9,100
Cooke	Erysipelas	59	35	6	0	0	94	—
"	Measles	21	39	33	4	0	46·5.	—
"	Scarlet Fever.	34	36	24	6	0	82	—
"	Acute lobar Pneumo.	54	26	15	2	0	90·5.	—
"	Syphilis	23	32	36	10	0	42·5	—
"	Phthisis.	41	29.	24	2	1	83·5	—
"	"	63	29	4	1	0	95·5	—
"	"	60	26	14	0	0	93.	—
"	"	33	36	25	6	0	81·5	—
Evans' Journ.	Pneumonia.	61	29	9	1	0	94·5	2nd day of Disease
" "	"	56	34	6	1	0	96	8th " " "
" "	"	23	46	23	6	2	80·5	11th " " "
" "	"	14	40	32	9	2	43	24th " " "
McDowal	Chronic Insanity	5·4	29·5	65·8	16·8	1·6	58·1	
T. E. Taylor.	Phthisis	18	64	14	1	0	90·5	
"	"	31	54	10	2	0	93	

Taking into consideration the mass of evidence which I have endeavoured to collect, one is forced to admit of the following conclusions

1st That the "Normal" Arneth count is variable within certain limits

It would appear that Class I may form anything from 5% to 12% of the total number of polymorphs. Similarly, Class II may provide 20% to 35% of the cells; Class III, 36% to 50%; Class IV, 15% to 30%., and Class V, 2% to 5%.

Likewise, a "normal" index may be said to be one which does not fall below 48 and does not exceed 62.



Schema, built up from the results of various observers, illustrating the ranges within which the cells of the various classes may be expected to occupy in health.

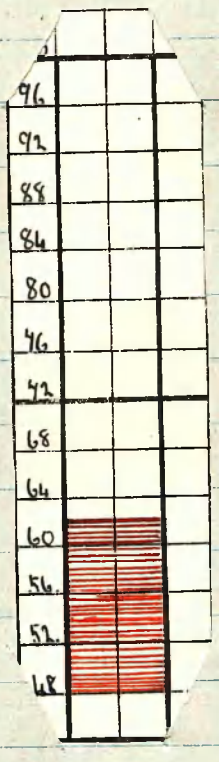


Figure to illustrate the ranges of the INDEX in health.

If it is suggested that the normal scope is too wide, then the only remedy which I can suggest is the one I have already enunciated, viz, that each clinician should establish for himself his own normal which will not, after some practice, be far off Arneth's normal. In my own case, my normal count differs but slightly from Arneth's, a fact which I attribute solely to the study I made of a dozen films prepared from individuals known to be healthy.

2nd That in certain diseased conditions there is an alteration in the nuclear picture of the polymorphonuclear leucocytes.

Reference to the counts preceding will show that in a variety of conditions one meets with an increase in the percentage of cells belonging to Classes I and II, and a corresponding diminution in the percentages of Classes III, IV and V. In order to satisfy myself that this was the case I have made 140 counts according to Arneth's method in 64 cases of pulmonary tuberculosis. The cases represent different phases of the disease, and when necessary, I have given notes on the physical signs in the chest together with any other remarks which I have deemed of special interest.

The blood films were made on glass slides, care being taken to obtain a thin film of blood. At least two films were taken from each patient, and the better film always examined, after staining with Leishman's stain. I selected Leishman's stain as the one most useful for the work in question, because of the excellent picture it gives of the nuclei. At the beginning of my investigations I made use of Jenner's stain, Ehrlich's Triacid stain and Giemsa's stain, but soon abandoned these in favour of Leishman's, for the reasons already given. In work like Haematology

consistency is of paramount importance, and despite the disadvantages of Leishman's stain, such as, for example, its frequent failure to stain myelocyte granules, yet the intense coloration given to the nuclei of the polymorphs more than compensates for the defect mentioned. At the outset of every differential count I enumerated first all the kinds of leucocytes, noting the nuclear arrangement of the neutrophile polymorphs at the same time. When 100 white cells had been counted, I confined my attention entirely to the neutrophile polymorphs until I had brought the total number of these particular cells up to one hundred. In this way I had not only a differential count of the leucocytes, but also a complete differential count of the nuclei of the polymorphs.

Chapter VI.

Some Observations on the Arneth Count in Pulmonary Tuberculosis.

As already stated, I find the normal Arneth count to be.

Class I	Class II	Class III	Class IV	Class V.	Index.
9%.	31%	43%.	15 %.	2 %.	61·5.

The great majority of the observations to be hereafter recorded were made from patients admitted to the Stanfield Sanatorium, Burslem, Staffs, where the average type of patient was one suffering from advanced tuberculous disease of the chest. By the kind permission, however, of Dr Magill, Tuberculosis Officer for the County Borough of Stoke-on-Trent, I was able to take films from several patients attending the Tuberculosis Dispensary in Stoke, and it was from these patients principally that I selected my early or "first stage" cases. In the first column of each page the letter F denotes "female", and the letter M, "male".

Case	Classes I	II	III	IV	V	Index	Date	Remarks.
1.F.	14	33	49	3	1	41·5	20·8·15	Act 20. Onset 8 mths previously. Up and About.
"	12	30	44	9	2	65·5	3·9·15	Left apex dull to percussion: a few crepitations heard at the end of inspiration posteriorly.
2F	10	32	41	16	1	62·5	23·9·15	Act 12. Patient up and about. No symptoms. High pitched breathing at rt. apex.
3.F	8	34	40	14	1.	62	23·9·15	Act 4. General condition good. Slight enlargement of cervical glands on both sides of neck. Chest examination negative.
4F	9	31	54	5	1	64	23·9·15	Act 19. Patient up and about. Poor air-entry all over the
"	15	44	31	4	0	44·5	20·10·15	chest. No adventitious sounds heard. Patient complaining of slight pain over left apical region on 20·10·15. Erection to be heard, - normal temperature.
5F	12	29	44	11	1	64·5	26·8·15	Act. 30. General condition good. R.M. deficient over rt apex. No signs of activity in chest.
6F	19	24	45	9	0	68·5	23·9·15	Act 5. Enlarged glands palpable both sides of neck A few sibilant rhonchi over rt. side of chest.
7F	18	28	46	8	0	69	26·8·15	Act 24. Chest normal to percussion. A few
"	14	24	44	15	0	63	4·9·15	moist sounds heard at rt. apex at end of inspiration.
"	12	29	42	15	2	62	8·10·15	General condition good.
8F	13	34	38	11	1	69	23·9·15	Act 4. General condition good. Slight paravertebral dulness. Von Pirquet +. Patient up and about.
9F	9	44	46	6	2	49	28·8·15	Act 22. Patient in bed. Tuberculous disease of dorsal
"	14	46	31	9	0	45·5	4·9·15	vertebrae. General condition good.
10F	10	40	42	4	1	41	25·8·15	Act 23. Patient in bed; temp 99·4; pulse 90. Rt upper lobe consolidated. Numerous crepitations heard.

Case	Classes I	II	III	IV	V.	Index	Date	Remarks
11 F	20	44	30	6	0	49	15-5-15	Ast 16. General condition good. Retraction of both apices
" "	13	39	36	11	1	70	26-9-15	Rt. apex dull to percussion. A few crepitations audible at at left apex ; one or two enlarged glands in neck.
12 F	13	42	31	12	2	40·5	23-9-15	Ast 5 General condition good. Von Pirquet +. Chest normal to examination.
13 M	14	40	38	4	1	43	2-9-15.	Ast 33. Chest normal to percussion. On auscultation, expiration was definitely prolonged, and a few rhonchi were audible. Patient complained of "asthmatic" attacks.
14 F	12	48	29	11	0	64·5	2-9-15	Ast 24. Rt side of chest impaired in resonance; also left apex. Numerous moist sounds heard. Tubercle bacilli present. General condition good.
15 M	14	46	36	4	0	48	18-8-15	Ast 26 Chest normal Enlarged glands left side of neck.
16 M	15	39	39	6	1	43·5	26-8-15	Ast 14. Rt apex dull to percussion ; R.M. markedly
" "	12	42	40	5	1	44	16-9-15	diminished. Mass of enlarged glands left side of neck.
17 F	19	32	44	8	3	64	16-8-15	Ast 16. General condition good. Chest examination
" "	12	30	46	9	3	65	31-8-15	negative, but for slight impairment of air entry over Rt. upper lobe. Old hip-joint disease; now healed
18 M	16	44	29	4	1	44·5	30-8-15	Ast 24. General condition good. Both upper
" "	14	40	39	6	1	73·5	16-9-15	lobes dull to percussion, and crepitation abundant. Temp. 99° F in evenings ; pulse 80-90.
19 F	22	41	32	5	0	49	30-8-15	Ast 14. General condition fair. Enlarged glands on both sides of neck. Crepts at left apex, and base.
20 F	14	44	34.	2	0	49·5	25-8-15	Ast 39. General condition good. Rt. upper lobe
" "	13	40	41.	5	1	73·5	16-9-15	dull to percussion. Moist sounds heard at Rt apex
" "	12	38	34.	8	3	69·5	14-10-15	V.R. and V.F exaggerated. Tub. bacilli in sputum.

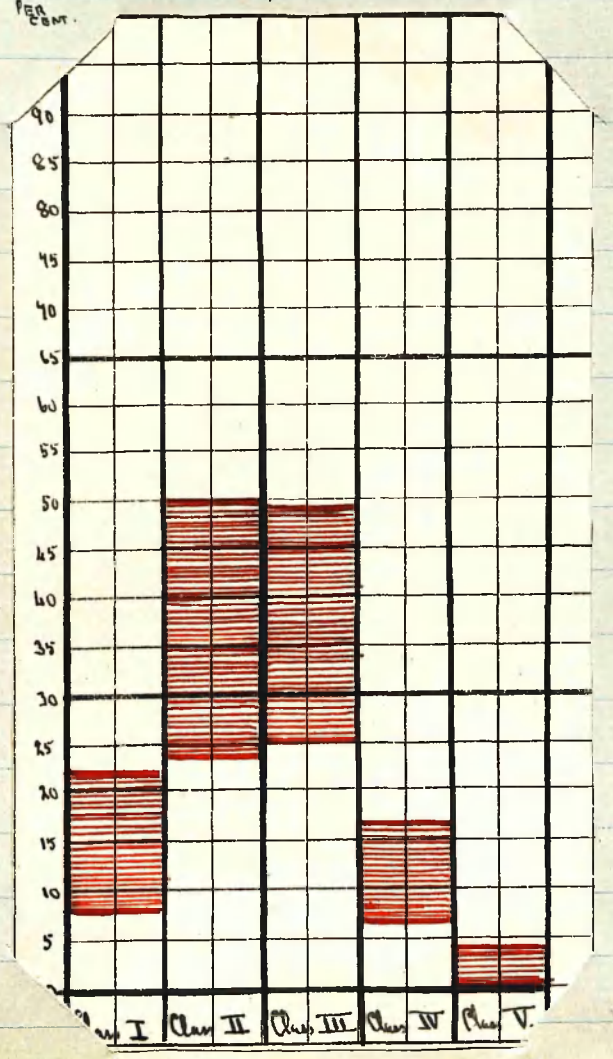
Case	CLASSES. I	II	III	IV	V	INDEX	DATE	REMARKS
21 F	18	44	32	5	1	80	23-9-15	Act 12. Both apices lacking in normal resonance. R.M. very harsh at both apices. Numerous crepitations heard over left lung. General condition good. Temp. normal.
22 F	20	41	34	2	0	49·5	30-9-15	Act 20. General condition excellent. Beyond a few creps. at R apex, chest was normal, as was also temperature and pulse-rate.
" "	18	38	31	11	2	71·5	8-10-15	
23 F	15	44	30	10	1	74	20-8-15	Act 20. R.M. a trifle harsh at R apex. General
" "	12	41	31	12	4	68·5	3-9-15	condition good. Family history had as regards phthisis.
24 F	8	48	31	10	0	71·5	28-8-15	Act 29. Past history of cough, expectoration and pleurisy. Chest now dull posteriorly on R side, with R.M. diminished. General condition good.
25 F	5	30	47	16	2	58·5	22-8-15.	Act 24 Previous history of pleurisy and empyema. No symptoms now; up and about. Temp. normal.
26 M.	12	50	25	10	3.	74·5	25-8-15.	Act 35. Patient feeling well. R. apex impaired to percussion, and a few moist sounds heard. Temp. 98·4

Looking over the cases just recorded (1 to 26), and taking the counts and indices in conjunction with the physical signs, one is compelled to admit that there is a deviation from normal nuclear arrangement in most of the cases. This deviation is not constant in every case, but it is nevertheless an indication that the blood condition, as regards the polymorphonuclear leucocytes in any case, is not normal. In most of the cases the lesion is slight; in some the diagnosis is doubtful altogether and it be presumptious to suppose, as some have done, that one is enabled to diagnose pulmonary tuberculosis from an index which differs so little from normal.

In some of the cases, eg. 1, 4, 9, 11, 18, 20, the effect of sanatorium

treatment is exemplified, or in other words, the increasing resisting powers of the individual are shown to be improving by successive readings made at monthly intervals.

The conclusion one comes to in regard to cases of early tuberculosis of the lungs is that, while there is a "dislocation" or "deviation to the left" (Arneth) of the nuclear blood-picture, this is of no definite value in diagnosis. It occurs in many other conditions, as we have seen. Such an opinion is shared by other writers on the subject. It is to be noted, however, that in some cases, e.g. 14, 18, 20 and 21, although the physical signs pointed to actual, and sometimes to extensive disease in the chest, yet the blood picture was remarkably little altered. Following the theory advanced by Arneth that the powers of resistance are to be gauged by the proximity of the nuclear count to normal, one may deduct positively from these cases that the prognosis is good, particularly if the count remains approximately normal at successive examination.



Schema illustrating the ranges within which the cells of the various classes may be expected to occupy in early pulmonary tuberculosis, or when the powers of resistance are a little impaired.

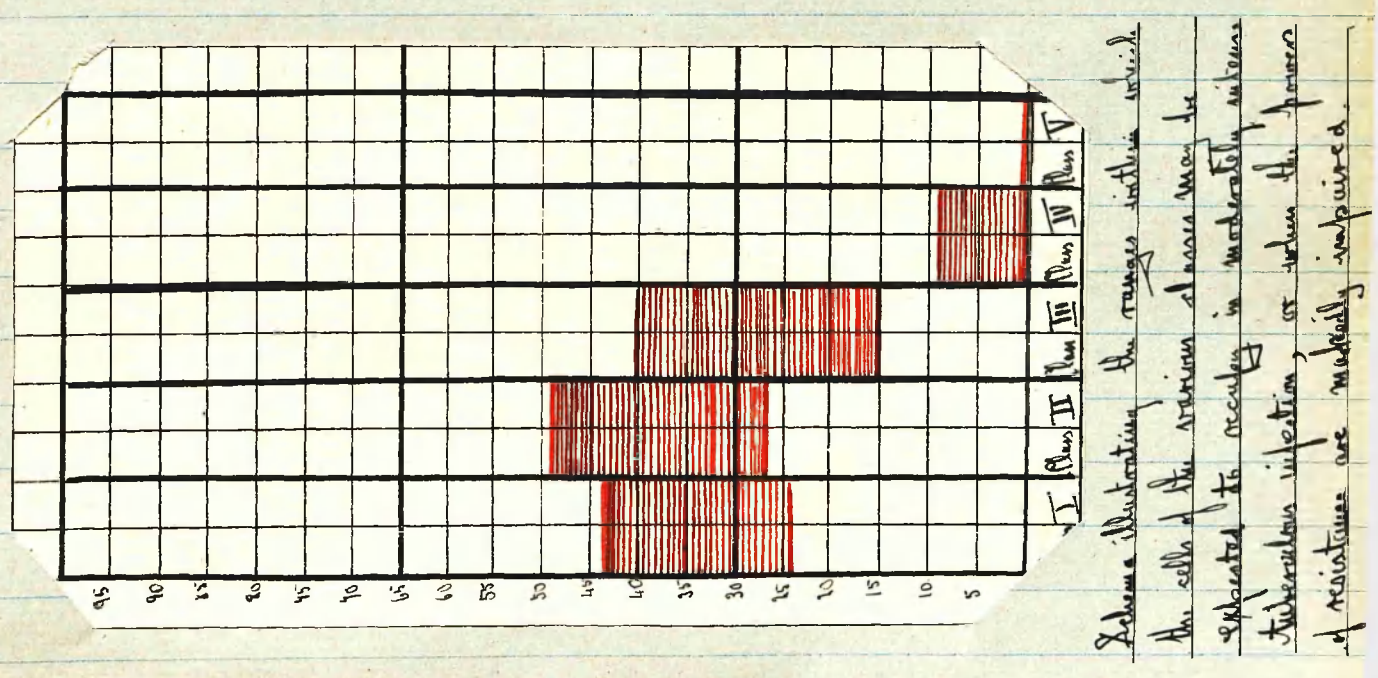
Case	Classes. I	II	III	IV	V	Index	Date	Remarks
24 F	36	31	32	1	0	83	16-9-15	Aet 26. Pleurisy 4 years ago. Haemoptysis at frequent
" "	31	31	34	1	0	80·5	4-10-15	intervals during July and August 1915. Family history bad. Both apices lacking in resonance, especially left. R.M. very harsh over both upper lobes; a few crepitations heard on deep inspiration.
28 M	34	33	33	0	0	89·5	16-5-15	Aet. 12. Patient was a delicate boy. Hectic fever on
" "	34	34	29	0	0	85·5	19-8-15	admission. Left upper lobe dull to percussion on Aug 21, 1915,
" "	40	34	23	0	0	88·5	2-9-15	and many rhonchi were heard. Under treatment, the
" "	41	36	23	0	0	88·5	25-9-15	temp. subsided to 99°. Tub. bac. Streptococci and staphylococci
" "	43	35	22	0	0	89	16-10-15	were found in sputum.
29 M	28	34	36	2	0	80	8-12-15	Aet 21. General condition good. Rt upper lobe dull to percussion; resp. murmur very harsh. No crepts heard.
30 F	24	36	36	1	0	81	23-9-15	Aet 12. Rt. base impaired in resonance, with diminished R.M. A few moist râles present in left axilla.
31 F	31	34	29	3	0	82·5	23-9-15	Aet. 10. Both sides of chest affected with bronchitis and at the apex of both lungs a few moist sounds were heard. General condition good.
32 F	14	35	39	9	0	41·5	4-9-15	Aet 35 Patient emaciated. Mother and paternal uncle
" "	20	39	36	5	0	44	21-9-15	died of phthisis. Both apices retracted; R. dull to
" "	30	38	29	3	0	82·5	1-10-15	percussion, with harsh breath sounds, and numerous
" "	36	42	21	1	0	88·5	24-10-15	crepitations. Streptococci et Tub. bacilli in sputum. Temperature normal.
33 F	39	45	15	1	0	91·5	14-9-15	Aet 23. General condition good. Both cords and
" "	36	41	22	1	0	88	4-10-15	arytenoid cartilages congested. Rt apex dull to percussion; a few crepitations heard.

Case	Classes I	II	III	IV	V.	Index	Date	Remarks
34 M	40	21	29	4	0	81·5	10-8-15	Act 49. Past history of recent pleurisy, influenza and bronchitis. Definite impairment of percussion note over both fronts; over post. aspect of rt. lung were definite signs of cavity formation. Temperature only slightly elevated. Pulse = 90. Tub. bac. in sputum. General condition good.
" "	31	29	40	0	0	80.	31-8-15	
" "	21	36	34	0	0	81·5	8-9-15	
" "	20	34	43	3	0	75·5	9-10-15	
35 F	32	41	26	1	0	86	18-8-15	Act 31. Rt. apex impaired in resonance. A few scattered crepitations at rt. apex. General condition good. Patient up and about. Temperature normal.
" "	30	40	28	2	0	84	31-8-15	
" "	29	43	24	1	0	85·5	23-9-15	
" "	29	41	29	1	0	84·5	11-10-15	
36 F	31	41	22	0	0	89	30-9-15	Act 10. Chest normal to percussion. Numerous moist sounds heard at left base posteriorly. Von Pirquet +. Temperature and pulse rate normal.
" "	35	30	28	1	0	85	14-10-15	
34 F	25	39	29	6	1	78·5	19-8-15	Act 41. Rt. apex dull to percussion. Small and scattered crepitations heard at both apices on successive examination.
" "	24	43	29	3	0	83·5	28-8-15	
" "	24	39	26	1	0	86	2-9-15	
" "	39	41	40	0	0	90	11-9-15	
" "	34	41	25	0	0	88·5	16-10-15	
38 M.	24	49	23	1	0	89·5	16-9-15	Act 28 Both apices were dull to percussion; Rhonchi and crepitations abundant all over the chest. Duration of disease said to be 4 years. General condition good.
39 M	19	49	18	4	0	72	20-8-15	Act 29. Rt side of chest was absolutely dull to percussion. The left side was clear and resonant. Crepitations were heard all over right side, and friction was audible at the angle of the scapula on rt side. General condition was good. Pulse rate slightly accelerated; temp. elevated to 99·4 in evenings.
	24	36	18	2	0	89	31-8-15	
	19	39	31	1	0	83·5	19-9-15	
	34	39	26	1	0	86	8-10-15	

Cases 24 to 39 are illustrative of patients suffering from tuberculous disease and in whom the nuclear index is, approximately, between 80 and 90. Comparing the physical signs in the chest and the clinical findings we see that the disease is, in most cases, more extensive than in patients 1 to 23. That this is not altogether so, however, is exemplified by Cases 29, 30 and 35 where the lesions in the chest are slight.

The deduction to be made from the Arneth count in these cases is that the count is an indication of the intensity of the process rather than of the extent of the lesion.

The last case recorded, No. 39, illustrates the association of tolerably extensive disease with an Arneth count only moderately deviated. Another point of importance is that in none of the above cases, in which several counts were made, were there any very definite improvement in the nuclear index, despite the fact that, in some, there was a substantial drop in the leucocyte of Class I. The paucity of polymorphs of the fourth class is a feature which also merits attention, and points to the fact that those particular cells appear to be extremely sensitive to a tuberculous infection.



Schema illustrating the manner in which the cells of the various classes may be affected in the course of tuberculous infection, or when the powers of resistance are markedly impaired.

The cases which now fall to be recorded are, almost without exception, cases of advanced or apparently advancing disease. The clinical findings are recorded in detail, and the conclusion is that, despite the remarkable variations in the symptoms and signs shown by the patients, yet there is one feature above all others which is outstanding and common to all, namely, a large amount of deviation to the left in the nuclear count. One case especially (No 56) is deserving of attention, and no other sign in clinical medicine could have convinced one that the case was acute and progressive. A similar case is recorded by Minot and Ringer. If the Arneth count served no other purpose than to distinguish acute from apparently chronic or early cases, its ~~service~~ service in clinical medicine would be enormous.

CASE	I	II	III	IV	V	INDEX	DATE	REMARKS.
OM	41	29	24	3	0	88·5	26-8-15	Act 20. Onset 2½ years previously. Rt. hip-joint diseased. Several discharging sinuses over hip and sacrum. Chest examination revealed poor air entry at both apices with a few crackling rales at rt. apex. Temp. 99°F.
"	44	40	15	1	0	91·5	23-9-15	
"	46	39	15	0	0	82·5	30-9-15	
"	46	40	13	1	0	92·5	16-10-15	
M	40	41	14	0	0	93	5-5-15	Act 34. Pleurisy 3 years previously. Both apices markedly retracted; left dull to percussion, vocal resonance exaggerated; crepitation heard all over left apex.
M	42	46	12	0	0	94	28-8-15	Act 24. Onset 3 months previously. Brother and sister died of phthisis. General condition poor. Temp. 99 - 102°F. Pulse 100 - 110 per minute. Left upper lobe dull to percussion and resonance impaired over rt. upper lobe. Numerous moist sounds heard all over left lung and over rt. upper lobe. Sputum contained Tub. bac., Streptococci, Staphylococci and Diplococci. Died 24-2-16
	47	45	8	0	0	96	19-9-15	
	48	45	4	0	0	96·5	8-10-15	

Case	Classes I	II	III	IV	V	Index	Date	Remarks
43 F	50	40	10	0	0	95	26-8-15	Aet 24 Bed patient. Temp 98-100. Rt. upper lobe
" "	49	41	10	0	0	95	28-8-15	dull; numerous crepts, and R.M. very intense amounting
" "	48	44	8	0	0	96	11-9-15	to bronchophony. Tub. Bac. and the common secondary
								organism abundant in sputum. Died 12.12.15.
44 M	44	40	15	1	0	91.5	26-8-15	Aet 33. General condition good. Rt. lung dull all
" "	47	44	9	1	0	95.5	19-9-15	over; numerous moist sounds heard. Cavity
" "	39	47	12	2	0	92	5-10-15	at upper lobe in left side. Pneumothorax developed
								on left side on 20.9.15. Patient recovered and felt
								better afterwards.
45 F	41	46	13	0	0	93.5	8-10-15	Aet 14 General condition poor. Both upper
" "	40	48	12	0	0	94	11-10-15	lobes dull to percussion. Large cavity involving
								upper left lobe. Crepitation heard all over both
								lungs. Temp. 98 to 101.6° F. Tub. Bac. abundant
								in sputum. Died 19-3-16.
46 M	38	34	20	4	1	85	19-8-15	Aet 39. General condition poor. Both lungs
" "	40	38	21	1	0	85.5	2-9-15	riddled with disease. Temperature only
" "	43	41	16	0	0	92	23-9-15	moderately elevated, - 99.6° F. Duration of
" "	40	42	14	1	1	90.5	14-10-15	illness said to be 5 years. N.B. There was no
								noticeable clinical exacerbation in the disease
								between 2-9-15 and 23-9-15. Still alive.
47 M	42	46	12	0	0	94	31-8-15	Aet 19. General condition good. Admitted with
	40	34	22	1	0	88	8-9-15 - at 12-30 pm.	temp 100 - 102° F.; pulse 100 - 110.
"	43	35	20	2	0	88	8-9-15 . at 5-30 pm.	Rt apex impaired in resonance; numerous
	40	34	21	2	0	84.5	11-9-15	moist crepitations heard; also well-
	31	34	23	9	3	76.5	19-10-15	marked bronchial breathing. Tubercle
								Bacilli in sputum. By 8-9-15 temp had subsided,
								and patient was feeling well. Rt apex still
								impaired in resonance on 19-10-15, but only a few
								scattered crepitations heard.

Case	I	II	III	IV	V	Index	Date	Remarks.
48F	46	45	9	0	0	95·5	3-9-15	Act 20. Both upper lobes dull. The R.M. evesyculum
"	40	39	19	2	0	88·5	23-9-15	accompanied by small moist rales. Cavity formation at left apex. Temp 99.-104° F.
49F	54	32	13	1	0	92·5	8-9-15 at 12-10 pm.	Act 34. Both apices retracted; a few
	49	34	16	1	0	91	8-9-15 at 5-10 pm.	moist sounds heard at rt apex. Cavity
	46	39	14	1	0	92	8-10-15.	at left apex. Numerous crepitation over apex of left lower lobe.
50M	44	42	12	2	0	92	20-8-15	Act. 54. General condition very poor. Temp 99-101.6°F.
	46	39	14	1	0	92	28-8-15	Pulse 100-110. A note made on 12-8-15. "Left lung
	50	39	11	0	0	96·5	19-9-15	is dull anteriorly and posteriorly. There are many
	51	42	7	0	0	96·5	8-10-15	crepitations to be heard over left side of chest; at the apex there is a cavity. The right lung is almost wholly excavated posteriorly. From the physical signs, it is doubtful whether any healthy lung tissue exists at all." Died 15-12-15.
51M	52	48	0	0	0	100	8-10-15	Act 16. General condition poor. Both lungs dull to percussion, anteriorly and posteriorly. Crepitations heard all over chest. Temp. 100-102.6°F. Pulse 120. Died 9-11-16.
52M	49	50	1	0	0	99·5	8-10-15	Act 15. Admitted with extensive cavity formation in left upper lobe. Crepitation numerous all over left lung and over rt. upper lobe. Died suddenly 16-10-15.
53F	43	49	8	0	0	96	31-8-15	Act 19. Patient very emaciated. Both apices
	42	50	8	0	0	96	8-9-15 at 12-30 pm.	dull to percussion. R.M. tubular all
	44	49	4	0	0	98	8-9-15 at 5-30 pm.	over chest; crepitations abundant on
	50	49	1	0	0	99·5	23-9-15	both sides; cavity in rt upper lobe. Temp. 100-103. Pulse 120. Died 15-11-15

Case	Classes. I	II	III	IV	V	Index	Date	Remarks
54M	46	48	6	0	0	94	19-9-15	Act 32. Patient was admitted with both feet swollen and oedematous. Rt apex impaired in resonance. Left lung dull posteriorly from apex to base. Both lungs crepitating all over. Died 2-1-16
" "	47	48	5	0	0	99.5	8-10-15	
55M.	50	48	2	0	0	99	22-5-15	Act 50. Poor general condition. R.M. very weak all over chest; moist sounds heard over both sides. Temperature normal; pulse 100 Died 14-7-16.
56M	44	42	11	0	0	96.5	22-5-15	Act 24. Patients father, mother and grandfather died of phthisis. General condition good. Right apex lacking in resonance. A few crepitations were heard at the end of inspiration. Temperature never above normal. Died 30-8-15, after profuse haemoptysis following an attack of "Influenza".
54M	48	50	2	0	0	99	18-8-15	Act 32. Onset 8 months previously. General condition very poor. Both apices much retracted; it dull to percussion, and crepitating. Temperature swinging between 99 at 102. Pulse 110. Died 4-9-15.
58F	50	49	1	0	0	99.5	5-5-15	Act 14. Films were taken when patient was extremely ill. Both lungs riddled with disease all over. Temp 103-4° F. Pulse 120(?) Died 4-5-15.
59F	48	49	3	0	0	98.5	20-8-15	Act 14 Onset 10 weeks previously. Diffuse
"	50	49	1	0	0	99.5	31-8-15	tuberculous broncho-pneumonia, with peritoneal involvement. Temp. 102° F. Pulse 110. Died 8-9-15

Case	Classes I	II	III	IV	V	Index	Date	Remarks.
60 M	36	39	23	2	0	86·5	20-8-15	Act 14. Rt. border of cardiac dulness 1½ ins. to the rt. of sternum.; left border in left anterior axillary line. Soft mitral systolic murmur heard at apex of heart and in left axilla. Rt apex dull to percussion; numerous crepn. heard. Ascites and oedema of feet & legs. Tub. bac. in sputum. Died 24-9-15.
" "	41	43	15	1	0	91·5	28-8-15	
61 F.	42	46	12	0	0	94	19-8-15	Act 28 Both upper lobes dull to percussion.
" "	46	49	4	0	0	96·5	28-8-15	Cavity formation at rt. upper lobe.
" "	45	46	9	0	0	96·5	4-9-15	Crepitation all over rt. lung and at apex of left.
" "	47	49	4	0	0	98	11-9-15	Temp 98-101° F. Died 12-12-15.
62 F	47	48	5	0	0	97·5	31-8-15	Act 14. General condition very poor. Left lung
" "	46	49	5	0	0	97·5	23 9 15	dull to percussion from apex to base. Crepitations
" "	50	48	2	0	0	99	8-11-15	abundant. Large cavity in rt. upper lobe. Tubercle bacilli in sputum, also other organisms. Temp 99-101. Pulse 110. Died 5-1-16.
63 F	49	50	1	0	0	99·5	11-9-15	Act 26. Onset, 4 months previously. Pleurisy
" "	50	48	2	0	0	99	8-10-15	3 weeks before. Both vocal cords infiltrated and white; epiglottis oedematous at base. Cavities at both apices with numerous crepitations all over lungs. Temp 99-102°. Pulse 100. Died 9-12-15.
64 M.	48	49	3	0	0	98·5	15-5-15.	Act 35 Emaciation extreme. Both lungs
" "	51	49	0	0	0	100	29-5-15	riddled with disease; large cavities in rt lung, in upper and lower lobes. Temp. 99-101°. Pulse 110. Died 29-5-15.
65 F.	44	50	3	0	0	98·5	8-5-15	Act 10. Extreme emaciation Wt. 2 st. 11¼ lbs. Abdomen distended and tympanitic. A few crepn. developed at left apex. Died 4-8-15

Case	Classes I	II	III	IV	V	Index	Date	Remarks
						Classes.		
66M	46	49	5	0	0	97·5	20·8·15	Adt 20. Chest little altered from normal to percussion. A few crepn. at both apices. Temp. 98–101 for four weeks after admission, but then came within normal limits. On 26·8·15 temperature was normal and general condition good. Died 31·10·15.
	50	44	6	0	0	99	26·8·15	
67M	48·50	2	0	0		99	31·8·15	Adt 14 Numerous crepitation heard all over R. side of chest. Temp 99–101°F. Pulse 90–110. Died 11·10·15.

In making my observations on the nuclear counts in the polymorphonuclear leucocytes, I was forced by dint of circumstances to take the majority of my patients from amongst cases of very advanced disease. The remarkable figures obtained show that in such cases, there is a very definite nuclear change in the polymorphonuclear leucocyte. In such cases as No 56, where the index is over 90., it behoves one to regard the case as a dangerous one, and for ordinary purposes, one must regard an index of 90 or more as an alarm signal, even when the patient's general condition is apparently good. The presence of a high index may be taken, then, as an indication of feeble resistance on the part of the patient, and, as a high index is synonymous with an excess of cells of Classes I and II, one may regard these cells as the last representatives of the defensive mechanism, and, consequently, of serious import. In certain cases (see Nos. 51 and 64) there is sometimes a complete obliteration of Classes III, IV and V., giving an index of 100. Such cases are grave in the extreme.

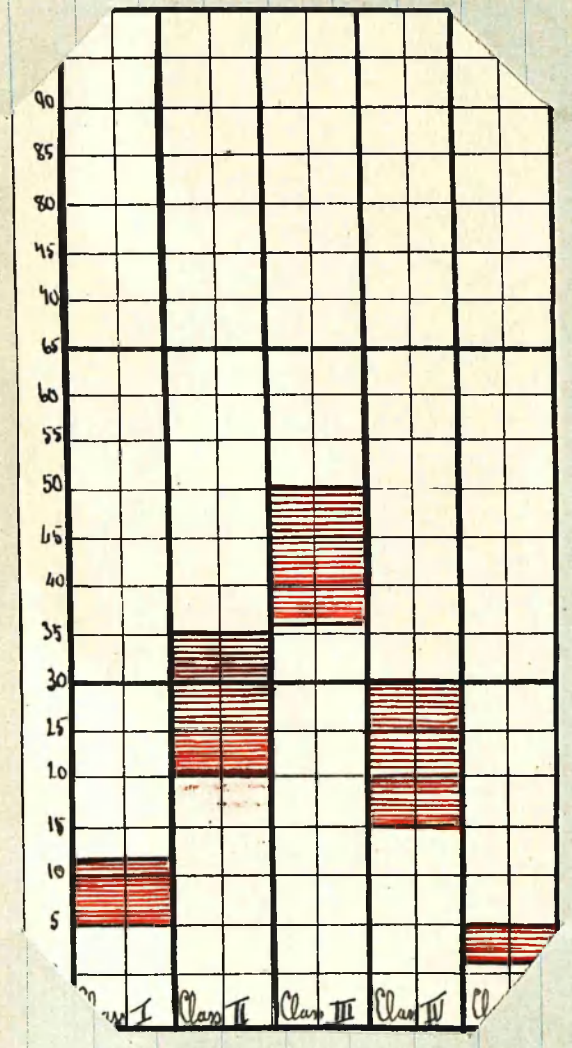
Most of the cases last recorded (Nos. 40 to 64) were cases of in what has been termed the "Third Stage" of the disease; the majority had swinging or hectic temperatures, tubercle bacilli and other organisms in the sputum, increased pulse-rate, and most of the other symptoms characteristic of extensive, or of acute and progressive disease. The effect of these secondary organisms

on the number of leucocytes in the circulating blood, I have shown already. Suffice it to say now that the long continued call on the leucocytes, such as is demanded by the so-called third-stage cases, must inevitably lead to a marrow exhaustion, in quality if not in quantity. In several of the above patients I had the opportunity of taking leucocyte counts, and in the succeeding chapter I shall endeavour to correlate the number of leucocytes with their morphology.

It is now possible to chart the various ranges within which it is possible for the different classes of polymorphs to occupy in various stages of the disease; or, to be more correct, it is now possible to make a chart of a particular patients powers of resistance.

Description of Diagrams on the Following Page.

1. Schema, built up from the results of various observers. illustrating the ranges within which the cells of the various classes may be expected to occupy in health.
2. Schema illustrating the ranges within which the cells of the various classes may be expected to occupy in early pulmonary tuberculosis, or when the powers of resistance are a little impaired
3. Schema illustrating the ranges within which the cells of the various classes may be expected to occupy in moderately intense tuberculous infection, or when the powers of resistance are markedly impaired.
4. Schema illustrating the ranges within which the cells of the various classes may be expected to occupy in severe cases of tuberculous infection, or when the powers of resistance are very feeble.


90
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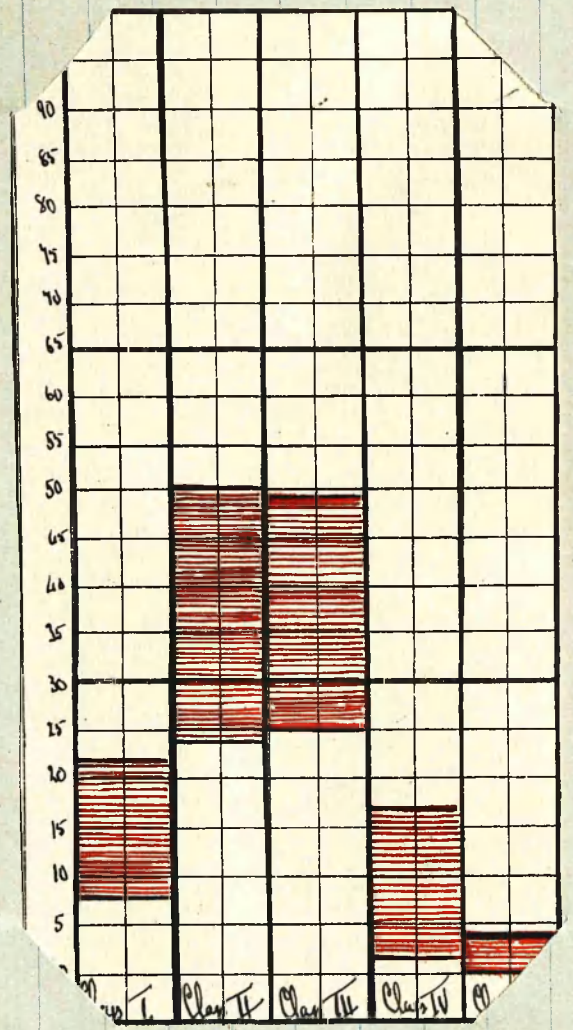
Class I
Class II
Class III
Class IV

1.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Class III
Class IV

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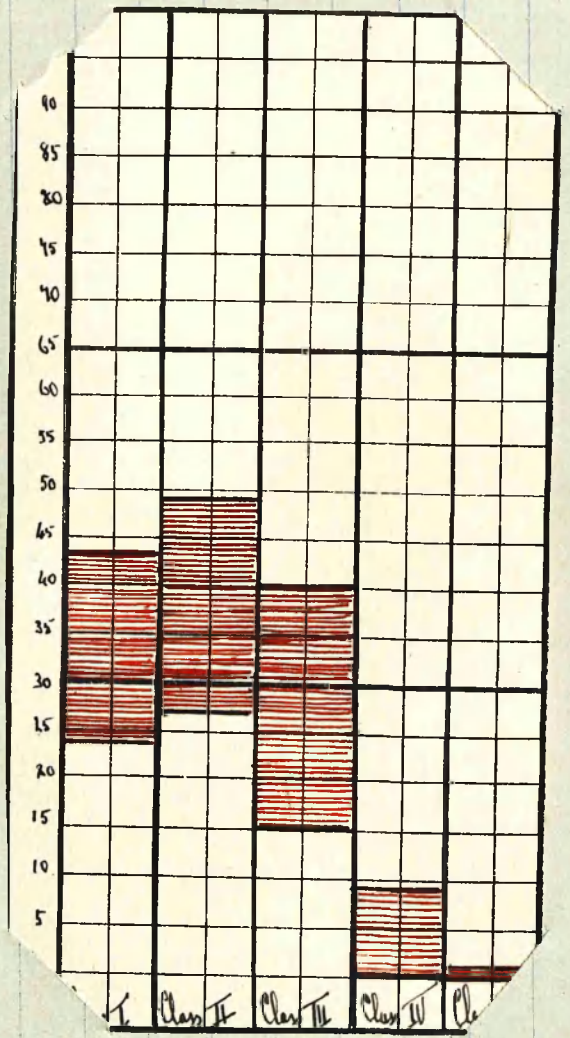
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Class I
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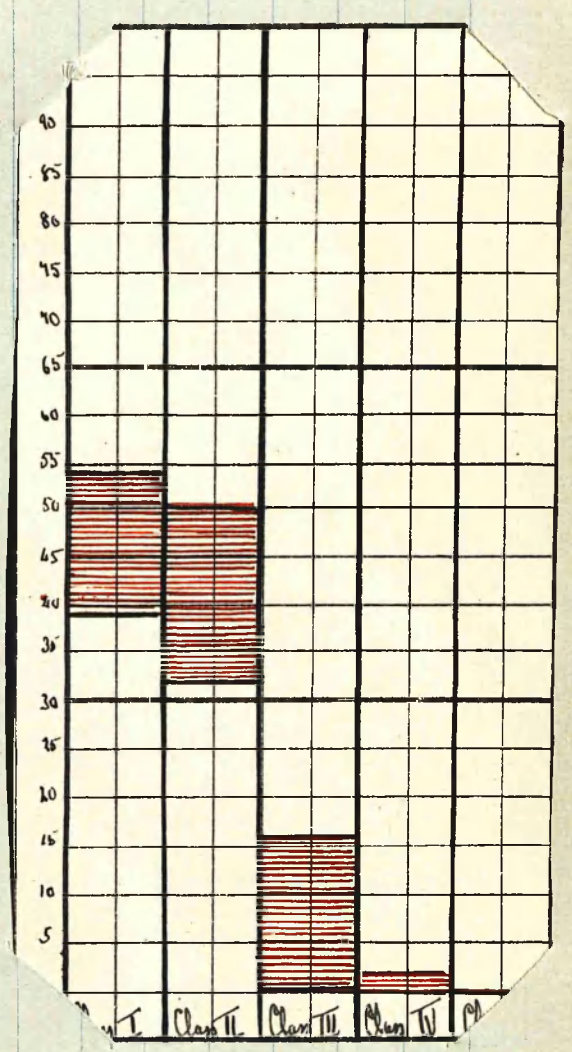
Class III
Class IV

3.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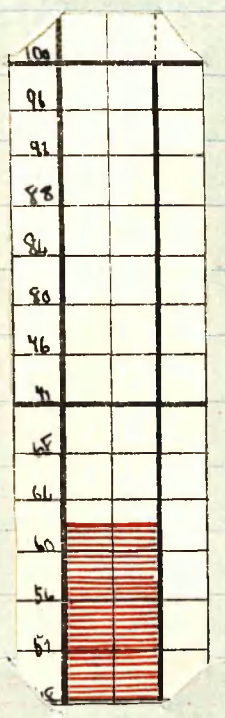
Class I
Class II
Class III
Class IV

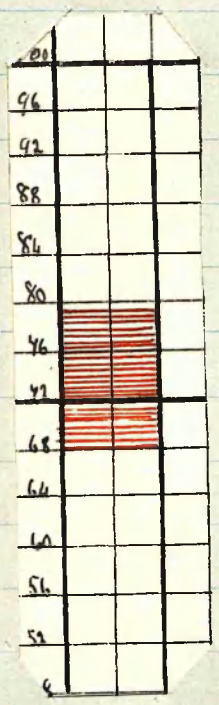
4.

Figures to Illustrate the Range of the "Index" in:

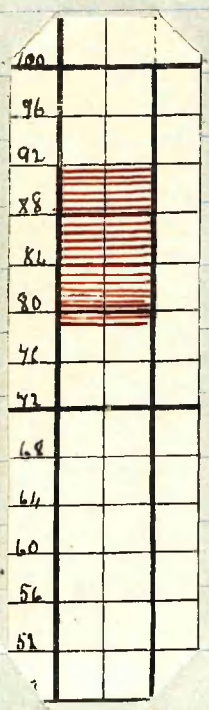
(a) Health.



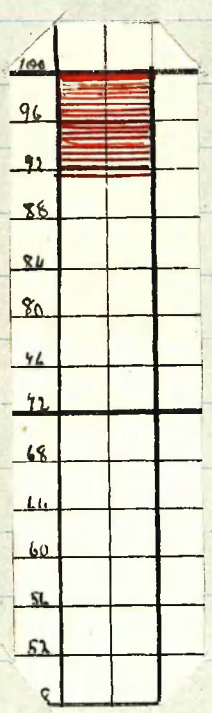
(b) Patients whose powers of resistance are a little impaired.



(c) Patients whose powers of resistance are markedly impaired.



(d) Patients whose powers of resistance are very feeble.



The foregoing charts show better than words could tell what is meant by the "deviation to the left"; the term used by Arneth to signify the preponderance of cells of the first and second classes.

The precise significance of this deviation to the left in the presence of an intoxication is problematical and the explanation depends entirely on the view one takes of the function of the polymorphonuclear leucocyte. There is, as I have said previously, much evidence to show that the relation of this cell to the immunising processes going on in the body, are more intimate than was at one time admitted. Accurate study of the neutrophile granules, which are said to be the source of complement, is not very easy for obvious reasons; but a priori, one might suggest that a cell lacking in nuclear matter, such as cells of Classes I and II, is not in a position to ~~formulate~~ fournish the ~~opt~~ same substance, whatever it is, as the cells of Classes III, IV and V, which are much richer in chromatin.

Be as it may, the fact remains that, with an ebbing immunity and an approaching death, the cells of Classes I and II predominate over the other classes, and, conversely, with an increasing immunity and improved health, there is a tendency for the nuclear picture to once more attain its normal outline.

Chapter VII

The Relation of the Consecutive Leucocyte Count to the Arneth Count.

We have seen that a leucocytosis, susceptible to great variation, is a feature of certain cases of pulmonary tuberculosis. In Chapter VI it has been pointed out also, that a change in the nuclear picture of the polymorphs has definite significance in the course of the same disease. The object of the present inquiry is to ascertain whether there is any relation between the two phenomena, and if possible, to arrive at some conclusion on the much debated point as to whether a leucocytosis is, prognostically, a favourable sign.

Ellon and Craig have asserted that an increase in the leucocytes is a most unfavourable sign, while Arneth considers that an increase in the total number of white cells is of ill omen. From a large series of observations on this point, I prefer take a middle course, and point out that, under certain conditions, a leucocytosis may be favourable, and that under circumstances, as Ellon and Craig suggest, it is of no value.

Altogether I have examined thirty different cases in order to come to my conclusions. These cases have already been cited either in Chapter II or in Chapter VI, so that in what follows, only reference will be made to the cases in question.

Taking the Arneth count as a sign of value in pulmonary tuberculosis, as indicative of the powers of resistance of the individual, we find that there are several possibilities.

1st. A consecutive leucocyte count within normal limits, accompanied by a normal Arneth count.

This is the condition which prevails in health, and which is

taken as the standard for comparing with the abnormal

2nd A consecutive leucocyte count within normal limits, accompanied by an Arneth count (a) slightly deviated to the left.
(b) more markedly deviated to the left.
(c) greatly deviated to the left.

2(a) This is the condition found in early cases of phthisis, when no secondary organisms are making their presence felt. It is, unfortunately, in those cases that we are confronted with the difficulty of making a positive diagnosis when the physical signs in the chest are doubtful. Personally, I should hesitate to make a diagnosis of phthisis with the presence of a normal leucocyte count and a slightly heightened index, (see Cases 4, 12, 23 Chapt. VI), for so many other conditions, — influenza, for example, may be accompanied by the same sign. The value of the Arneth count even when associated with a normal leucocyte count is doubtful from a diagnostic point of view, and he would be a rash person who would say otherwise. Too much depends on the personal equation for one to dogmatise on this particular point. It is different, however, when we are considering a case such as Case XXIX, Chapt. V, where, at the first examination, there was a definite leucocyte swing with a moderately deviated index, and volume, at the last examination, the successive leucocyte counts were within normal limits and associated, at the same time, with a nuclear picture, only slightly deviated to the left. This case shows the value of repeated blood examination, and helps to confirm the opinion formed by physical examination of the patient, viz, that the disease was becoming quiescent.

2(b) In this case the value of the findings is of greater import, and is found in cases of pure tuberculosis when the powers of resistance are more markedly impaired than in the

case of 2(a). Tubercle bacilli may be present in the sputum but other organisms are very scarce if present at all. Such cases tend to run a more or less normal temperature and a normal pulse-rate (Cases 4, 14, 18 Chapt. VI.).

2(c) The presence of a normal consecutive leucocyte count with an Index greatly deviated to the left is a combination with which I am not very familiar in pulmonary tuberculosis. No writer has, so far as I know, made the necessary combined observation on acute influenza, in which diseases one might anticipate a normal leucocyte count with a much deviated nuclear picture. I have, however, to record one case (No 59. Chapt. VI) where, on the date mentioned (20-8-15), seven successive leucocytes were found to be within normal limits, and yet the Arneth Index registered 98-6. In this case, death followed a fortnight later. The deduction which I make from this case is that the intensity of the tuberculous process was very great, and that the response on the part of the marrow was extremely feeble, from a qualitative view more especially. Before coming to more definite conclusions on this point I should prefer to get other cases with a series of leucocyte counts within normal limits accompanied by a much deviated nuclear picture; as I have said, the former is the exception in pulmonary tuberculosis. It is convenient to discuss here the relation between the leucocyte count and the nuclear index in such a case as Case I, Chapt. II, where, at different intervals, the leucocyte count tends to come within normal limits.
In this particular patient, the series of counts made on Feb. 22 1916 was more in keeping with normal that they had been previously, yet the following observations were made:

		Classes.					Index.
		I	II	III	IV	V.	
14-XII-15.	4 p.m.	41.	28	28	3	0	83.
	5 pm.	40	32	25	3	0	84·5.
18-XII-15	4·15 a.m.	39	33	26	2	0	85
26-I-16	12 noon.	45	40	14	1	0	92.
	4 pm.	43	40	16	1	0	91.
22-II 16	2 pm.	44	41	12	0	0	94.
	4 pm.	48	41	11	0	0	94·5.

Although, then, the leucocyte counts were more within normal range as time went on, yet the nuclear index was much higher on Feb. 22, 1916 than it had been at any previous time. The sudden termination to the patient's life on Feb. 29, 1916 lends stress in favour of the argument that the leucocyte count was adversely affected both qualitatively and quantitatively.

3rd A consecutive leucocyte count below normal limits i.e. a leucopoenia with an Arneth count (a) slightly deviated to the left
(b) more markedly deviated to the left.
(c) greatly deviated to the left.

The three conditions may be discussed together. Whilst the occurrence of a leucopoenia in miliary tuberculosis and in enteric fever is recognised, there is also evidence to show that the Arneth count is also deviated to the left in these diseases. So far as pulmonary tuberculosis is concerned, however, I have no data to show that there is ever a continued leucopoenia, not even in the terminal stages of the disease, so that the above combination of circumstances does not apply to tuberculosis of the lungs so far as I am aware.

4th. A consecutive leucocyte count above normal limits i.e. a leucocytosis, with an Arneth count (a) slightly deviated to the left.
(b) more markedly deviated to the left.
(c) greatly deviated to the left.

I have not been able to satisfy myself that a consecutive leucocytosis is characteristic of phthisis. On the contrary, I should say that it is the exception, for the reasons already given. (Chapt. IV) In some cases, however, even where tubercle bacilli are found in the sputum, the leucocyte count does tend towards a leucocytosis, but in such cases, we cannot, in the light of our present knowledge of tuberculosis of the lungs, regard the infection as a purely tuberculous one; even although tubercle bacilli are found in the sputum and the temperature be a normal one. In Case XV Chapt. II, the nuclear index was between 80 and 90 in all of five different films; consequently I should place the case in 4(b).
Of course, it might be argued that the Arneth count is not peculiar to phthisis; but neither is a constant leucocytosis. How, then, are we to explain the presence of tubercle bacilli in the sputum, the deviated nuclear picture and the more or less constant leucocytosis in Case XV Chapt II. The leucocytosis is, I believe, caused by the preponderance of secondary organisms. In the case of simple bronchitis there is usually an inflammatory leucocytosis amounting to 12, or 14,000 cells per cub. mm.; the patient alluded to had a well marked bronchitis as well as the pulmonary lesion. The sputum examination in this case, also, showed numerous secondary organisms, some of which were actually cultivated on blood agar. As I have mentioned above, the deviation in the nuclear picture is not peculiar to phthisis, and the tubercle bacilli in the sputum were, in this case, the subordinate organisms, for the time being at least. It is only by

such a process of reasoning that the results are admissable. I have notes of a similar case, (Case 31 Chapt. VI), which presented a leucocytosis of 12 to 14,000 and a nuclear index of 84.5, where bronchitis was the prominent lesion but where also a few crepitations were heard in the left axilla. I have ascertained since making that examination, that the bronchitis and the crepitations have disappeared entirely, and that the patient is now in perfect health.

It appears, therefore, that a series of leucocyte counts, amounting to a sustained, and approximately constant leucocytosis, together with a deviated nuclear blood picture, speaks against rather than for tuberculosis of the lungs.

5th A "swing" in the leucocyte count accompanied by an Arneth count (a) slightly deviated to the left.
(b) more markedly deviated to the left.
(c) greatly deviated to the left.

5 (a) Bearing in mind that the Arneth count is an index of resistance, and that the leucocyte count is an index of activity of pyogenic and, perhaps, other organisms, one is in a position to subdivide this fifth possibility into three classes, the first of which we are considering now, and which deals with the majority of so called "early" cases of phthisis, i.e. those showing a slight, but yet appreciable swing in the leucocyte count, and a nuclear index slightly deviated to the left. Case III, Chapt II is a case in point. Here the leucocytes are seen to vary from 6,600 to 16,200; the nuclear index was only 68.5 or an average of three readings. viz:

20-XII-15.	TIME	12:30 pm.	5-30 pm.	4 pm.
	INDEX	69	67.	69

I have noted two similar cases where the Index was below 49·5 with the leucocytes averaging between 6,000 and 16,000 per cub. mm., at periodical examinations.

Returning once more to the phrase "so-called early" cases, one can scarcely admit that Case III, Chapt. II should fall into this category. On the contrary, the patient was a "third-stage" case; but the blood findings appear at first sight to contradict this statement. In an earlier chapter I have maintained that the extent of the lesion in the chest is no criterion of its pathology. A very intense tuberculous infection, – so long as it remains tuberculous, – is not necessarily associated with a leucocytosis. Such an event only happens on the advent of other organisms. The sputum examination in Case III Chapt. II gives further strength to my argument. The comparatively low index for such an 'advanced' case of phthisis is merely another way of saying that the leucocyte response was qualitatively good.

In such cases as 5 (a), (the group we are considering), the temperature may be normal and the pulse rate only slightly elevated, and tubercle bacilli may be present in the sputum. As a rule, however, it is exceptional to meet with advanced physical signs in the chest in these cases. More often the lesion is a small one to physical examination, and tubercle bacilli absent from the sputum. (Case 22 Chapt. VI).

5 (b) Cases in which the nuclear index varies between 49·5 and 41·5 are usually accompanied by a consecutive leucocyte count with the maximum number of leucocytes at or about 22,000 per cub. mm. (Cases 39 Chapt VI; XI, Chapt II.) The physical signs are most frequently easy to find, and tubercle bacilli are seldom absent from the sputum.

Conversely, in any particular case where bacilli are absent from

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(b) more markedly deviated to the left.
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is that the leucocytosis is a useless one both from the humoral and from the phagocytic points of view. For an active phagocytosis, there must be a satisfactory leucocyte response. As we have seen, in all the cases which come under this heading (5c), the leucocytosis is usually high enough, but the cells are evidently too young, too immature, to thwart the infection.

Chapter VIII

Conclusion

In the preceding chapter I have endeavoured to justify the conclusion that in tuberculosis of the lungs, the polymorphonuclear leucocyte plays a most important part in the clinical pathology of the disease. This is by no means a new conclusion. For years back, physicians have pinned their faith on certain drugs, the outstanding action of which is to aid the leucocytes of the blood in their antagonism to the disease. It seems almost as if the experience of years had at last made itself felt, and the fruits of the ripe experience have given us the necessary "specifics" for the scourge of tuberculosis. Certain it is that many physicians, who have tried almost every drug in the pharmacopoia in tuberculosis, fall back ultimately on the use of one or other of the so-called "specifics", some of which may be tabulated below.

1/ Nucleic Acid — Nuclein acid stands apart as the best example of leucocyte-producing drugs. It is contained in tuberculin, and given in the form of yeast, after the manner advocated by Huggard and Moorland, it is claimed to have beneficial effects. I have used for the past twelve months, Nuclein (P. D and Co.) hypodermically, dose 10 to 60 m. This preparation contains 5% of Nucleinic Acid, prepared from yeast. I have given it with and without tuberculin and in the limited number of patients on my record whom I have so treated, I have noted a decided improvement in the blood picture. The breath index improves and the leucocyte count tends to come within normal limits after about ten weeks treatment, giving doses twice weekly in increasing amounts. So far, my cases are too few

to entitle me to be dogmatic on this method of treatment, but I hope to be able to publish results when the number of cases is larger. How much benefit accrues from the nuclein I am not prepared to say at present, because all the patients to whom I have given Nuclein were undergoing Sanatorium treatment coincidently.

2 Cinnamic Acid. This drug was first used by Landerer, who advocated its use in phthisis in virtue of its double action, firstly, as a stimulator of leucocyte formation, and secondly, as a stimulator of fibrous tissue growth round a tubercular focus. The modification of Cinnamic Acid most used nowadays is sodium cinnamate, also known as "Hetol" My predecessor at Crossley Sanatorium has spoken to me favourably of Sodium cinnamate, but I have no personal knowledge of its efficacy in tuberculosis of the lungs. Cantorowitz and R. Weissmann have collected 1160 papers on the subject, a large majority being favourable to its use.

3 Iodine. Apart altogether from the action of potassium iodide in bronchitis, there is a fair collection of evidence to prove that Iodine is beneficial in phthisis. Some of its potency may be in virtue of its power to excite phagocytosis.

4, Other drugs which have been used in phthisis with the hope that leucocyte formation may be helped are, Colchicum, Camphor, Benzoic Acid, Ether and Quinine.

None of the above drugs can be said to be in any way specific for Phthisis pulmonalis, but it is the spirit which prompts their use which I am desirous of

emphasizing.

I have maintained that the leucocyte response in phthisis is a response to the invasion of the body by secondary organisms. Once these organisms are present, there are obviously two ways in which the body can protect itself against the infection; the one is by attacking the organisms directly, and the other is by attacking them indirectly. The direct method of attack is by the administration of antiseptic inhalations, which are in such common use in tuberculosis of the lungs. The indirect method is by encouraging the natural foes of these secondary invaders, namely, the leucocytes, to become as efficient as possible, and it is with this intention that the above drugs have been used in phthisis. It does not follow, as I have pointed out before, that a mere increase in number of leucocytes is the object to be aimed at; on the contrary, the correct numerical quantity may be an actual diminution in the existing number. It is the quality, the normal nuclear picture, which should be the ultimate aim of treatment.

How far syntrosis increases or diminishes the virulency of the ordinary secondary organisms so commonly met with in association with tuberculosis of the lungs it is difficult to say, but it is clear, from clinical experience, that they are extremely difficult to overcome by medicinal measures. The satisfactory restoration of a leucocyte count to normal limits, and the improvement in the hæmoglobin count obtained in many cases of phthisis by ordinary Sanatorium treatment without the introduction of any medicines whatever, indicate that in the usual well-regulated Sanatorium regime we have a more than useful weapon for attack. It is to be remembered however, that Sanatorium regime does not mean merely fresh air and good food, an interpretation too often put on it. At Crosby Sanatoriums, we have used

a system of graduated exercise, in most of the cases with excellent results, with the hope of increasing the immunising processes by small, and repeated autoinoculation, after the manner detailed by Paterson. The effects of these autoinoculation are not always manifested by an increase in the temperature, although careful observations on the pulse rate will frequently provide an indication of systemic infection. All the patients who were "up and about" (Chapt. II) had graduated exercise, and the blood-findings, when taken in conjunction with the line of treatment and the theories on which it depends, are significant. The combination of Sanatorium treatment, antiseptic inhalations and nuclein or some such leucocyte stimulating substance appears to me to be the most beneficial line of treatment at present at our disposal. Such is the opinion I have formed as a result of the observations I have made on the role of the polymorpho-nuclear leucocyte in pulmonary tuberculosis.

In times of advance in histology and pathology we are forced to combine the findings of the sciences. So far as the polymorph is concerned, we know that it plays a very minor part in the histology of the pure tuberculous focus; and it plays no part whatever in the construction of the miliary tubercle. But in speaking of the pathology of the disease, as it presents itself clinically, we are dealing with a totally different thing; the rôle given by Metchnikoff to the polymorph in immunity brings this cell to the forefront as a most important factor in the processes of immunity and phagocytosis, and, as I have shown, in the presence of secondary infection, the tuberculous process itself is of minor importance.

It must not be for clinicians to be pessimistic of the result of this battle between organisms and tissue cells, for such it is, with the tubercle bacilli

the main offenders and the polymorphonuclear leucocytes their chief foes. Apparently, as yet, we have no specific cell which may be regarded as the specific enemy of the tubercle bacillus. We have, however, certain cells, - the polymorphs, - which are tissue cells definitely inimicable to the great majority of organisms which affect the lungs secondarily, and to which we can attribute much of the damage done in the pulmonary substance. Let us make full use of their function.

Evolution works slowly; who can say but that these same cells, the polymorphs; or some other cells, eg. the mononuclears, may be gradually educating themselves to respond "to the chemical aroma" of the tubercle bacilli just as they have learned in the past to deal with the lesser complex foes of the human body.

As matters are at present, I shall conclude with a quotation from Bushnell, "An objective proof that a toxic absorption is present in a degree which constitutes a tax on the resistances of the afebrile patient, is one of the great desiderata in the treatment of pulmonary tuberculosis."

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