

A STUDY of the CORRELATION of the SEDIMENTATION
RATE of the ERYTHROCYTES with the LEUCOCYTE
COUNT and the CHOLESTEROL CONTENT of the
BLOOD in CERTAIN INFECTIVE DISEASES.

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A Thesis presented for the Degree of M.D.,
at the University of Glasgow,

By

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In presenting the findings the following arrangement has been adopted:

PART I. The Sedimentation Rate of the Red Blood Corpuscles.

Section 1. Introduction.

- " 2. Value of the Test.
- " 3. Explanation of the Phenomenon of Increased Sedimentation Rate.
- " 4. Technique employed and Comparison with other Methods.
- " 5. Results in Present Investigation.
- " 6. Conclusion.
- " 7. References.

PART II. Estimation of the Cholesterol Content of the Blood Plasma.

Section 1. Introduction.

- " 2. Technique.
- " 3. Results.
- " 4. Conclusion.
- " 5. References.

General Conclusions and Summary.

P A R T I.

THE SEDIMENTATION RATE OF RED BLOOD CORPUSCLES.

Section 1: Introduction

In the early days of medicine Galen demonstrated that in certain cases when blood was allowed to stand, it separated into two layers, an upper clear layer and a lower opaque red layer. This he called the "Crusta Phlogistica". John Hunter⁽¹⁴⁾ in 1791, in describing the same phenomenon, referred to it as the "buffy coat" and in the course of his investigation on the sedimentation rate recorded the fact that this rate varied in different specimens of blood. He further pointed out that the phenomenon was of general rather than of local significance, since blood from an inflamed part did not differ in this respect from blood from an unaffected part. Biermacki published excellent papers on the subject in 1894 and in his conclusion claimed that the test had clinical value.

Attention was again focussed on the subject by Fåhræus⁽¹⁰⁾ who, in his observations in 1918, found that in pregnancy the red cells sink much more rapidly than

normally, and he introduced a method of estimating this rate of fall, by measuring the distance through which erythrocytes sediment in a given time. This method has since been modified by Linzenmeier, Westergren, Zeckwer and Goodell⁽¹⁹⁾⁽³⁵⁾⁽³⁶⁾ and much important recent work has been done which, owing to the variation in technique used, we have found difficult to correlate.

Section 2: Value of the Sedimentation Test.

Most workers are agreed that the sedimentation of erythrocytes is increased in pregnancy, acute inflammatory conditions, active tuberculosis, malignancy, and in the later stages of syphilis. It is therefore obvious that the test cannot be used per se as diagnostic of any one of these conditions. We must then consider it along with clinical findings.

In cases of tuberculosis, Raykowski⁽²⁸⁾ found a satisfactory parallelism between the clinical data and this laboratory test, while Dreyfus⁽⁸⁾ affirmed that it furnished a more exact and more reliable indicator in regard to the course of the infection in a given case than observation⁽²⁷⁾ of the temperature curve. Popper and Kreindler in a

study of over 250 cases, go even further and maintain that as a general rule all progressing pulmonary affections show acceleration of sedimentation even with minimal lesions not yet discoverable on clinical and radiographic examination. Other workers who advocate the test as an aid to diagnosis and prognosis of tuberculosis include Katz, Hecht, Poindecker and Siess, Bochalli, Frosch, Morris and Rubin, and Hunt.

(7) (24) (3)
 (21) (13)
 (20)
 Löhr has found sedimentation useful in differentiating inflammatory from non-inflammatory conditions.

(31)
 In a study of malignant tumours, Rubin confirms Dreyfus' statement that the test is a better guide to the condition of the patient than the temperature chart.

(2)
 Baer and Reis in a series of gynaecological cases, found the test more useful than the temperature curve in determining the presence or absence of infection and advocate it as a further aid in determining the safe time for operation. Hildebrande, Alexander, Polak and Mazzola, Tollefson, and Elinor Jackson share this view. The latter in a series of 533 gynaecological cases showed that, in inflammatory lesions of the pelvis, of 13 patients operated on with a sedimentation rate of over 30 per cent above normal, 9 or 69.2 per cent developed

septic complications after operation, whereas in the large group of 61 cases operated on with a sedimentation rate of under 30 per cent above normal - only 4 or 6.5 per cent caused any anxiety. She also expresses the opinion that the test, though not infallible, is undoubtedly of value in the differential diagnosis between ectopic pregnancy and an inflammatory swelling. As a direct result of her investigations carried out in 1930, the test has been adopted as a routine in the gynaecological wards of the Glasgow Royal Infirmary.

In estimating the sedimentation rate in typhoid and paratyphoid conditions Sabrazès, Pauzat and Jaffry⁽³²⁾ show that the rate, which usually decreased with the onset of the convalescent stage, rises again rapidly with a relapse or at the onset of a complication, thus offering a reliable prognostic index of the course of the disease.

⁽⁵⁾
Dawson and Boots make use of the test in the differential diagnosis of rheumatoid and osteoarthritis.

⁽⁴⁾
Finally Bonet suggests sedimentation as a test for malingering.

⁽²³⁾
On the other hand, Pinner, Knowleton and Kelly, working on a series of tuberculosis cases, concluded that although a higher average rate was found in active tuber-

culosis than in normal conditions, this increase was far from constant and did not parallel the extent and progressiveness of the lesions. The prognostic value, they say, is therefore minimal, and with the exception of extremely rare instances, this test is not apt to furnish information beyond that gained by clinical and bacteriological observation.

In direct contrast to the work of Elinor Jackson, are the results of Gladys Dodds and Florence Telfer⁽⁷⁾ who found that the sedimentation rate was of no value in the differential diagnosis between pelvic abscess and ectopic pregnancy, and furthermore that it was no aid in the diagnosis of malignant conditions.

Similarly in a study of 304 cases of circulatory disturbances, Groedel and Hubert⁽¹²⁾ found the sedimentation test of no diagnostic value.

From the evidence above, it would therefore appear that many observers have found that the test has value -

- (1) as an aid to the diagnosis and prognosis of tuberculous conditions;
- (2) in differentiating inflammatory from non-inflammatory conditions;
- (3) as an indication of the condition of the patient with malignant disease;

- (4) in the differential diagnosis of gynaecological conditions and in determining the safe time for operation;
- (5) as a reliable prognostic index in the course of typhoid and paratyphoid fevers;
- (6) in differentiating rheumatoid from osteoarthritis;
- (7) and finally, it has been used as a test for malingering, but opinion is not uniform.

Section 3: Explanation of the Phenomenon of
Increased Sedimentation Rate.

The cause of this phenomenon is not yet clearly understood, but numerous theories have been put forward dealing with the alteration in the chemical and physical properties of the blood, whereby agglutination of the corpuscles takes place. These views may be summarised briefly as follows:-

(a) Tissue Destruction.

As has already been mentioned, the sedimentation rate of the erythrocytes has been found increased in acute inflammatory conditions, pregnancy, active tuberculosis and malignancy. In each of these conditions a greater or lesser degree of tissue destruction is going on. Accord-

(17) ing to Katz, Frosch and Starlinger, the sedimentation rate is determined by the fibrinogen content of the blood, the latter increasing with the number of cells undergoing disintegration. There are many supporters of this theory, including Linzenmeier, Westergren, Alexander and Newham. (22) The latter found that while a case of anaesthetic leprosy showed no signs of acceleration of the sedimentation rate, the nodular type, especially if associated with ulceration and breaking down of the nodules, showed an increased rate. This statement has recently been confirmed by Landeiro. Following up his theory, Newham estimated the fibrinogen content of the blood in 14 cases, 5 of which showed increased sedimentation rates, but found it normal in all cases.

M.E.Wylie in a recent thesis on "A Clinical and Laboratory Study of several infective Fevers with particular reference to Scarlet Fever" found that the sedimentation rate was not influenced by the age of the patient, nor by the height of the fever per se. "It is probable" she says "that the rate of sedimentation is determined by the amount of tissue destruction." (29)

In cases of Scarlatina Rodin concluded that on the whole, no definite relationship exists between the variations of the plasma protein and the sedimentation rate curve.

(23) Pinner, Knowleton and Kelly, could not establish a quantitative relationship between the fibrin content of the

blood and the sedimentation rate in clinical tuberculosis.

(b) Leucocytosis.

(29)

In the same study of Scarlatina, Rodin found that to a certain extent the leucocytosis followed the variations of the sedimentation rate curve, i.e. high sedimentation rate values were accompanied by marked leucocytosis and temporary decreases in leucocytosis occurred in connection with the "characteristic phases". Although in general agreement with this statement, Newham (22) points out that leucocytosis is not essential for rapid sedimentation, and quotes cases in his investigation of Sprue and Kala-azar where rapid sedimentation occurred with a leucopenia.

(c) Increased Cholesterol.

Kurten first suggested an increased cholesterol content in the blood as a possible cause of increased sedimentation rate.

(22)

Newham, however, in a series of 15 cases of which 13 had rapid rates and 2 were normal, found only one - a cholecystitis with gallstones - with an increased cholesterol content of the blood, the others being normal. He pointed out also that in Sprue, although the sedimentation rate is rapid, the cholesterol content is below normal.

In 59 cases of tuberculosis, Salomon, de Potter, and (33) Valtis showed that in grave tuberculosis, the amount of cholesterol in the blood is decreased, while the sedimentation is accelerated. In normal persons with a high cholesterol content, sedimentation is retarded; in pregnant women, the normal as well as the tuberculous, hypercholesterolaemia is associated with an increased speed. They therefore conclude that acceleration of sedimentation is not connected with the cholesterol content of the blood.

(d) Electric Theory.

Fahræus originally suggested that the phenomenon was due to a difference in electric charge of the various elements of the blood, but was unable to establish his theory by experimental evidence and later suggested that viscosity might be a factor.

Wells' view is that red blood corpuscles are negatively charged particles, and their mutual repulsion will be decreased by positively charged proteins in the serum, of which fibrinogen and globulin are the most important. Hence, if the proportion of fibrinogen and globulin be high as compared with albumen, the electro-positive protein in the blood is increased and sedimentation is more rapid.

In a highly technical article on "The Stability of Suspensions", published in the Proceedings of the Royal Society of Edinburgh of 1928-1929, Kermack, Gray, McKendrick and Ponder (18) studied the sedimentation rate from the electrical point of view - and conclude that it is along this line which more work may prove helpful.

A great many workers suggest that more than one factor must be taken into account, e.g. Cooper suggests that an increased fibrinogen + globulin + cholesterol cause a rapid rate. (22)

Newham provides evidence that the phenomenon is resident in the corpuscles rather than the plasma while Puxeddu affirms that it is solely located in the plasma. (22) In an investigation into the blood group Newham found that these had no bearing on the question. He also found that sedimentation was more rapid at 37°C than at 15°C., but thinks this may be due to altered viscosity of the plasma and suggests further investigation along that line.

Section 4: Technique employed in present Investigation and Comparison with other Methods.

The method employed was a combination of Westergren's modification of the Fahræus' technique and the method of

Zeckwer and Goodell. The citrated blood was procured by the former method, but the results were read according to the latter, i.e. the column of sedimenting cells was measured instead of the supernatant fluid. For this purpose a 1 cc. pipette, 30 cm. long and 7 mm. in diameter, graduated from above downwards in hundredths of a cc, was used, and the readings were recorded at room temperature at the end of 15, 30, 60, 120, 180 and 240 minutes.

Two facts, which were noted during the carrying out of the experiments, are perhaps worthy of note. Firstly, in most of the rapidly sedimenting bloods, the upper border of sedimenting cells was very indistinct and difficult to determine exactly in readings taken during the first hour. A maximum and minimum was therefore observed at each reading for the purposes of greater accuracy. According to Engel⁽⁹⁾ this phenomenon occurs in anaemic bloods with a haemoglobin content of under 40 per cent and is due to "currents and shifting of the larger agglutinates of erythrocytes - made possible by a greater dilution of the blood." Secondly, we are in agreement with Salomon⁽³⁴⁾ and Valtis that citrated blood sediments in 3 layers, from below upwards - red blood cells, white corpuscles, and citrated plasma. At the end of four hours, the three

layers were easily recognisable.

The above method was chosen in preference to that of Linzenmeier, as Newham ⁽²²⁾ affirms that small bore tubes (Linzenmeier tubes are 3-4 mm. in diameter) give inaccurate results because of capillary attraction. It has the advantage also over that of Zeckwer and Goodell, in that it requires a smaller amount of citrated blood - 2 ccs. as compared with 10 ccs. in the latter method.

Section 5: Results in the Present Investigation.

The following investigations were carried out in the City of Glasgow Fever Hospital and Tuberculosis Sanatorium, Ruchill, by kind permission of Dr. Elliott, Superintendent, and Dr. McCracken, Sanatorium Superintendent.

In all 158 sedimentation tests were performed, each with its corresponding leucocyte count in duplicate from which an average was taken and recorded.

In the first series of cases the test was made on the day of the patient's admission to Hospital and repeated again on the fourth day. Doubtful cases or cases with mixed infection were carefully excluded. The diseases studied were (1) Scarlet Fever; (2) Pneumonia;

(3) Tuberculosis (febrile and -afebrile); and (4) Enteric Fever.

The patients represented all types in the social scale, and included school children, apprentices, nurses, ward-maids, housewives and unemployed persons. The room temperature, diet and medical treatment in each group of cases were essentially the same, except for the administration of antitoxin in severe cases of scarlet fever. In the tuberculosis groups, the fresh-air, diet and amount of exercise taken were carefully regulated so that in similar groups these influences did not vary in individual cases.

(1) Among the scarlet group, the ages of the patients varied from 9 to 31 years. The commonest symptoms included headache, sore throat, sickness and vomiting. No case was selected which did not have an initial rise of temperature and pulse rate, a greater or lesser degree of faucial inflammation, a peeling tongue and a generalised erythematous rash with or without flexural staining, followed by "pin-hole" desquamation on fingers and toes. Cultures were taken from the throat swab of each patient on admission, and after an incubation of 24 hours on Loeffler's medium, these were examined microscopically to ex-

clude any atypical case of diphtheria. In severe cases, requiring scarlatinal antitoxin, the first specimen of blood was taken prior to the injection of the antitoxin.

Table I shows that rapid sedimentation does not depend solely on leucocytosis. Case No.12 with a leucocytosis of 30,400 had a slower sedimentation rate than case No.5 with a leucocytosis of less than half that figure (13,800). Cases No.6 and No.10 with the same leucocytosis, at the end of 2 hours' sedimentation showed a difference of 27 per cent and at the end of 4 hours a difference of 23 per cent in the sedimentation rate. On the other hand, case No.2 and case No.5 at the end of 4 hours had the same sedimentation rate whereas the leucocytosis of the latter was only a little over half that of the former. Cases No.1 and No.11 having an equally rapid sedimentation rate showed leucocytosis of 23,000 and 21,000 respectively.

The slowest rate of sedimentation found in case No.6 had the third lowest leucocyte count which was 6,000 below the average. The most rapid sedimentation rate occurred in cases No.1 and No.11 whose leucocytoses were both above the average for the group.

Table I.
SCARLET FEVER (1st Day)

| No. | $\frac{1}{4}$ hr | $\frac{1}{2}$ hr | 1 hr | 2 hr | 3 hr | 4 hr | Leucocytes |
|-------------|------------------|------------------|--------------|--------------|--------------|--------------|------------|
| 1 | 1 0.97 | 0.90 0.86 | 0.67 0.67 | 0.56 0.56 | 0.40 0.40 | 0.35 0.35 | 23,000 |
| 2 | 1 0.98 | 0.98 0.93 | 0.83 0.79 | 0.66 0.66 | 0.60 0.60 | 0.59 0.59 | 26,600 |
| 3 | 1 0.99 | 0.97 0.96 | 0.90 0.88 | 0.75 0.73 | 0.60 0.57 | 0.51 0.49 | 24,600 |
| 4 | 1 0.99 | 0.99 0.98 | 0.91 0.90 | 0.75 0.74 | 0.60 0.60 | 0.50 0.50 | 14,200 |
| 5 | 1 0.98 | 0.95 0.95 | 0.86 0.84 | 0.69 0.69 | 0.63 0.63 | 0.59 0.59 | 13,800 |
| 6 | 1 0.99 | 1 0.98 | 0.96 0.95 | 0.87 0.87 | 0.80 0.80 | 0.75 0.74 | 14,800 |
| 7 | 1 0.97 | 0.94 0.93 | 0.85 0.83 | 0.69 0.67 | 0.60 0.60 | 0.57 0.57 | 25,800 |
| 8 | 1 1 | 0.99 0.98 | 0.95 0.94 | 0.85 0.83 | 0.77 0.75 | 0.69 0.68 | 23,000 |
| 9 | 0.99 0.97 | 0.93 0.91 | 0.84 0.82 | 0.69 0.68 | 0.64 0.62 | 0.59 0.57 | 19,200 |
| 10 | 0.99 0.97 | 0.93 0.90 | 0.80 0.78 | 0.60 0.60 | 0.55 0.55 | 0.53 0.51 | 14,800 |
| 11 | 0.96 0.94 | 0.80 0.78 | 0.63 0.61 | 0.40 0.40 | 0.36 0.36 | 0.35 0.35 | 21,400 |
| 12 | 1 0.99 | 0.97 0.97 | 0.91 0.90 | 0.75 0.75 | 0.66 0.66 | 0.62 0.61 | 30,400 |
| Maximum | 0.995 | 0.95 | 0.84 | 0.69 | 0.60 | 0.55 | 20,965 |
| Mean | 0.99 | 0.94 | 0.83 | 0.685 | 0.595 | 0.545 | |
| Minimum | 0.98 | 0.93 | 0.82 | 0.68 | 0.595 | 0.545 | |
| 0.75 & over | 12 | 12 | 10 | 3 | 2 | 0 | |
| 0.5 to 0.75 | | | 2 | 8 | 8 | 9 | |
| 0.5 & under | | | | 1 | 2 | 3 | |

Table II shows the results of similar tests on the same group of patients 3 days later.

The highest leucocytosis occurred in case No.11 which gave the most rapid sedimentation rate. Case No.9 with the lowest leucocyte count showed an average rate of sedimentation. Comparing cases with the same leucocytosis: cases No.6 and No.8 have comparable sedimentation rates: cases No.7 and No.10 show a difference of 6 per cent in the sedimentation rates: cases No.1 and No.12 have a difference of 32 per cent, i.e. the former sediments twice as quickly as the latter.

Of the cases with a similar rate of sedimentation rate after 4 hours: cases No.3 and No.4 have similar leucocytoses (1,000 of difference): cases No.6 and No.12 have also comparable counts (difference of 1,200). Of the whole group the blood showing the most rapid sedimentation had also the greatest leucocytosis.

The slowest sedimentation rate occurred in case No.8 which had a leucocytosis below the average for the group:

Comparing Tables I and II, it will be seen that the average number of leucocytes was almost 5,000 less on the 4th day than on the first estimation, but that the sedi-

Table II.SCARLET FEVER (4th Day)

| No. | $\frac{1}{4}$ hr | $\frac{1}{2}$ hr | 1 hr | 2 hr | 3 hr | 4 hr | Leucocytes |
|----------------|------------------|------------------|--------------|--------------|--------------|--------------|------------|
| 1 | 0.96 0.92 | 0.82 0.77 | 0.56 0.56 | 0.40 0.40 | 0.37 0.37 | 0.35 0.35 | 16,000 |
| 2 | 1 0.97 | 0.95 0.92 | 0.80 0.74 | 0.61 0.61 | 0.55 0.55 | 0.50 0.50 | 16,400 |
| 3 | 1 0.99 | 1 0.96 | 0.86 0.86 | 0.70 0.70 | 0.65 0.65 | 0.64 0.62 | 11,800 |
| 4 | 1 0.99 | 0.98 0.95 | 0.88 0.86 | 0.71 0.71 | 0.67 0.66 | 0.63 0.63 | 12,800 |
| 5 | 0.97 0.94 | 0.88 0.86 | 0.68 0.68 | 0.53 0.53 | 0.48 0.48 | 0.46 0.46 | 22,600 |
| 6 | 1 1 | 0.97 0.97 | 0.93 0.93 | 0.81 0.80 | 0.74 0.72 | 0.67 0.66 | 14,800 |
| 7 | 0.98 0.98 | 0.95 0.93 | 0.85 0.80 | 0.60 0.60 | 0.56 0.55 | 0.53 0.52 | 15,800 |
| 8 | 1 0.99 | 0.98 0.98 | 0.95 0.95 | 0.86 0.84 | 0.77 0.75 | 0.71 0.69 | 14,800 |
| 9 | 1 1 | 0.94 0.92 | 0.83 0.80 | 0.68 0.68 | 0.62 0.61 | 0.55 0.55 | 9,600 |
| 10 | 1 0.98 | 0.97 0.96 | 0.90 0.87 | 0.75 0.72 | 0.64 0.64 | 0.59 0.58 | 15,800 |
| 11 | 0.85 0.80 | 0.60 0.48 | 0.36 0.36 | 0.32 0.32 | 0.31 0.31 | 0.31 0.31 | 27,800 |
| 12 | 1 0.99 | 0.99 0.98 | 0.93 0.90 | 0.80 0.77 | 0.70 0.70 | 0.68 0.66 | 16,000 |
| Maximum | 0.98 | 0.92 | 0.79 | 0.65 | 0.58 | 0.55 | 16,183 |
| Mean | 0.97 | 0.90 | 0.785 | 0.645 | 0.58 | 0.545 | |
| Minimum | 0.96 | 0.89 | 0.78 | 0.64 | 0.58 | 0.54 | |
| 0.75 & over | | | 8 | 3 | 1 | | |
| 0.5 to 0.75 | | | 3 | 7 | 8 | 9 | |
| 0.5 & under | | | 1 | 2 | 3 | 3 | |

mentation rate at the end of 4 hours was practically identical in each group, i.e. the leucocyte count agrees more closely with the clinical course of the disease. This parallel is true not only of the group as a whole, but also in cases developing complications as illustrated in the following cases:-

Eight cases out of the twelve showed a decrease in the leucocytosis on the 4th day: four did not. Of these, one, (case No.6) was stationary. This girl complained of transient pains in shoulders and arms on the 3rd day. Case No.10 showed a slight increase. The temperature in this case had not completely settled and was still 99^oF. on the 5th day. Apart from a transitory albuminuria, no further complications ensued. Cases No.5 and No.11 had definite increases in leucocytosis on the 4th day. The former had still a temperature of 100^oF. which did not finally become normal until 2 days later and the latter developed Scarlatinal Rheumatism on the 3rd day after admission, her temperature rising to 102^o by the 4th day. This was followed later by a transient albuminuria.

Of these 4 abnormal cases, case No.6 had the lowest leucocyte count and showed the slowest sedimentation rate. Case No.11 which had the greatest leucocytosis sedimented

much more quickly than any of the others. Therefore, in these complicated cases of scarlet fever a high leucocyte count was associated with a rapid sedimentation rate.

Comparing the relationship of clinical course in the abnormal cases with the leucocytosis and sedimentation rate: case No.11, which was the most severe clinically, showed the highest leucocyte count and also the most rapid sedimentation rate. Case No.5 - clinically the second in severity - had the second highest leucocytosis and the second highest sedimentation rate. Cases No.10 and No.6 - both less severe - had respectively the third and lowest leucocyte counts and also the third and slowest sedimentation rates.

It would appear, therefore, that in complicated cases of scarlet fever, there is a close relationship between the clinical course, the leucocytosis and the sedimentation rate. The more severe the clinical symptoms, the greater the leucocytosis and the faster is the sedimentation rate.

Comparing the sedimentation rates of Tables I and II:- of the uncomplicated cases i.e. these where there was a definite decrease in the leucocytosis of the 4th day - only 4 or 50 per cent had a slower sedimentation rate than normal. One (case No.1) remained stationary

although the leucocytes had fallen by 7,000. The remaining three cases (Nos.2, 7 and 9) had faster sedimentation rates with a decrease in leucocytosis.

It is rather noteworthy that of these 4 exceptional cases, two (cases No.1 and No.9) were of severe type and had been given 10 cc. of antitoxin intramuscularly before the 4th day tests were applied.

(2) The majority of the cases in the pneumonia group were admitted during the influenza epidemic of 1929. Some had been on the waiting-list for admission to hospital for several days, so that the lung condition was well established before those cases were seen - some being admitted on 4th, 5th, 7th and 8th day of illness. The age groups varied from 10 to 53 years, the majority occurring between 20 and 30 years of age.

The commonest symptoms in the order of their greatest frequency were: pain in the chest or back, cough, fever, headache, shivering, sickness and vomiting, and one case (No.6) was delirious. The temperatures on admission were all over 101° with one exception (case No.4); the respirations were rapid, laboured and superficial, the colour in some cases being quite cyanosed. Their tongues were furred and in all cases there was a definite involvement

of one or more lobes as evidenced by impaired percussion note, tubular breathing and fine crepitations.

One case (No.2) had a second degree burn over the right base posteriorly where a poultice had been applied and case No.5 was complicated by pregnancy, terminating in a $2\frac{1}{2}$ -3 months' abortion 8 days after admission. Case No.6, who was delirious on admission, died on the 16th day, 8 days after admission, with no remission of temperature.

A glance at Tables III and IV will show that the sedimentation rates in Pneumonia were distinctly more rapid, the average leucocytoses being also greater than in the Scarlet Fever group. By the 4th day the average leucocyte count in Pneumonia had fallen by over 7000 and this was accompanied by a slowing of the sedimentation rate although not to the same degree. The average sedimentation rates in all the Pneumonia groups were greater than in Scarlet Fever. This seems contrary to the findings of Roger and Binet. (30) They found that oxygenation accelerates sedimentation and makes it more complete. Variations in the sedimentation rate, they say, do not depend on direct interference with the lung; they vary with changes in size of the corpuscles dependent itself

Table III.
PNEUMONIA (1st Day)

| No. | $\frac{1}{4}$ hr | $\frac{1}{2}$ hr | 1 hr | 2 hr | 3 hr | 4 hr | Leucocytes |
|-------------|------------------|------------------|--------------|--------------|--------------|--------------|-------------------------------|
| 1. | 0.85 0.78 | 0.61 0.57 | 0.51 0.46 | 0.40 0.40 | 0.39 0.39 | 0.38 0.38 | 20,000 |
| 2 | 1 0.94 | 0.78 0.70 | 0.51 0.51 | 0.44 0.44 | 0.42 0.41 | 0.42 0.40 | 31,400 |
| 3 | 1 1 | 1 0.97 | 0.86 0.80 | 0.65 0.65 | 0.59 0.59 | 0.55 0.54 | 49,600 |
| 4 | 0.98 0.92 | 0.75 0.65 | 0.51 0.51 | 0.41 0.41 | 0.36 0.36 | 0.32 0.32 | 25,400 |
| 5* | 1 0.96 | 0.90 0.82 | 0.52 0.52 | 0.44 0.44 | 0.42 0.42 | 0.40 0.40 | 31,400 |
| 6 | 0.85 0.75 | 0.55 0.47 | 0.35 0.35 | 0.32 0.31 | 0.31 0.30 | 0.30 0.29 | 28,600 (died 8 days later) |
| 7 | 0.90 0.86 | 0.70 0.65 | 0.46 0.46 | 0.40 0.40 | 0.35 0.35 | 0.30 0.30 | 17,400 |
| 8 | 0.98 0.95 | 0.90 0.86 | 0.68 0.66 | 0.50 0.50 | 0.45 0.44 | 0.43 0.41 | 24,400 |
| 9 | 0.95 0.95 | 0.90 0.86 | 0.65 0.65 | 0.49 0.49 | 0.43 0.43 | 0.42 0.42 | 15,200 |
| 10 | 0.91 0.90 | 0.85 0.80 | 0.56 0.56 | 0.42 0.42 | 0.37 0.37 | 0.36 0.35 | 12,000 |
| 11 | 1 0.98 | 0.96 0.96 | 0.87 0.87 | 0.72 0.72 | 0.65 0.64 | 0.60 0.59 | 12,200 |
| 12 | 0.90 0.87 | 0.80 0.73 | 0.50 0.50 | 0.38 0.38 | 0.36 0.36 | 0.36 0.35 | 28,800 |
| Maximum | 0.94 | 0.81 | 0.58 | 0.46 | 0.42 | 0.40 | 24,700 |
| Mean | 0.92 | 0.78 | 0.575 | 0.46 | 0.42 | 0.395 | |
| Minimum | 0.90 | 0.75 | 0.57 | 0.46 | 0.42 | 0.39 | |
| 0.75 & over | 12 | 7 | 2 | 0 | 0 | 0 | |
| 0.5 to 0.75 | - | 5 | 8 | 3 | 2 | 2 | |
| 0.5 & under | - | - | 2 | 9 | 10 | 10 | |

* Pregnant aborted eight days later.

Table IV.PNEUMONIA (4th Day)

| No. | $\frac{1}{4}$ hr | $\frac{1}{2}$ hr | 1hr | 2hr | 3hr | 4hr | Leucocytes |
|-------------|------------------|------------------|------|-------|-------|-------|------------|
| 1 | 0.98 | 0.85 | 0.50 | 0.41 | 0.38 | 0.35 | 25,500 |
| | 0.94 | 0.66 | 0.46 | 0.39 | 0.36 | 0.34 | |
| 2 | 1 | 0.98 | 0.80 | 0.63 | 0.58 | 0.53 | 22,800 |
| | 1 | 0.93 | 0.73 | 0.63 | 0.58 | 0.53 | |
| 3 | 1 | 0.98 | 0.90 | 0.72 | 0.59 | 0.53 | 11,800 |
| | 1 | 0.97 | 0.87 | 0.68 | 0.58 | 0.52 | |
| 4 | 1 | 0.98 | 0.86 | 0.66 | 0.63 | 0.61 | 21,200 |
| | 0.98 | 0.96 | 0.71 | 0.64 | 0.62 | 0.60 | |
| 5 | 1 | 0.98 | 0.78 | 0.59 | 0.52 | 0.45 | 10,400 |
| | 1 | 0.91 | 0.75 | 0.59 | 0.52 | 0.45 | |
| 6 | 0.85 | 0.57 | 0.39 | 0.34 | 0.32 | 0.31 | 14,400 |
| | 0.80 | 0.52 | 0.39 | 0.33 | 0.31 | 0.30 | |
| 7 | 0.92 | 0.80 | 0.51 | 0.39 | 0.36 | 0.35 | 22,800 |
| | 0.87 | 0.70 | 0.51 | 0.39 | 0.36 | 0.35 | |
| 8 | 1 | 0.92 | 0.79 | 0.63 | 0.55 | 0.50 | 18,800 |
| | 0.98 | 0.91 | 0.79 | 0.63 | 0.55 | 0.50 | |
| 9 | 0.98 | 0.87 | 0.60 | 0.44 | 0.40 | 0.38 | 7,000 |
| | 0.94 | 0.80 | 0.58 | 0.44 | 0.40 | 0.38 | |
| 10 | 0.97 | 0.92 | 0.73 | 0.53 | 0.49 | 0.49 | 18,400 |
| | 0.96 | 0.88 | 0.70 | 0.52 | 0.48 | 0.47 | |
| 11 | 0.98 | 0.96 | 0.87 | 0.74 | 0.65 | 0.62 | 15,400 |
| | 0.98 | 0.95 | 0.87 | 0.74 | 0.65 | 0.60 | |
| 12 | 0.93 | 0.80 | 0.52 | 0.41 | 0.38 | 0.37 | 21,200 |
| | 0.88 | 0.75 | 0.52 | 0.41 | 0.38 | 0.36 | |
| Maximum | 0.97 | 0.88 | 0.69 | 0.54 | 0.49 | 0.46 | 17,475 |
| Mean | 0.955 | 0.855 | 0.67 | 0.535 | 0.485 | 0.455 | |
| Minimum | 0.94 | 0.83 | 0.65 | 0.53 | 0.48 | 0.45 | |
| 0.75 & over | | | 6 | 0 | 0 | 0 | |
| 0.5 to 0.75 | | | 5 | 7 | 6 | 5 | |
| 0.5 & under | | | 1 | 5 | 6 | 7 | |

on the CO₂ content of the blood - the corpuscles becoming greater in diameter, the richer the CO₂ content of the blood. Dochez ⁽⁶⁾ points out that the coagulation time of the blood is generally prolonged during the acute stage of lobar pneumonia and that this is probably due to an increase in the circulating fibrinogen. This being so, it would appear that an increase in the fibrinogen content of the blood is associated with an increased sedimentation rate.

The majority of bloods in Table III had sedimented to half their volume in 2 hours' time and to over a third of their volume in 4 hours. By the 4th day, although the leucocytes had fallen by 7,000 or almost 30 per cent, the sedimentation rate was not retarded to any great degree, the difference being only 6 per cent.

A more detailed scrutiny of Table III shows that the lowest leucocyte count occurred in case No.10 which had the fourth quickest sedimentation rate. The highest leucocyte count occurred in case No.3 which was the second slowest to sediment. Equal leucocytosis in cases No.2 and No.5 showed similar sedimentation rates. On the other hand, cases No.10 and No.12 with the same sedimentation rates had very different leucocyte counts,

the former being less than half the latter. The slowest sedimentation rate was found in case No.11. This patient had the second lowest leucocyte count. The quickest sedimentation rate occurred in case No.6 and had the fifth highest leucocyte count which was 4,000 above the average for the group. This was the most severe case clinically. Four days later, although her leucocyte count had fallen to almost half its previous figure, the sedimentation rate was practically stationary. It would seem that this falling count was due to a falling in the resistance of the patient and that here the sedimentation rate was a better indication of the course of the disease, as the patient died on her 8th day after admission.

The lowest leucocyte count of Table IV occurred in case No.9 which had the fourth quickest sedimentation rate. The highest leucocyte count (case No.1) showed the second quickest sedimentation rate. Of the cases with equal leucocytosis: cases No.8 and No.10 had similar sedimentation rates: cases No.2 and No.7 showed a difference of 17 per cent: and cases No.4 and No.12 a difference of 22 per cent. The slowest sedimentation rate occurred in case No.4 which had the fourth highest

leucocyte count and the quickest sedimentation rate occurred in case No.6 which was the worst clinically and had a comparatively low count probably due to diminishing resistance on the part of the patient.

In eight cases out of twelve, there was a decrease in leucocytosis on the 4th day after admission. Of these eight cases two, No.3 and No.9, had more rapid sedimentation rates with diminishing leucocytoses. The former had a pseudo-crisis on the fourth day after admission, the temperature becoming finally settled on the following day. Of the 4 cases with greater leucocyte counts on the fourth day, only one (case No.1), who was at the crisis, had a more rapid sedimentation rate.

Conclusions.

In acute lobar pneumonia 8 out of 12 cases had a leucocytosis of 20,000 and over. Of these, 7 had very rapid sedimentation rates, the red cells sedimenting in four hours to less than 50 per cent of their original volume. One, case No.3, sedimented to 55 per cent. In acute lobar pneumonia, therefore, where there is a marked leucocytosis, there is a rapid sedimentation rate.

Eight cases out of twelve showed a fall in leuco-

cytosis between the 1st and 4th day of 4,000 per cc. or more. Of these, six cases showed a slower sedimentation rate, the fall ranging from 1 per cent to 28 per cent less than at the original test. Two cases, No.3 and No.9, showed increased sedimentation rates with a falling leucocytosis, in the former case an increase of 2 per cent and in the latter of 4 per cent. On the whole therefore in acute lobar pneumonia, where there is a rapid fall in the leucocyte count, there is a fall in the sedimentation rate.

The clinical symptoms agree with the leucocyte count and the sedimentation rate, i.e. the leucocyte count and the sedimentation rate are more closely related in pneumonia than in scarlet fever.

(3) I am indebted to Dr. McCracken for the classification in the Tuberculosis cases. Unfortunately, no further details of their clinical condition are available.

A study of the results in Tables V and VI shows (a) that the sedimentation rate is greater in acute tuberculosis than in the acute stages of either lobar pneumonia or scarlet fever, and (b) a striking fact that although the average sedimentation rate is more rapid in acute than

Table V.TUBERCULOSIS (Acute) Febrile

| No. | $\frac{1}{4}$ hr | $\frac{1}{2}$ hr | 1 hr | 2 hr | 3 hr | 4 hr | Leucocytes |
|-------------|------------------|------------------|--------------|--------------|--------------|--------------|------------|
| 1 | 0.98 0.96 | 0.90 0.88 | 0.66 0.66 | 0.54 0.54 | 0.47 0.47 | 0.44 0.44 | 35,000 |
| 2 | 1 0.97 | 0.95 0.93 | 0.77 0.76 | 0.63 0.63 | 0.55 0.54 | 0.49 0.49 | 22,200 |
| 3 | 0.97 0.95 | 0.90 0.87 | 0.66 0.64 | 0.44 0.44 | 0.38 0.37 | 0.36 0.34 | 18,800 |
| 4 | 0.70 0.68 | 0.53 0.53 | 0.40 0.40 | 0.33 0.33 | 0.29 0.29 | 0.26 0.25 | 25,400 |
| 5 | 0.90 0.83 | 0.75 0.65 | 0.51 0.50 | 0.38 0.38 | 0.35 0.34 | 0.33 0.33 | 17,000 |
| 6 | 0.98 0.97 | 0.85 0.77 | 0.57 0.55 | 0.43 0.43 | 0.40 0.40 | 0.38 0.38 | 26,400 |
| 7 | 0.92 0.90 | 0.80 0.75 | 0.55 0.55 | 0.38 0.38 | 0.35 0.34 | 0.32 0.31 | 18,000 |
| 8 | 0.75 0.66 | 0.65 0.52 | 0.38 0.38 | 0.25 0.25 | 0.20 0.20 | 0.15 0.15 | 17,800 |
| 9 | 0.93 0.93 | 0.85 0.83 | 0.61 0.61 | 0.46 0.46 | 0.39 0.39 | 0.36 0.36 | 11,600 |
| 10 | 0.95 0.93 | 0.78 0.73 | 0.49 0.49 | 0.38 0.38 | 0.37 0.37 | 0.35 0.35 | 12,800 |
| 11 | 0.97 0.97 | 0.90 0.87 | 0.67 0.66 | 0.48 0.48 | 0.43 0.42 | 0.37 0.36 | 11,400 |
| 12 | 0.98 0.97 | 0.90 0.88 | 0.63 0.62 | 0.49 0.49 | 0.39 0.39 | 0.35 0.35 | 13,200 |
| Maximum | 0.92 | 0.81 | 0.58 | 0.43 | 0.38 | 0.35 | 19,133 |
| Mean | 0.905 | 0.79 | 0.57 | 0.43 | 0.38 | 0.345 | |
| Minimum | 0.89 | 0.77 | 0.56 | 0.43 | 0.38 | 0.34 | |
| 0.75 & over | 12 | 12 | 1 | 0 | 0 | 0 | |
| 0.5 to 0.75 | - | - | 8 | 2 | 1 | 0 | |
| 0.5 & under | - | - | 3 | 10 | 11 | 12 | |

in chronic tuberculosis - the average leucocyte count is greater in the latter than in the former. This seems to point again to the fact that a rapid sedimentation rate is not dependent solely on leucocytosis.

Looking at the individual cases in Table V one is impressed with their uniformly rapid sedimentation rates. At the end of 2 hours, ten cases out of the twelve have sedimented to half their original volume, and at the end of 4 hours, all have sedimented to less than half — some to a third or even less of their original volume. There is the same irregularity in the comparisons between similar final sedimentation points and the corresponding leucocytosis. Cases No.10 and No.12 with the same sedimentation rates, have comparable leucocyte counts (12,800 and 13,200); similarly with cases No.9 and No.11. On the other hand case No.8, with the most rapid sedimentation rate, has a leucocytosis which is less than that of case No.2 with the slowest sedimentation rate and equal to less than half that of case No.1, whose sedimentation rate is slowest but one (case No.2) of the whole series.

It would seem, therefore, that there is very little correlation between the leucocyte count and the sedimentation rate in acute tuberculosis.

Table VI.

TUBERCULOSIS (Chronic) Afebrile

| No. | $\frac{1}{4}$ hr | $\frac{1}{2}$ hr | 1 hr | 2 hr | 3 hr | 4 hr | Leucocytes |
|-------------|------------------|------------------|--------------|--------------|--------------|--------------|------------|
| 1 | 0.85 0.78 | 0.70 0.67 | 0.51 0.51 | 0.44 0.43 | 0.40 0.40 | 0.39 0.39 | 24,600 |
| 2 | 0.92 0.89 | 0.80 0.78 | 0.58 0.58 | 0.45 0.45 | 0.38 0.38 | 0.34 0.34 | 20,000 |
| 3 | 0.97 0.93 | 0.90 0.80 | 0.59 0.58 | 0.45 0.45 | 0.40 0.40 | 0.39 0.39 | 25,200 |
| 4 | 1 0.98 | 0.97 0.95 | 0.85 0.81 | 0.65 0.65 | 0.61 0.61 | 0.57 0.57 | 32,200 |
| 5 | 1 1 | 0.97 0.96 | 0.90 0.86 | 0.68 0.68 | 0.64 0.64 | 0.61 0.61 | 16,200 |
| 6 | 0.93 0.88 | 0.75 0.61 | 0.49 0.48 | 0.37 0.37 | 0.35 0.34 | 0.33 0.33 | 26,400 |
| 7 | 0.90 0.83 | 0.65 0.58 | 0.43 0.43 | 0.28 0.28 | 0.25 0.25 | 0.23 0.22 | 14,200 |
| 8 | 1 0.99 | 0.97 0.97 | 0.94 0.93 | 0.82 0.80 | 0.77 0.75 | 0.71 0.70 | 15,800 |
| 9 | 1 0.98 | 0.95 0.87 | 0.69 0.69 | 0.54 0.54 | 0.51 0.51 | 0.49 0.49 | 12,600 |
| 10 | 0.95 0.92 | 0.72 0.69 | 0.54 0.54 | 0.41 0.41 | 0.38 0.38 | 0.38 0.37 | 22,000 |
| 11 | 0.96 0.96 | 0.86 0.84 | 0.59 0.59 | 0.43 0.43 | 0.39 0.39 | 0.38 0.37 | 22,400 |
| 12 | 0.88 0.85 | 0.67 0.67 | 0.43 0.43 | 0.39 0.39 | 0.37 0.37 | 0.37 0.36 | 16,600 |
| Maximum | 0.95 | 0.83 | 0.63 | 0.49 | 0.454 | 0.432 | |
| Mean | 0.93 | 0.80 | 0.625 | 0.49 | 0.453 | 0.43 | 20,683 |
| Minimum | 0.92 | 0.78 | 0.62 | 0.49 | 0.452 | 0.43 | |
| 0.75 & over | 12 | 12 | 3 | 1 | 1 | 0 | |
| 0.5 to 0.75 | - | - | 6 | 3 | 3 | 3 | |
| 0.5 & under | - | - | 3 | 8 | 8 | 9 | |

Of the chronic cases (Table VI) the lowest leucocyte count (case No.9) had a more rapid sedimentation rate than that with the greatest leucocytosis (case No.4). Of these cases with similar leucocyte counts: cases No. 10 and No.11 had equal sedimentation rates: cases No.5 and No.12 showed a difference of 25 per cent. Of the cases with equal sedimentation rates: cases No.1 and No.3 had similar leucocyte counts: case No.7, which sedimented most quickly of the group, had a lower leucocyte count than case No.8, whose sedimentation rate was the slowest.

In acute and chronic tuberculosis, therefore, a high leucocytosis is not associated with a rapid sedimentation, nor is a low count associated with a slow sedimentation.

(4) At the time of this investigation, only a few cases of Enteric Fever were available. The main clinical features were as follows:-

Case No.1 was a man of 20 years, suffering from a B. Typhosus infection. He had been ill for two to three weeks prior to admission to hospital, with diarrhoea, loss of appetite, slight cough, pain in the back and general weakness. On examination he appeared acutely

ill; his skin was hot and clammy but showed no rose spots; his tongue was dry and furred and his temperature was 102°F., although his pulse and respiration were normal, (P.90 : R.26). The heart sounds, although regular, were of poor quality. The spleen was not palpably enlarged. He was mentally confused. The pupils were normal in size and reacted to light and accommodation. The knee-jerks were absent, the other reflexes being normal. There was a trace of albumen in the urine and the motions were loose. A specimen of blood was taken for a Widal reaction. The result was positive for B. Typhosus in every dilution (1 in 250). Towards the end of his fourth week of illness, his temperature began to settle and the mental symptoms cleared. At the beginning of the sixth week he had marked bradycardia and some coarse moist râle was found at the bases of the lungs. His condition improved in the seventh week, his pulse becoming stronger and more rapid and the chest clearing. He was put on light diet. At the beginning of his eighth week he took a relapse which lasted fourteen days. Thereafter his convalescence was uneventful except for a slight thrombosis in his left leg in the tenth week.

The sedimentation readings were taken during the acute

stage of his disease and show on both occasions a comparatively rapid sedimentation rate considering the leucopenia present. The greater the leucopenia became, however, the slower was the sedimentation rate.

Cases No.2 and No.3 were Paratyphoid B. infections occurring in adolescents. Case No.2 was an optician's assistant of 15 years, who had been ill for two weeks before admission to hospital, and had suffered from shivering, headache, abdominal pains and general weakness, with vomiting on the first day. There was a short attack of epistaxis on his sixth day of illness. His bowels were rather constipated. He appeared, on examination, only moderately ill, his temperature being only 99°F. and the pulse and respirations normal. Numerous rose spots (50 to 60) were present on the chest and abdomen. His tongue was practically clean though dry. There was slight tenderness over the splenic area although there was no palpable enlargement of that organ. The blood was positive for B. Paratyphosus B. (1 in 250) and the faeces showed the presence of the same organism, although the urine was negative.

Apart from transient pains in the head and neck and slight earache, his convalescence was uneventful.

The sedimentation curve here again is comparatively rapid for such a low leucocyte count, and compares with the results of case No.1 in that a greater number of leucocytes is associated with increased sedimentation speed. Case No.3 which showed a moderate leucocytosis in contrast to the leucopenias, had the most rapid sedimentation rate.

(22)

It has been suggested by Newham that the increased sedimentation in these cases where there is some derangement of the liver might be due to some disturbance in the metabolic substance normally present in the plasma. To this end urea estimations were carried out in three of the most rapidly sedimenting bloods, but no abnormal proportions were found.

Unfortunately the numbers are too few to allow of any general conclusions, - but at least they consistently show that in Enteric Fever an increasing leucopenia is associated with a slower sedimentation rate.

Section 6: Conclusions.

(1) The sedimentation rate of the erythrocytes is increased in active tuberculosis, lobar pneumonia, chronic tuberculosis, scarlet fever, and enteric fever.

Table VII
ENTERIC FEVER
 (1st Day of Investigation.)

| | $\frac{1}{4}$ hr | $\frac{1}{2}$ hr | 1hr | 2hr | 3hr | 4hr | Leucocytes |
|----|------------------|------------------|------|------|------|------|------------|
| 1. | 1 | 0.98 | 0.9 | 0.81 | 0.68 | 0.64 | 6,900 |
| | 0.98 | 0.94 | 0.86 | 0.75 | 0.68 | 0.64 | |
| 2. | 0.98 | 0.93 | 0.82 | 0.68 | 0.61 | 0.57 | 7,600 |
| | 0.98 | 0.93 | 0.82 | 0.68 | 0.61 | 0.57 | |

Table VIII
ENTERIC FEVER
 (4th Day of Investigation)

| | $\frac{1}{4}$ hr | $\frac{1}{2}$ hr | 1hr | 2hr | 3hr | 4hr | Leucocytes |
|----|------------------|------------------|------|------|------|------|------------|
| 1. | 1 | 0.99 | 0.96 | 0.88 | 0.80 | 0.74 | 6,200 |
| | 0.99 | 0.98 | 0.96 | 0.88 | 0.80 | 0.74 | |
| 3. | 1 | 1 | 0.90 | 0.75 | 0.68 | 0.56 | 13,600 |
| | 1 | 0.97 | 0.82 | 0.67 | 0.59 | 0.56 | |

(2) With the convalescent stage the rate is considerably retarded again as was seen in lobar pneumonia and enteric fever , after an interval of 4 days.

(3) In all these acute fevers, with the exception of enteric, the increased sedimentation rate is accompanied generally by a considerable increase in leucocytosis.

(4) The sedimentation rate, however, is not dependent solely on leucocytosis.

(5) In uncomplicated cases of scarlet fever, the leucocyte count agrees more closely with the clinical condition of the patient than does the sedimentation rate.

(6) There is a closer relationship between the leucocytosis, sedimentation rate and clinical symptoms in pneumonia and complicated cases of scarlet fever than in the acute stages of simple scarlatina. The more severe the condition clinically, the more rapid the sedimentation rate and the greater the leucocytosis.

(7) In acute and chronic tuberculosis, there is very little correlation between the sedimentation rate and the leucocytosis.

(8) In enteric fever an increasing leucopenia is associated with a decreasing sedimentation rate.

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P A R T II.ESTIMATION OF THE CHOLESTEROL CONTENT OF THE BLOOD PLASMA.Section 1: Introduction.

Cholesterol was first isolated from the blood in 1775. The total cholesterol is made up of free cholesterol and cholesterol combined with fatty acids to form cholesterol esters. According to Richter-Quittner⁽¹⁰⁾ in normal conditions the total cholesterol is divided about equally between the blood corpuscles and the plasma. In pathological conditions it is found in abundance in the plasma. For this reason the plasma was always utilised in these investigations. Strathmann-Herweg⁽¹⁴⁾ says that, if they are thriving, both breast-fed and artificially fed infants present normal cholesterin values in the blood serum, irrespective of whether their diet is rich or poor in fats. According to Shope⁽¹²⁾ there is a marked and rather rapid increase in the serum cholesterol from birth for a relatively short period of time during the early life of the animal and there is a less marked and more gradual decline with advancing age.

The normal cholesterol content of the blood is generally accepted as between 150 - 180 mgm. per 100 c.c.

in healthy subjects. This amount is increased in pregnancy, the early stages of malignant disease, arteriosclerosis, nephritis, nephrosis, obstructive jaundice, and certain skin conditions. It is reduced in anaemias, acute infective fevers, febrile tuberculosis, and, according to Cornell,⁽³⁾ in the blood of dogs there is an immediate fall from 10 - 30 per cent within 10 - 30 minutes after eating.

Section 2: Technique Employed.

The method used was that of Myers and Wardell. 1 cc. of the blood plasma was allowed to drop on to about 5 gms. of plaster of Paris in a crucible and allowed to dry in a hot air oven at 100°C. for two hours. It was found that certain grades of plaster of Paris were more suitable than others, and that used was the clover-leaf plaster. When dry, the mixture was finely powdered in this dish by a pestle and transferred into an extraction thimble. A Soxhlet extraction apparatus was used with chloroform as solvent, and extraction was allowed to proceed four times over the blood plaster mixture. A standard solution of cholesterol in chloroform was used for comparison in the colorimeter. To avoid any moisture getting into

the mixture, the glass parts of the apparatus were cleaned with chloroform and kept in a hot air oven when not in use. The stoppers used were of cork.

Simplified methods have been described by Leiboff⁽⁷⁾ and Ling⁽⁸⁾ but according to Brunton⁽¹⁾ the former method is liable to leave traces of water in the final chloroform extract which prevents development of the colour with acetic anhydride and sulphuric acid, thus giving lower results than with the method of Myers and Wardell.

Section 3: Results in the Present Investigation.

In all, 84 cholesterol estimations were performed. The conditions studied were as follows:- (1) Scarlet Fever, 21 cases; (2) Pneumonia, 13; (3) Acute Phthisis, 6; Chronic Tuberculosis, 12; (4) Enteric Fever, 9; (5) Erysipelas, 16; and Facial Erysipelas, 7. In the majority of cases the corresponding leucocyte count and sedimentation rate are recorded for comparison with the cholesterol content.

The clinical features of the Scarlet Fever, Pneumonia, and Enteric groups have already been described in Part I.

(1) In the Scarlet Fever group the readings were taken in the acute stage, while the rash was still present. It

Table IX.SCARLET FEVER (Acute)

| No. | $\frac{1}{4}$ hr | $\frac{1}{2}$ hr | 1 hr | 2 hr | 3 hr | 4 hr | Leucocytes | Cholesterol of Blood. mgm/100 ccs. |
|-----|------------------|------------------|--------------|--------------|--------------|--------------|------------|--|
| 1 | 0.99 0.99 | 0.98 0.98 | 0.94 0.94 | 0.86 0.86 | 0.79 0.79 | 0.74 0.74 | 27,200 | 141.5 |
| 2 | 0.99 0.99 | 0.85 0.85 | 0.77 0.77 | 0.70 0.70 | 0.64 0.64 | 0.61 0.60 | 22,000 | 140.35 |
| 3 | 0.99 0.99 | 0.98 0.98 | 0.96 0.96 | 0.94 0.94 | 0.90 0.90 | 0.86 0.86 | 18,200 | 135.6 |
| 4 | 0.98 0.98 | 0.95 0.95 | 0.88 0.88 | 0.75 0.75 | 0.67 0.66 | 0.63 0.62 | 23,600 | 140.35 |
| 5 | 0.99 0.99 | 0.98 0.98 | 0.95 0.95 | 0.89 0.89 | 0.83 0.82 | 0.79 0.79 | 22,600 | 177.7 |
| 6 | 0.96 0.96 | 0.90 0.90 | 0.80 0.79 | 0.65 0.65 | 0.58 0.58 | 0.55 0.55 | 13,800 | 168.4 |
| 7 | 0.98 0.98 | 0.96 0.94 | 0.86 0.84 | 0.72 0.72 | 0.60 0.60 | 0.55 0.55 | 15,000 | 150.9 |
| 8 | 0.98 0.98 | 0.90 0.90 | 0.79 0.79 | 0.65 0.65 | 0.58 0.58 | 0.52 0.51 | 11,400 | 119.4 |
| 9 | 0.95 0.95 | 0.90 0.90 | 0.82 0.82 | 0.68 0.68 | 0.60 0.60 | 0.55 0.55 | 18,800 | 188.2 |
| 10 | 0.96 0.96 | 0.85 0.85 | 0.70 0.70 | 0.56 0.56 | 0.48 0.46 | 0.45 0.43 | 19,800 | 152.4 |
| 11 | 0.99 0.99 | 0.97 0.97 | 0.91 0.91 | 0.76 0.76 | 0.67 0.67 | 0.64 0.64 | 25,200 | 98.2 |
| 12 | 0.97 0.97 | 0.90 0.88 | 0.73 0.73 | 0.59 0.59 | 0.52 0.52 | 0.48 0.47 | 16,600 | 116.8 |
| 13 | 0.97 0.96 | 0.95 0.94 | 0.80 0.80 | 0.67 0.67 | 0.58 0.58 | 0.50 0.50 | 10,200 | 164.9 |

Table IX (contd.)

| No. | $\frac{1}{4}$ hr | $\frac{1}{2}$ hr | 1hr | 2hr | 3hr | 4hr | Leucocytes | Cholesterol of Blood. |
|---------|------------------|------------------|--------------|--------------|--------------|--------------|------------|--------------------------|
| 14 | 0.98 0.98 | 0.97 0.97 | 0.92 0.92 | 0.78 0.78 | 0.70 0.70 | 0.65 0.65 | 16,800 | 101.3 |
| 15 | 0.98 0.98 | 0.95 0.93 | 0.85 0.83 | 0.65 0.65 | 0.58 0.58 | 0.56 0.54 | 18,000 | 141.6 |
| 16 | 0.99 0.99 | 0.98 0.98 | 0.95 0.95 | 0.83 0.83 | 0.75 0.75 | 0.68 0.68 | 8,200 | 146.8 |
| 17 | 0.99 0.99 | 0.98 0.98 | 0.95 0.95 | 0.92 0.92 | 0.87 0.87 | 0.81 0.81 | 18,400 | 87.8 |
| 18 | 0.99 0.99 | 0.98 0.98 | 0.95 0.95 | 0.87 0.87 | 0.80 0.80 | 0.72 0.72 | 39,800 | 120.3 |
| 19 | - | - | - | - | - | - | - | 123.07 |
| 20 | - | - | - | - | - | - | - | 177.7 |
| 21 | - | - | - | - | - | - | - | 153.8 |
| Maximum | 0.98 | 0.94 | 0.86 | 0.75 | 0.67 | 0.63 | | |
| Mean | 0.98 | 0.94 | 0.86 | 0.75 | 0.67 | 0.625 | 19,200 | 140.3 |
| Minimum | 0.98 | 0.94 | 0.86 | 0.75 | 0.67 | 0.62 | | |

will be seen from Table IX that the cholesterol values varied from 87.8 to 188.2 mgm. per 100 c.c. of plasma. (4) This is comparable to the results of Gavriila and Berariu who found variations between 80 and 160 mgms. per 100 c.c. in the febrile period. The average cholesterol content of the blood (140.3 mgm. per 100 c.c.) is below normal for healthy individuals and corresponds with an average leucocytosis of 19,200. This is in agreement with the findings of Szirmai (15) who says that the cholesterol is generally decreased in Scarlet Fever.

Two cases in the group gave cholesterol readings of under 100 mgm. per 100 c.c. of blood plasma. The lower of these - case No.17 - showed an average leucocytosis and the second slowest sedimentation rate for the group. The other case, No.11, showed a relatively high leucocytosis and an average sedimentation rate. The highest cholesterol estimate was found in case No.9, which had an average leucocytosis and a rapid sedimentation rate. The same cholesterol estimations found in cases No.2 and No.4 showed similar leucocyte counts and sedimentation rates. Comparing cases with similar leucocyte counts, e.g. in No.9 and No.17: case No.9 showed a high cholesterol estimate with a rapid sedimentation rate, while No.17 showed a low

cholesterol reading with a slow sedimentation rate.

It would therefore appear that blood with a high cholesterol content sediments much more rapidly than blood that has a low cholesterol content, the leucocytosis being equal.

It is interesting to note that three cases reached the same final sedimentation point, viz. cases No.6, No.7 and No.9. Although this was a rapid sedimentation rate compared with the average for the group, the leucocytosis in all three cases was below the average, while the cholesterol estimations were all high, none being below 150 mgms.

A rapid sedimentation rate is more often associated with a high cholesterol content than with a high leucocyte count and vice versa in the acute stages of Scarlet Fever.

(6)

(2) H.A. Kipp found 129 mgm. and 151 mgm. of cholesterol per 100 c.c. of blood before crisis in pneumonia: in broncho-pneumonia 151 - 171 mgm. per 100 c.c. The cases recorded here were of the lobar type of pneumonia, the readings having been taken also before the crisis, but the results show distinctly lower values ranging from 66.6 mgm. to 136.7 mgm. per 100 c.c. According to Kipp's conclusion, the variation in cholesterol in the blood serum in pneumonia is dependent upon the activity of the

leucocytes and being transferred by them to the area of acute inflammation acts as an antitoxic substance, neutralising the bacterial toxins and those arising from the disintegration of tissue in the process of the inflammatory reaction. He goes on to say that the utilisation of cholesterol in acute toxic infections is directly proportional to the severity of the disease, i.e. the more seriously ill the patient, the lower is the cholesterol content of the blood in toxic conditions. This is borne out by the cases shown in Table X.

Case No.1, who was the most seriously ill, had a very high leucocyte count, a very rapid sedimentation rate and a low cholesterol content. The next in severity, case No.5, had also a high leucocyte count, rapid sedimentation and a low cholesterol content.

The lowest cholesterol estimation was found in case No.11 which had an average sedimentation rate and a lower leucocytosis than the average for the group. Case No.7 which was also low in cholesterol value had an average leucocytosis and a slower sedimentation rate than the average. The highest cholesterol content occurred in case No.4 which showed a slow sedimentation rate and a lower leucocyte count than average. Similar cholesterol

Table X.

PNEUMONIA (before crisis)

| No. | $\frac{1}{4}$ hr | $\frac{1}{2}$ hr | 1hr | 2hr | 3hr | 4hr | Leucocytes | Cholesterol of Blood |
|---------|------------------|------------------|--------------|--------------|--------------|--------------|------------|-------------------------|
| 1 | 0.90 0.88 | 0.75 0.72 | 0.52 0.52 | 0.38 0.38 | 0.35 0.35 | 0.34 0.33 | 65,800 | mgm/100 ccs 78.8 |
| 2 | 0.97 0.97 | 0.95 0.95 | 0.87 0.85 | 0.67 0.66 | 0.59 0.59 | 0.52 0.51 | 16,400 | 101.3 |
| 3 | 0.96 0.94 | 0.75 0.72 | 0.59 0.59 | 0.52 0.52 | 0.49 0.48 | 0.48 0.46 | 30,800 | 100.0 |
| 4 | 0.97 0.97 | 0.94 0.94 | 0.86 0.86 | 0.73 0.72 | 0.59 0.59 | 0.59 0.59 | 18,000 | 136.7 |
| 5 | 0.97 0.96 | 0.90 0.87 | 0.65 0.65 | 0.52 0.52 | 0.46 0.46 | 0.43 0.43 | 30,600 | 94.1 |
| 6 | 0.97 0.97 | 0.93 0.92 | 0.86 0.83 | 0.69 0.69 | 0.64 0.64 | 0.62 0.61 | 25,000 | 117.6 |
| 7 | 0.97 0.97 | 0.92 0.91 | 0.84 0.82 | 0.66 0.64 | 0.62 0.62 | 0.56 0.55 | 24,600 | 76.2 |
| 8 | 0.96 0.96 | 0.88 0.86 | 0.80 0.74 | 0.57 0.57 | 0.52 0.52 | 0.50 0.50 | 18,000 | 103.9 |
| 9 | 0.96 0.96 | 0.83 0.80 | 0.66 0.66 | 0.54 0.54 | 0.47 0.46 | 0.45 0.45 | 21,200 | 123.1 |
| 10 | 0.97 0.96 | 0.85 0.82 | 0.68 0.68 | 0.57 0.56 | 0.51 0.51 | 0.47 0.46 | 22,800 | 75.5 |
| 11 | 0.98 0.98 | 0.87 0.87 | 0.75 0.75 | 0.64 0.64 | 0.56 0.56 | 0.50 0.50 | 18,200 | 66.6 |
| 12 | 0.98 0.98 | 0.92 0.92 | 0.86 0.83 | 0.67 0.67 | 0.55 0.55 | 0.52 0.52 | 18,200 | 104.6 |
| Maximum | 0.96 | 0.875 | 0.75 | 0.60 | 0.53 | 0.50 | | |
| Mean | 0.96 | 0.87 | 0.74 | 0.595 | 0.53 | 0.495 | 25,750 | 98.2 |
| Minimum | 0.96 | 0.86 | 0.73 | 0.59 | 0.53 | 0.49 | | |
| 13 | 0.98 0.98 | 0.93 0.88 | 0.75 0.71 | 0.53 0.53 | 0.47 0.47 | 0.44 0.44 | 18,400 | 106.6 |

contents were found in cases No.8 and No.12. These cases showed also very similar leucocytosis and sedimentation rates. Cases No.11 and No.12 had the same leucocytosis. The former had a much lower cholesterol content than the latter and showed an average sedimentation; the latter with a cholesterol content above the average had a very slightly slower sedimentation rate. Equal sedimentation rates in cases No.8 and No.11 showed equal leucocytosis - although the cholesterol content of the former was considerably higher than that in the latter.

Contrasting the mean of the results in Tables IX and X we find that in Acute Lobar Pneumonia, the sedimentation rate is more rapid, the leucocytosis greater and the cholesterol much less than in the acute stage of Scarlet Fever.

(2)

(3) Chauffard, Richet and Grigaut state that in tuberculosis the cholesterol content of the blood depends upon the character of the disease, whether apyretic or febrile. In the afebrile tuberculosis it remains normal, while in the febrile form the cholesterol content of the blood is constantly lowered and markedly so when the general condition is very bad or the fever very high. The depression of the cholesterol in the blood is evidently proportionate to the intensity of the disease. SaTomon, de Potter and Valtis (11)

showed that in grave tuberculosis the amount of cholesterol in the blood is decreased, while sedimentation is accelerated.

In contrast to those opinions are the findings of Strathmann-Herweg, ⁽¹⁴⁾ who said "In various infections - sepsis, pyodermia and tuberculosis, the values (of cholesterin) were usually normal but occasionally increased." L. Jullien and ⁽⁵⁾ Martin Rossel calculated the cholesterol in the blood serum of twenty-four patients with different forms of tuberculosis. They found that the amount was not modified under the influence of the infection.

From the results shown in Tables XI and XII we are in agreement with the first group of workers. The cholesterol content was found lowered in acute or febrile tuberculosis, while the sedimentation rate was accelerated. On the other hand in the afebrile type of tuberculosis no such marked change in the cholesterol was encountered, all the readings being within the limits for normal individuals.

(4) The ages of the Enteric Fever group ranged from 10 to 60, the majority being between 20 and 26 years of age. The commonest symptoms in order of their greatest frequency were: shivering, sickness and vomiting, diarrhoea, abdominal pains, headache, cough, epistaxis and deafness. Two cases

Table XI.
TUBERCULOSIS (Acute)

| No. | $\frac{1}{4}$ hr | $\frac{1}{2}$ hr | 1hr | 2hr | 3hr | 4hr | Leucocytes | Cholesterol of Blood. |
|---------|------------------|------------------|--------------|--------------|--------------|--------------|------------|--------------------------|
| 1 | 0.93 0.90 | 0.75 0.73 | 0.55 0.47 | 0.33 0.33 | 0.28 0.28 | 0.26 0.85 | 10,200 | 119.5 |
| 2 | 0.92 0.88 | 0.80 0.75 | 0.65 0.59 | 0.42 0.42 | 0.34 0.34 | 0.31 0.30 | 20,400 | 126.9 |
| 3 | 0.95 0.95 | 0.84 0.82 | 0.70 0.62 | 0.45 0.45 | 0.38 0.38 | 0.36 0.36 | 11,800 | 160.0 |
| 4 | 0.98 0.97 | 0.92 0.91 | 0.80 0.78 | 0.61 0.61 | 0.56 0.56 | 0.53 0.53 | 19,000 | 103.2 |
| 5 | 0.96 0.94 | 0.86 0.84 | 0.74 0.69 | 0.54 0.54 | 0.50 0.50 | 0.49 0.48 | 38,800 | 76.1 |
| 6 | 0.96 0.93 | 0.85 0.85 | 0.56 0.54 | 0.41 0.41 | 0.38 0.38 | 0.36 0.36 | 10,400 | 73.7 |
| Maximum | 0.95 | 0.84 | 0.66 | 0.46 | 0.41 | 0.385 | | |
| Mean | 0.94 | 0.825 | 0.635 | 0.46 | 0.41 | 0.38 | 18,450 | 109.9 |
| Minimum | 0.93 | 0.81 | 0.61 | 0.46 | 0.41 | 0.38 | | |

Table XII.
TUBERCULOSIS (chronic)

| No. | $\frac{1}{4}$ hr | $\frac{1}{2}$ hr | 1hr | 2hr | 3hr | 4hr | Leucocytes | Cholesterol of Blood. |
|---------|------------------|------------------|--------------|--------------|--------------|--------------|------------|--------------------------|
| 1 | 0.95 0.93 | 0.87 0.85 | 0.68 0.68 | 0.54 0.54 | 0.45 0.45 | 0.40 0.40 | 21,000 | 150.9 |
| 2 | 0.95 0.95 | 0.93 0.89 | 0.75 0.72 | 0.55 0.55 | 0.45 0.45 | 0.40 0.40 | 15,800 | 106.6 |
| 3 | 0.98 0.98 | 0.88 0.88 | 0.78 0.78 | 0.65 0.65 | 0.55 0.55 | 0.50 0.50 | 18,000 | 155.3 |
| 4 | 0.98 0.98 | 0.92 0.92 | 0.84 0.84 | 0.66 0.66 | 0.60 0.60 | 0.54 0.54 | 23,400 | 192.8 |
| 5 | 0.93 0.92 | 0.80 0.75 | 0.59 0.59 | 0.43 0.43 | 0.41 0.41 | 0.39 0.39 | 12,800 | 160.0 |
| 6 | 0.99 0.99 | 0.98 0.98 | 0.96 0.96 | 0.84 0.84 | 0.75 0.75 | 0.70 0.70 | 17,200 | 177.7 |
| 7 | 0.95 0.95 | 0.60 0.60 | 0.49 0.49 | 0.41 0.41 | 0.40 0.40 | 0.39 0.39 | 20,000 | 175.8 |
| 8 | 0.99 0.99 | 0.96 0.95 | 0.84 0.83 | 0.68 0.68 | 0.63 0.63 | 0.59 0.59 | 9,400 | 152.4 |
| 9 | 0.95 0.93 | 0.75 0.73 | 0.48 0.48 | 0.35 0.35 | 0.34 0.34 | 0.33 0.32 | 10,800 | 105.3 |
| 10 | 0.98 0.98 | 0.95 0.94 | | 0.71 0.70 | 0.63 0.63 | 0.60 0.60 | 19,600 | 133.3 |
| 11 | 0.97 0.97 | 0.94 0.92 | | 0.59 0.59 | 0.54 0.54 | 0.51 0.51 | 13,600 | 139.5 |
| 12 | 0.96 0.95 | 0.90 0.86 | 0.75 0.71 | 0.52 0.52 | 0.45 0.45 | 0.40 0.40 | 32,000 | 111.1 |
| Maximum | 0.965 | 0.87 | 0.72 | 0.58 | 0.52 | 0.48 | | |
| Mean | 0.96 | 0.865 | 0.715 | 0.58 | 0.52 | 0.48 | 17,800 | 146.7 |
| Minimum | 0.96 | 0.86 | 0.71 | 0.58 | 0.52 | 0.48 | | |

were delirious on admission, cases No.1 and No.4. Two cases showed evidence of rose spots, cases No.3 and No.5. The temperatures varied from 98° to 103°F. and the pulses from 84 to 120 per minute. The blood gave a positive Widal reaction in all cases: six were positive for B typhosus (four in every dilution to 1 in 250 and the remaining two to a dilution of 1 in 125). In case No.1 the presence of B typhosus was demonstrated in the faeces, the urine and in the blood.

(12)

According to Shope, plasma obtained from blood in which either sodium citrate or potassium oxalate have been used as anti-coagulents contains less cholesterol bound as ester than does serum from blood drawn from the same animal and at the same time. In case No.6 of Table XIII two cholesterol readings are given for blood taken from the same person at the same time. In the one case the serum cholesterol was estimated and in the other the plasma. It will be seen from the results that in agreement with Shope we found that plasma estimations showed slightly less cholesterol than serum taken from the same individual.

(2)

Chauffard, Laroche and Grigaut in investigating cases of typhoid found a primary hypocholesterolaemia succeeded by a gradual rise above the normal content attain-

ing a maximum from the 27th to the 56th day and falling again to a normal figure on approximately the 73rd day. Malerba (9) says he found cholesterol values below normal in severe cases of pneumonia or typhoid.

(4)
Gavrila and Berariu found a hypocholesterolaemia in the febrile stage of 80 - 140 mgm. per 100 c.c. This is followed after 10 days of apyrexia by a hypercholesterolaemia which finally returns to a normal figure.

We have not been able to demonstrate a hypocholesterolaemia to the same degree as that quoted. In the few cases of Enteric Fever shown the cholesterol content varied from 95.2 - 200 mgm. per 100 c.c. plasma, the average being 138.5mgm. It is interesting to note, however, that the cases investigated up to and including the 20th day of illness showed less cholesterol on the whole than those investigated after the 20th day of illness.

Table XIV shows a case of B.typhosus B. The first estimation was carried out on the 14th day and the second 8 days later, i.e. on the 22nd day of illness. The first cholesterol reading was above normal, but by the 24th day it had returned to normal, the leucocyte count had increased and the sedimentation rate slightly retarded.

Contrasting Tables XIII and XIV, it will be seen that in paratyphoid fever the sedimentation rate was less

Table XIII.

ENTERIC FEVER (B. Typhosus)

| No. | $\frac{1}{4}$ hr | $\frac{1}{2}$ hr | 1 hr | 2 hr | 3 hr | 4 hr | Leuco- cytes | Choles- terol. | Day of Illness |
|---------|------------------|------------------|--------------|--------------|--------------|--------------|-----------------|-----------------------------------|-------------------|
| 1 | 0.97 0.97 | 0.94 0.92 | 0.79 0.78 | 0.70 0.69 | | 0.63 0.61 | 4,000 | 114.3 | 7th |
| 2 | 0.98 0.98 | 0.90 0.87 | 0.68 0.68 | 0.52 0.52 | 0.42 0.42 | 0.39 0.39 | 9,000 | 155.3 | 10th |
| 3 | 0.90 0.75 | 0.70 0.45 | 0.29 0.29 | 0.25 0.25 | 0.23 0.23 | 0.20 0.20 | 9,700 | 95.2 | 16th |
| 4 | 0.99 0.99 | 0.98 0.98 | 0.97 0.97 | 0.92 0.92 | 0.87 0.87 | 0.86 0.83 | 3,000 | 128.0 | 20th |
| 5 | 0.99 0.99 | 0.97 0.97 | 0.90 0.90 | 0.80 0.80 | 0.74 0.74 | 0.68 0.68 | 2,400 | 200.0 | 24th |
| 6 | 0.98 0.92 | 0.94 0.93 | 0.88 0.84 | 0.70 0.70 | 0.56 0.56 | 0.50 0.50 | 8,000 | Serum 142.9 Plasma 135.6 | 46th |
| Maximum | 0.97 | 0.90 | 0.74 | 0.65 | 0.56 | 0.54 | | | |
| Mean | 0.955 | 0.875 | 0.735 | 0.65 | 0.56 | 0.535 | 6,016 | 138.5 | |
| Minimum | 0.94 | 0.85 | 0.73 | 0.65 | 0.56 | 0.53 | | | |

Table XIV.

ENTERIC FEVER (B. Paratyphosus B)

| No. | $\frac{1}{4}$ hr | $\frac{1}{2}$ hr | 1 hr | 2 hr | 3 hr | 4 hr | Leuco- cytes. | Choles- terol | Day of Illness |
|--------------------------|------------------|------------------|--------------|--------------|--------------|--------------|------------------|------------------|-------------------|
| 1 | 0.97 0.97 | 0.94 0.92 | 0.84 0.82 | 0.69 0.67 | 0.59 0.59 | 0.55 0.54 | 6,800 | 173.9 | 14th |
| Same 8 days later. | 0.98 0.98 | 0.93 0.93 | 0.83 0.81 | 0.64 0.64 | 0.58 0.58 | 0.56 0.56 | 7,800 | 140.3 | 22nd |
| Maximum | 0.975 | 0.935 | 0.835 | 0.665 | 0.585 | 0.555 | | | |
| Mean | 0.975 | 0.93 | 0.825 | 0.66 | 0.585 | 0.55 | 7,300 | 157.1 | |
| Minimum | 0.975 | 0.925 | 0.815 | 0.655 | 0.585 | 0.55 | | | |

the leucocytosis and the cholesterol content greater than in the typhoid group. The clinical condition of the former group having been more severe than the latter - it would appear that the more serious the case is clinically in Enteric Fever, the more rapid is the sedimentation rate, the lower is the leucocyte count and cholesterol content.

(5) Erysipelas was considered in two subdivisions, that on the face, and elsewhere. In the first group were patients between the ages of 32 and 53 with a single instance at 29 years. In the latter group ages were considerably higher - varying from 40-65 years. We have, of course, excluded cases of Erysipelas neonatorum, who, on account of their youth, were unsuitable for investigation purposes. The cases of Erysipelas elsewhere than on the face occurred mostly on the legs and spread from chronic varicose ulcers, septic sores, following on an injury, or after an operation. The prevailing symptoms in both groups were headache, sickness, shivering, pain and swelling of the affected part, vomiting, giddiness and constipation. The temperatures in the facial group varied from 98° to 102° and in the non-facial from 98° to 103° , the majority being under 100° .

(4)

Gavrila and Berariu estimated the cholesterol content in the acute stage of erysipelas to be between 85 and 180 mgm. in the majority of cases under 155 mgm. Hypocholesterolaemia, they say, is therefore marked. In one to two days after defervescence, there is in every case a slow tendency to hypercholesterolaemia. In five to ten days of normal temperature in half the cases hypercholesterolaemia is over 200 mgm. and in the other cases the hypocholesterolaemia of the febrile period slowly returns to normal. Hypercholesterolaemia then begins to return to normal, but after 15 days of apyrexia the return is not yet complete.

The results found in the acute stage of Erysipelas are shown in Table XV. The cholesterol estimations agree fairly closely with those of Gavrila and Berariu already quoted. Variations were found from 100 - 195.1 mgm. per 100 c.c., the average being 146.08 mgm. A series of cases was investigated after 8 - 10 days of normal temperature (see Table XVI). The cholesterol readings in these cases varied from 119.4 to 205.1 - the average reading being 157.1 mgm. per 100 c.c. This shows an average increase of 11.02 mgm. in the convalescent stage. The sedimentation rate meanwhile had become considerably retarded.

Table XV.

ERYSIPĒLAS.

| No. | $\frac{1}{4}$ hr | $\frac{1}{2}$ hr | 1hr | 2hr | 3hr | 4hr | Leucocytes | Cholesterol of Blood. |
|---------|------------------|------------------|--------------|--------------|--------------|--------------|------------|--------------------------|
| 1 | 0.99 0.99 | 0.95 0.95 | 0.88 0.88 | 0.80 0.80 | 0.60 0.60 | 0.45 0.45 | 12,400 | 188.2 |
| 2 | 0.85 0.68 | 0.48 0.48 | 0.38 0.38 | 0.35 0.35 | 0.34 0.34 | 0.33 0.33 | 10,400 | 170.2 |
| 3 | 0.90 0.88 | 0.80 0.77 | 0.49 0.49 | 0.39 0.39 | 0.35 0.35 | 0.33 0.33 | 9,200 | 195.1 |
| 4 | 0.97 0.97 | 0.94 0.91 | 0.80 0.77 | 0.58 0.58 | 0.49 0.49 | 0.45 0.44 | 15,200 | 113.5 |
| 5 | 0.96 0.96 | 0.92 0.92 | 0.82 0.82 | | 0.60 0.60 | 0.56 0.56 | 20,000 | 152.4 |
| 6 | 0.98 0.98 | 0.94 0.94 | 0.83 0.83 | 0.68 0.68 | 0.61 0.61 | 0.57 0.57 | 13,400 | 131.1 |
| 7 | 0.97 0.96 | 0.88 0.88 | 0.77 0.74 | 0.58 0.58 | 0.52 0.52 | 0.48 0.48 | 18,800 | 100.0 |
| 8 | 0.99 0.99 | 0.96 0.96 | 0.91 0.91 | 0.78 0.78 | 0.69 0.69 | 0.59 0.59 | 8,000 | 139.1 |
| 9 | 0.96 0.96 | 0.78 0.70 | 0.54 0.54 | 0.42 0.42 | 0.40 0.40 | 0.39 0.38 | 15,800. | 135.6 |
| 10 | 0.99 0.99 | 0.97 0.97 | 0.89 0.86 | 0.70 0.70 | 0.65 0.65 | 0.62 0.62 | 13,600 | |
| 11 | 0.95 0.95 | 0.90 0.85 | 0.80 0.73 | 0.50 0.50 | 0.47 0.47 | 0.46 0.46 | 5,600 | 135.6 |
| Maximum | 0.95 | 0.87 | 0.74 | 0.58 | 0.52 | 0.48 | | |
| Mean | 0.945 | 0.86 | 0.73 | 0.58 | 0.52 | 0.475 | 12,945 | 146.08 |
| Minimum | 0.94 | 0.85 | 0.72 | 0.58 | 0.52 | 0.47 | | |

Table XVI.

ERYSIPELAS (after 8-10 days' normal temperature)

| No. | $\frac{1}{4}$ hr | $\frac{1}{2}$ hr | 1hr | 2hr | 3hr | 4hr | Leucocytes | Cholesterol of Blood. |
|---------|------------------|------------------|--------------|--------------|--------------|--------------|------------|--------------------------|
| 1 | 0.99 0.99 | 0.98 0.98 | 0.93 0.93 | 0.85 0.85 | 0.75 0.75 | 0.66 0.66 | 11,200 | 152.4 |
| 2 | 0.52 0.52 | 0.44 0.44 | 0.39 0.39 | 0.34 0.34 | 0.32 0.32 | 0.31 0.31 | 9,800 | 205.1 |
| 3 | 0.93 0.88 | 0.80 0.77 | 0.65 0.60 | | 0.35 0.35 | 0.33 0.33 | - | 156.8 |
| 4 | 0.99 0.99 | 0.97 0.97 | 0.94 0.94 | 0.88 0.88 | 0.81 0.81 | 0.75 0.75 | - | 119.4 |
| 5 | 0.99 0.99 | 0.98 0.98 | 0.93 0.93 | 0.80 0.80 | 0.71 0.71 | 0.63 0.63 | - | 175.8 |
| 6 | 0.99 0.99 | 0.98 0.98 | 0.93 0.93 | 0.80 0.80 | 0.70 0.70 | 0.64 0.64 | - | 133.3 |
| Maximum | 0.90 | 0.86 | 0.80 | 0.73 | 0.61 | 0.55 | | |
| Mean | 0.895 | 0.855 | 0.795 | 0.73 | 0.61 | 0.55 | | 157.1 |
| Minimum | 0.89 | 0.85 | 0.79 | 0.73 | 0.61 | 0.55 | | |

We are in agreement therefore with Gavriila and Berariu, that in the acute stage of Erysipelas there is a slight hypocholesterolaemia followed after 8-10 days of normal temperature by a return to within normal limits. The rising cholesterol is associated with a retarding sedimentation rate.

Comparing Tables XV and XII it is interesting to note that the cholesterol content and the sedimentation rates were almost identical in the series of cases of Acute Erysipelas and Chronic Tuberculosis, but there is a difference in the leucocytosis of nearly 5,000 per c.c. more in the Tuberculosis cases.

One would, therefore, conclude that just as the sedimentation rate is not dependent solely on leucocytosis neither is the cholesterol content of the blood.

A few cases of Facial Erysipelas (Table XVII) were investigated as apart from the general Erysipelas group. In these we found a marked hypercholesterolaemia in the acute stage of the disease, the average content being 212.9 mgm. per 100 c.c., although the final sedimentation figures were practically equivalent to these of the general Erysipelas group (Table XV). The leucocytosis was slightly greater in the facial type. These cases were on the

Table XVII.

ERYSIPELAS (Acute Facial)

| No. | $\frac{1}{4}$ hr | $\frac{1}{2}$ hr | 1hr | 2hr | 3hr | 4hr | Leuco- cytes | Choles- terol | Temp. | P. | R. |
|---------|------------------|------------------|--------------|--------------|--------------|--------------|-----------------|------------------|-------|-----|----|
| 1 | 0.98 0.98 | 0.93 0.92 | 0.82 0.80 | 0.61 0.61 | 0.54 0.54 | 0.50 0.50 | 6,200 | 200.0 | 98.0 | 88 | 20 |
| 2 | 0.99 0.99 | 0.97 0.97 | 0.95 0.95 | 0.90 0.90 | 0.85 0.85 | 0.80 0.80 | 10,200 | 457.1 | 98.4 | 84 | 24 |
| 3 | 0.96 0.96 | 0.85 0.85 | 0.65 0.65 | 0.50 0.50 | 0.45 0.44 | 0.43 0.42 | 15,000 | 205.1 | 98.4 | 120 | 26 |
| 4 | 0.68 0.68 | 0.51 0.51 | 0.42 0.42 | 0.34 0.34 | 0.31 0.31 | 0.30 0.30 | 20,400 | 108.1 | 98.6 | 108 | 26 |
| 5 | 0.96 0.96 | 0.75 0.75 | 0.53 0.53 | 0.40 0.40 | 0.37 0.37 | 0.36 0.36 | 19,000 | 188.2 | 100.2 | 120 | 26 |
| 6 | 0.97 0.97 | 0.92 0.85 | 0.60 0.50 | 0.41 0.41 | 0.39 0.39 | 0.38 0.38 | 20,000 | 139.1 | 102.8 | 120 | 28 |
| 7 | 1.0 1.0 | 0.97 0.97 | 0.85 0.85 | 0.68 0.68 | 0.59 0.59 | 0.54 0.54 | 17,400 | 192.8 | - | - | - |
| Maximum | 0.93 | 0.84 | 0.69 | 0.55 | 0.50 | 0.47 | | | | | |
| Mean | 0.93 | 0.835 | 0.68 | 0.55 | 0.50 | 0.47 | 15,486 | 212.9 | 99.4 | 106 | 25 |
| Minimum | 0.93 | 0.83 | 0.67 | 0.55 | 0.50 | 0.47 | | | | | |

whole of a clinically severer type than the cases of Table XV. Therefore the leucocyte count and the cholesterol content of the blood are a better indication of the severity of the disease in Erysipelas than is the sedimentation rate.

It may be that the severer the case the shorter is the stage of hypocholesterolaemia, and that this may account for the much higher value found in the Facial cases.

Is the cholesterol content of the blood in no way modified by differences in temperature of the patients? In Table XVII the first six cases are arranged according to the temperature of the patient when the blood was drawn off:- case No.1 had a moderate temperature, case No.2 slightly higher and so on to a maximum of 102.8°F. in case No.8. Two cases, No.2 and No.3, had equal temperatures. The cholesterol content of the former was more than double that of the latter, while the sedimentation rate in case No.2 was only about a third of case No.3.

It is interesting to note, however, that the higher the temperature, if anything, the lower is the cholesterol content. Cases No.4, No.5 and No.6, which have in that order the three highest temperatures, have all cholesterol contents below the average for the group. Incidentally

these three cases show also the three most rapid sedimentation rates and the three highest leucocyte counts.

. In acute facial Erysipelas, therefore, the severity of the condition is paralleled by a lowered cholesterol content, a rapid sedimentation rate and a definite leucocytosis.

Section 4: Conclusions.

(1) The cholesterol content of the blood plasma is markedly decreased below normal limits in the acute stages of lobar pneumonia and tuberculosis and also, but to a lesser degree, in the acute stages of typhoid fever, scarlet fever and erysipelas.

(2) Generally speaking - the more serious the condition clinically, the lower is the cholesterol content of the blood.

(3) In tuberculosis, the cholesterol content depends on the type of the disease. In afebrile or chronic tuberculosis the cholesterol is within normal limits, while in the febrile type it is markedly reduced.

(4) This hypocholesterolaemia of the acute fevers disappears in the convalescent stage, as was shown in the erysipelas and typhoid cases when the cholesterol increased

to within normal limits.

(5) Plasma cholesterol values are slightly lower than serum cholesterol of blood taken from the same individual and at the same time.

(6) The decreased cholesterol in the acute fevers is associated, generally speaking, with a rapid sedimentation rate and a high leucocytosis, although there are many individual exceptions to this rule.

(7) In the enteric group - the hypocholesterolaemia is associated with a rapid sedimentation rate but a leucopenia or normal leucocyte count.

(8) Blood cholesterol, however, is not dependent solely either on the number of leucocytes in the blood or on the sedimentation rate of the erythrocytes.

(9) The higher the temperature of the patient (as shown in facial erysipelas) the lower is the cholesterol content of the blood, the more rapid the sedimentation rate, and the greater the leucocytosis.

GENERAL SUMMARY AND COMMENT.

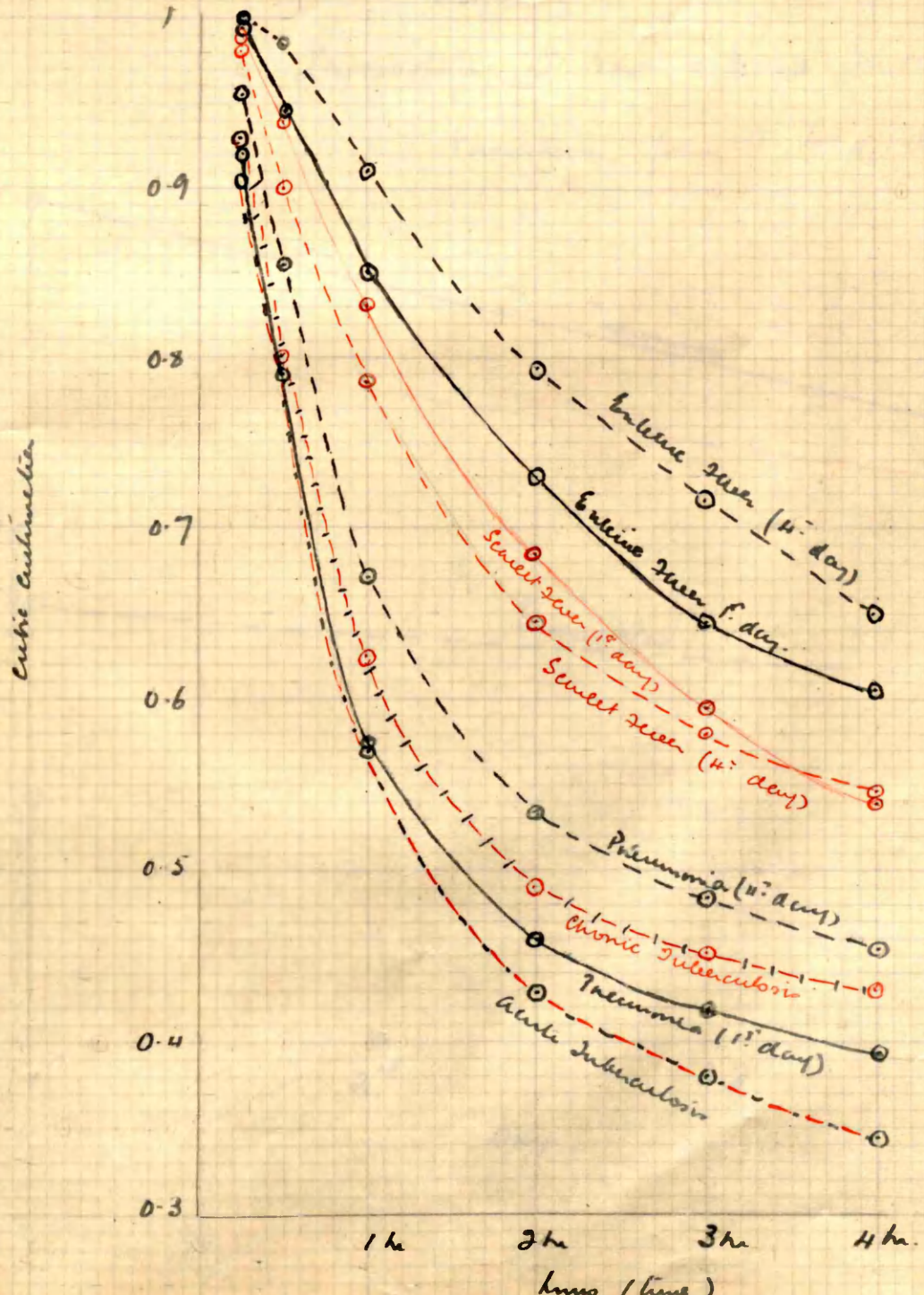
In the acute stages of certain infective fevers the sedimentation rate of the erythrocytes is markedly accelerated above normal and although this is in general associated with a marked leucocytosis and a lowered cholesterol content of the blood, this relationship is in no case a strict parallel and there are many individual exceptions and discrepancies in certain diseases. In view of this, the conclusion must be drawn that the three factors are not entirely interdependent nor are they controlled by a single agent, and that the true explanation of the behaviour of the sedimentation of the red cells in particular has not yet been established.

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Section 5: References.

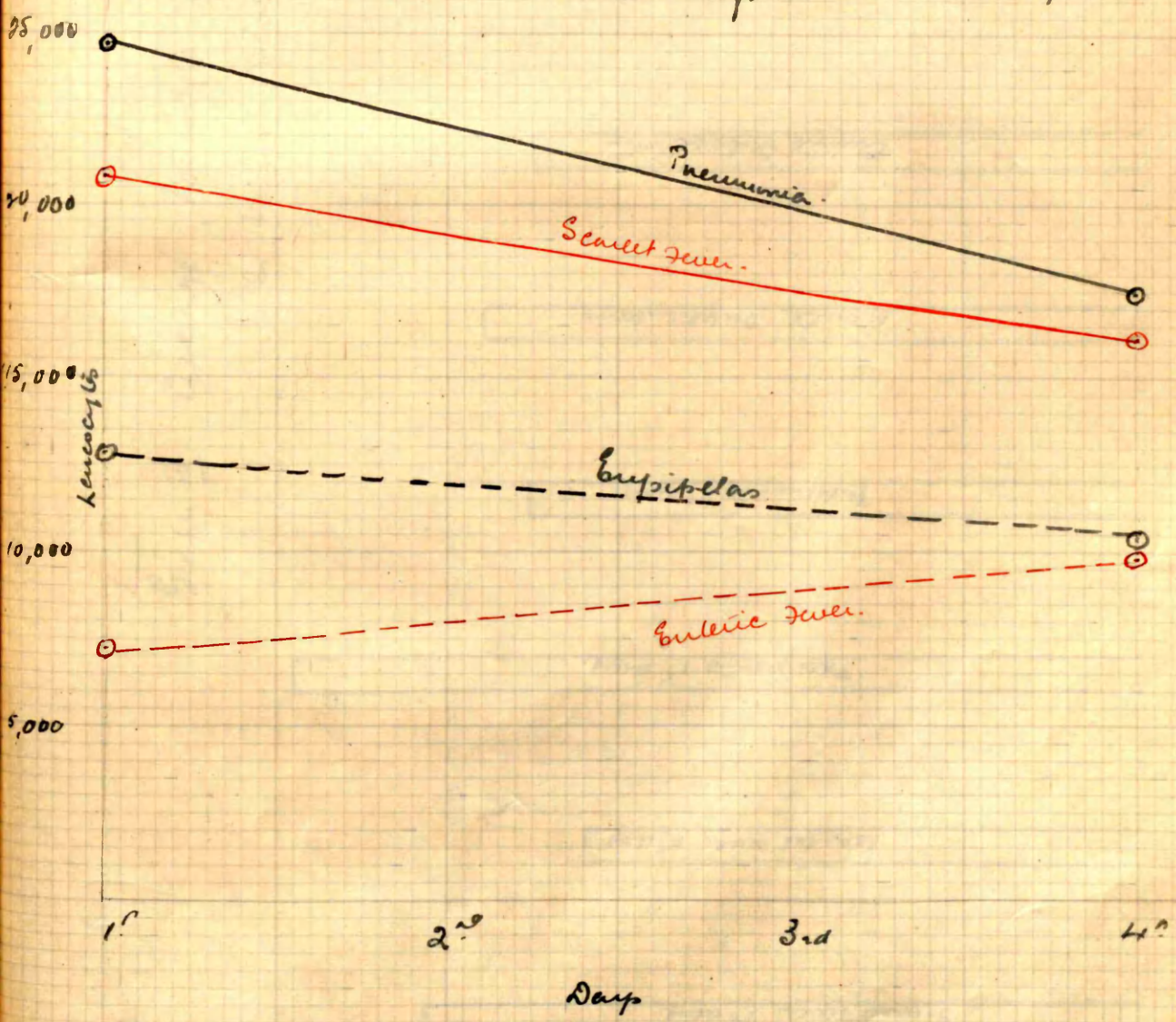
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Graph I Average sedimentation Rate in Various Acute Fevers.



Graph II
Leucocytosis in Various Acute Fevers.

Variations from 1st to 4th Day.



Graph III Average Leucocyte Counts

in Various Fevers.

