THE PLASMA PROTEINS IN THE ACUTE INFECTIVE FEVERS.

A study of the variations in the Fibrin, Albumen and Globulin content of the plasma in certain of the acute infectious diseases. This investigation was carried out in the City of Glasgow Fever Hospital, Ruchill, by kind permission of Dr W.Elliott, Medical Superintendent of the Hospital.

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Introduction.

It has been demonstrated by a number of observers that various circumstances may modify the protein constituents of the blood plasma. Thus, slightly different figures have been reported in the different sexes (1) and, again, definite alterations in the constituent proteins occur in a variety of conditions in which the metabolism of the individual is deranged. For example, in normal pregnancy (2) the Fibrin content of the plasma is increased while the Albumen and Globulin are diminished in amount. These abnormalities are further modified by the onset of a toxaemia or the supervention of nephritis. (3) Changes similar to those associated with pregnancy are present in a number of pathological conditions. Renal damage may be inferred if the Albumen content is much diminished and if the Total Protein is low: a low Fibrin content is indicative of impaired hepatic efficiency. (4) An increase in Globulin has been described in malignant tumours (5) and it has long been known that in certain infections such as pneumonia or acute suppurative conditions the Fibrin and Globulin of the plasma are increased.

Nature and Scope of the Present Investigation.

In view of these results it was considered probable that definite alterations in the various plasma proteins might be encountered in the infective fevers, and it appeared desirable to investigate this point. In the course of the work it was soon evident that such changes did occur, and that further, as will be fully demonstrated in the appropriate sections, the changes produced by some of the infections differed sharply from those produced by others. At the same time it was recognized that the findings/

findings had been determined in a very limited number of normal cases and therefore as a preliminary to the main investigation, the normal values of the proteins were worked out in a series of fifty cases.

Nature of the Material studied.

The cases investigated fall into two groups:-

A. A series of 50 normal controls.

B. A series of 208 estimations in the acute fevers which comprised

I.	Erysipelas	35 estimations.
II.	Scarlet Fever	33 estimations.
III.	Pneumonia	41 estimations.
IV.	Other Respiratory diseases	8 estimations.
V.	Tuberculosis	29 estimations.
VI.	Typhus Fever	11 estimations.
VII.	Typhoid Fever	23 estimations.
VIII.	Typhoid Fever & Bronchiectasis	2 estimations.
IX.	Paratyphoid Fever	12 estimations.
X.	Miscellaneous Infections	14 estimations.

Method employed in the Chemical Analysis.

The blood was withdrawn in the usual manner from a superficial vein in the antecubital fossa into a test tube containing powdered Potassium Oxalate. The test tube was agitated during the withdrawal of the blood and was then inverted several times to mix the blood and oxalate. The blood was then centrifugalised. The technique employed in the actual estimation of the plasma proteins was the colorimetric method of Hsien Wu (6). The details are as follows:-

Determination of Fibrin.

To 1 cc. of plasma add 28 cc. of 0.8% NaCl and 1 cc. of 2.5% $CaCl_2$ solution. Mix and allow to stand for 20 minutes. Break up the jelly by shaking slightly. Transfer to a dry filter. While filtering, remove the fibrin by whipping with a pointed glass rod. Slip the Fibrin off the rod, press dry between filter paper and put it in a centrifuge tube. Add 4 ccs. of 1% NaOH, place in a water bath at 100°C. and stir with a rod until the Fibrin is dissolved. The calcium oxalate is now in suspension. Add 10 ccs. of water, mix and centrifuge. Transfer the supernatant fluid to a 25 cc. volumetric flask and cool. Add 1 cc. of 5% H_2SO_4 and 0.5 cc. Phenol Reagent* and dilute to 20 ccs. Add 3 ccs. of 20% Na_2CO_3 solution. Shake. Add 1 drop of ether to dissipate the foam. Make up to 25 ccs. Mix.

To prepare the standard: place 1 cc. Standard Tyrosine Solution* in a 25 cc. volumetric flask. Add 0.5 Phenol Reagent, dilute to 25 ccs. and mix.

The unknown and the standard must be prepared simultaneously. Both solutions are allowed to stand for 15 minutes when they are compared in the colorimeter. The standard is set at 20.

Calculation: Standard at 20. Unknown = R.

Amount of apparent Tyrosine = $\frac{20}{R} \times \frac{0.2}{\quad}$ mgms.

Since 1 mgm. Tyrosine = 16.4 mgms. Fibrin

∴ Fibrin in 1 cc. of plasma = $\frac{20}{R} \times \frac{0.2}{\quad} \times \frac{16.4}{\quad}$ mgms.

∴ Percentage fibrin = $\frac{20}{R} \times 0.328$ mgms.

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* Folin's Phenol Reagent

	Ammonium molybdate	34 gms.
	10% Sodium Hydroxide	140 ccs.
	Distilled Water	150 ccs.
Boil together for 20 minutes to free from ammonia.		
Add	Sodium Tungstate	100 gms.
	85% Phosphoric Acid	50 ccs.
	Concd. Hydrochloric Acid	100 ccs.
	Distilled water to 700-800 ccs.	

Cover the flask with a filter funnel and watch glass and boil for 4 hours, making additions of water as needed to keep up the bulk. Cool and dilute to 1000 ccs.

Determination of Albumen.

To 1 cc. of plasma, add 9 ccs. of 5/9 Saturated $(NH_4)_2SO_4$. Mix and allow to stand 30 minutes. Filter. Place 1 cc. of the filtrate in a centrifuge tube, add 12 ccs. of water, 1 cc. 10% Sodium Tungstate Solution and 1 cc. of 2/3 N H_2SO_4. Stir with a slender rod. Centrifuge. Decant off fluid. (Should the precipitate be less than 0.5 cc., use an additional 1 cc. of filtrate). Add to precipitate 1-2 drops of 20% Na_2CO_3. Stir till the precipitate dissolves. Transfer to a 25 cc. volumetric flask. (Rinse the tube twice with 3 ccs. of water). Add 0.5 ccs. of the Phenol Reagent and 3 ccs. of 20% Na_2CO_3. Shake with a drop of ether. Make up to 25 ccs. Mix. Prepare the standard as in the fibrin estimation. Allow to stand for 15 minutes and compare.

Determination of Albumen + Globulin.

Take 2 ccs. of the filtrate from the fibrin determination in a centrifuge tube and proceed as in the Albumen estimation from the point marked .

Calculation: Standard at 20.

Reading for Albumen = Ra. Dilution 1-10.

Reading for Albumen + Globulin = Rb.

Then. Total apparent Tyrosine = $15 \times \frac{20}{Rb} \times 0.2$ mgms.

Apparent Tyrosine in 1 cc. of plasma = $10 \times \frac{20}{Ra} \times 0.2$ mgms

The apparent Tyrosine of Globulin

$$= (15 \times \frac{20}{Rb} \times 0.2) - (10 \times \frac{20}{Ra} \times 0.2) = \frac{60}{Rb} - \frac{40}{Ra} \text{ mgms.}$$

Since 1 mgm. Tyrosine = 25.2 mgms Globulin
= 27.5 mgms. Albumen

Then percentage Globulin $= \frac{(\frac{60}{Rb} - \frac{40}{Ra}) \times 25.2 \times 100}{1000}$ mgms.

$$= \frac{6}{Rb} - \frac{4}{Ra} \times 25.2 \text{ mgms.}$$

Then percentage Albumen $= \frac{(10 \times \frac{20}{Ra} \times 0.2) \times 27.5 \times 100}{1000}$

$$= \frac{20}{Ra} \times 5.44.$$

* Standard Tyrosine Solution Tyrosine 50.0 mgms.
N/10 Hydrochloric Acid to 250 ccs.

SECTION A.

Results obtained in Fifty Normal Cases.

The findings in fifty control cases are shown in Table I. The Fibrin, Albumen and Globulin were estimated by the above method and the Total Proteins and the ratio of Albumen to Globulin was determined. Of these cases four only were males (Nos. 3, 4, 5 and 6) and forty-six were females. For the most part the normal subjects were members of the Hospital staff; the remainder were patients in another Hospital who were suffering from purely surgical conditions and who were free from infection of any kind. Owing to the limited number of male controls it is impossible to confirm the differences in readings between the sexes reported by H.A.Salvesen (1) who found that the Albumen/Globulin ratio in males was 1.72 and in females 1.62. As will be shown later, the variation in normal subjects of either sex are wide and therefore in the present series, sex has been entirely disregarded as a factor that may modify the plasma proteins.

NORMAL CONTROL CASES. TABLE I.

Fibrin.	Albumen.	Globulin.	Total.	Albumen. / Globulin	No.	Fibrin.	Albumen.	Globulin.	Total.	Albumen / Globulin
0.328	4.534	1.609	6.471	2.8	26	0.305	4.836	1.761	6.902	2.7
0.298	4.185	1.431	5.914	2.9	27	0.437	4.837	2.661	7.935	1.8
0.354	5.308	2.646	8.308	2.0	28	0.336	5.182	1.777	7.295	2.9
0.364	4.837	1.513	6.714	3.1	29	0.437	5.308	3.602	9.347	1.4
0.305	4.268	3.804	8.377	1.1	30	0.354	4.946	1.868	7.168	2.6
0.312	4.353	2.041	6.706	2.1	31	0.320	4.107	2.772	7.199	1.4
0.364	5.440	2.161	7.965	2.5	32	0.354	4.837	2.347	7.538	2.0
0.364	4.534	2.102	7.000	2.1	33	0.345	4.387	2.762	7.494	1.5
0.385	4.353	2.843	7.581	1.5	34	0.410	4.925	2.453	7.788	2.0
0.354	4.837	2.587	7.778	1.8	35	0.385	4.770	3.180	8.335	1.5
0.385	4.441	3.449	8.275	1.2	36	0.345	4.692	3.274	8.311	1.4
0.437	5.182	3.160	8.779	1.6	77	0.423	4.650	2.288	7.361	2.0
0.345	4.630	1.885	6.860	2.4	38	0.323	4.925	2.794	8.042	1.7
0.423	4.353	2.141	6.917	2.0	39	0.399	4.353	3.170	7.922	1.3
0.328	5.182	2.119	7.629	2.4	40	0.426	4.732	3.375	8.533	1.4
0.364	5.440	2.918	8.722	1.8	41	0.322	4.770	2.493	7.585	1.9
0.312	5.182	2.763	8.257	1.8	42	0.350	4.946	3.175	8.471	1.5
0.364	5.440	2.716	8.520	2.0	43	0.437	4.591	2.521	7.549	1.8
0.345	4.534	2.376	7.255	1.9	44	0.360	4.030	3.142	7.532	1.2
0.328	4.742	2.194	7.264	2.1	45	0.298	5.182	3.069	8.549	1.6
0.312	5.308	2.119	7.739	2.5	46	0.435	4.030	2.843	7.308	1.4
0.385	4.441	2.762	7.588	1.6	47	0.468	5.084	3.271	8.823	1.5
0.354	4.534	2.376	7.264	1.9	48	0.372	4.516	2.376	7.264	1.9
0.410	4.534	1.850	6.794	2.4	49	0.375	4.692	2.339	7.406	2.0
0.410	4.732	2.820	7.962	1.6	50	0.358	4.591	2.332	7.281	1.9

ABSTRACT OF FINDINGS IN CONTROL CASES. TABLE II.

	MEAN.	Standard Deviation.	Coefficient of variation.	Range.
Fibrin	0.366 ± 0.0041	0.043	9.194 ± .625	0.298 - 0.468
bumen	4.745 ± 0.0353	0.370	7.796 ± .529	4.030 - 5.440
obulin	2.560 ± 0.0533	0.559	21.822 ± 1.494	1.431 - 3.804
tal Proteins	7.671 ± 0.0660	0.692	9.022 ± .613	5.914 - 9.347

In this table the first column gives the Arithmetic Mean with the probable Error of the Mean. The Probable Error of the Determination of any value gives the measure of unreliability of the Determination : that is to say that the Probable Error is a pair of values lying one above and the other below the value determined. The Probable Error of the Mean is determined by the following formula:-

$$\text{Probable Error} = \pm .67449 \times \frac{SD}{\sqrt{N}}$$

when SD = Standard deviation

N = Number of observations.

As the Mean represents only one aspect of the observations, it seemed advisable to investigate the dispersion of the series and this is represented in the second column as the "Standard Deviation". These figures are obtained for each protein by taking the square of the individual variations, adding them together and taking the square root of the average:

i.e. Standard Deviation = $\sqrt{\frac{\Sigma d^2}{n}}$

when d = individual deviation

Σ = sum of ditto.

λ = number of observations.

The Standard Deviation is of little value for purposes of comparison as it merely represents an absolute variation, independent of the size/

size of the Mean, so that the next step was to determine the Coefficient of Variation. The Coefficient of Variation represents a relative as compared with an absolute variation and is determined by taking the Standard Deviation divided by the Mean and expressing it as a percentage.

i.e. Coefficient of Variation = $\frac{SD \quad x\ 100}{M}$

when SD = standard deviation

M = mean.

For purposes of accurate comparison the Mean, the Probable Error of the Mean, the Standard Deviation and Coefficient of Variation have been determined in each of the following sections that contain a sufficient number of cases.

Fibrin.

These readings are very constant and the normal range of the Fibrin moiety is considerably less than that of either of the other constituent proteins. In 36 cases (72%) the amount present is between 0.30 and 0.40 gms. per 100 cc. In 12 cases the quantity is over 0.40 gms. per 100 ccs. and in 2 of these, it exceeds 0.45 gms. per 100 cc. In 2 cases the reading is less than 0.30 gms. per 100 cc. and in both of these, the amount by which it falls short is only 0.002 gms. per 100 cc.

It may be concluded therefore that any Fibrin reading that is above 0.45 gms. per 100 cc. or that is definitely below 0.30 gms. per 100 cc. is abnormal.

Albumen.

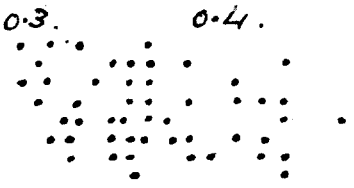
The Albumen readings vary between 4.030 gms. per 100 cc. and 5.440 gms. per 100 cc., a range of 1.410 gms. In 12 cases the quantity exceeds 5.00 gms. per 100 cc. and in 76% the amount is above 4.500 gms. per 100 cc. It will be seen later that in no diseases are the readings higher than in certain of these normal cases. On the other

hand/

NORMALS (MODE) GRAPH I

FIBRIN

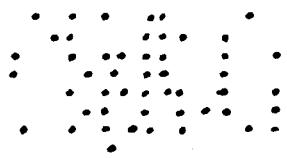
0·2. 0·3. 0·4.



Scale = 1/10 = ·01 gms.

ALBUMEN

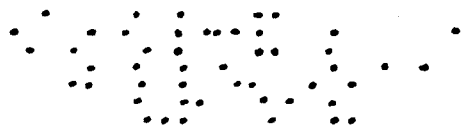
3·0 4·0 5·0 6·0.



Scale = 1/10 = ·10 gms

GLOBULIN

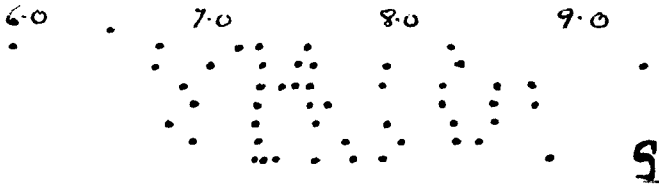
1·0 2·0 3·0 4·0



Scale = 1/10 = ·10 gms

TOTAL PROTEINS

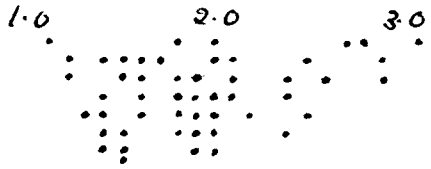
6·0 7·0 8·0 9·0



Scale = 1/10 = ·10 gms

ALBUMEN GLOBULIN

1·0 2·0 3·0



Scale 1/10 = ·10.

hand, in various pathological conditions, the readings fall below 4.00 gms. per 100 cc. Findings, therefore, below 4.00 gms. are certainly abnormal and are probably indicative of impaired renal function.

Globulin.

These results are extremely variable and show a range of 2.373 gms. between the highest and lowest readings. The Coefficient of Variation is 21.822,as compared with 7.796 in the Albumen readings. In 12 cases the reading is above 3.00 gms. per 100 cc. but in only 2 of these is the reading over 3.5 gms. per 100 cc. In 1 case the amount is less than 1.5 gms. per 100 cc. For practical purposes the Globulin can be considered abnormal, only if the amount exceeds 3.5 gms. per 100 cc. or is less than 1.4 gms. per 100 cc.

Total Proteins.

The Total Protein figures also show a wide range: the difference between the highest and lowest readings is as much as 3.433 per 100 cc. In 56% of cases the Total is between 7.0 gms. per 100 cc. and 8.0 gms. per 100 cc., in 28% it is above 8.0 gms. per 100 cc. and in 18% it is below 7.0 gms. per 100 cc.

The relation of the constituents to each other.

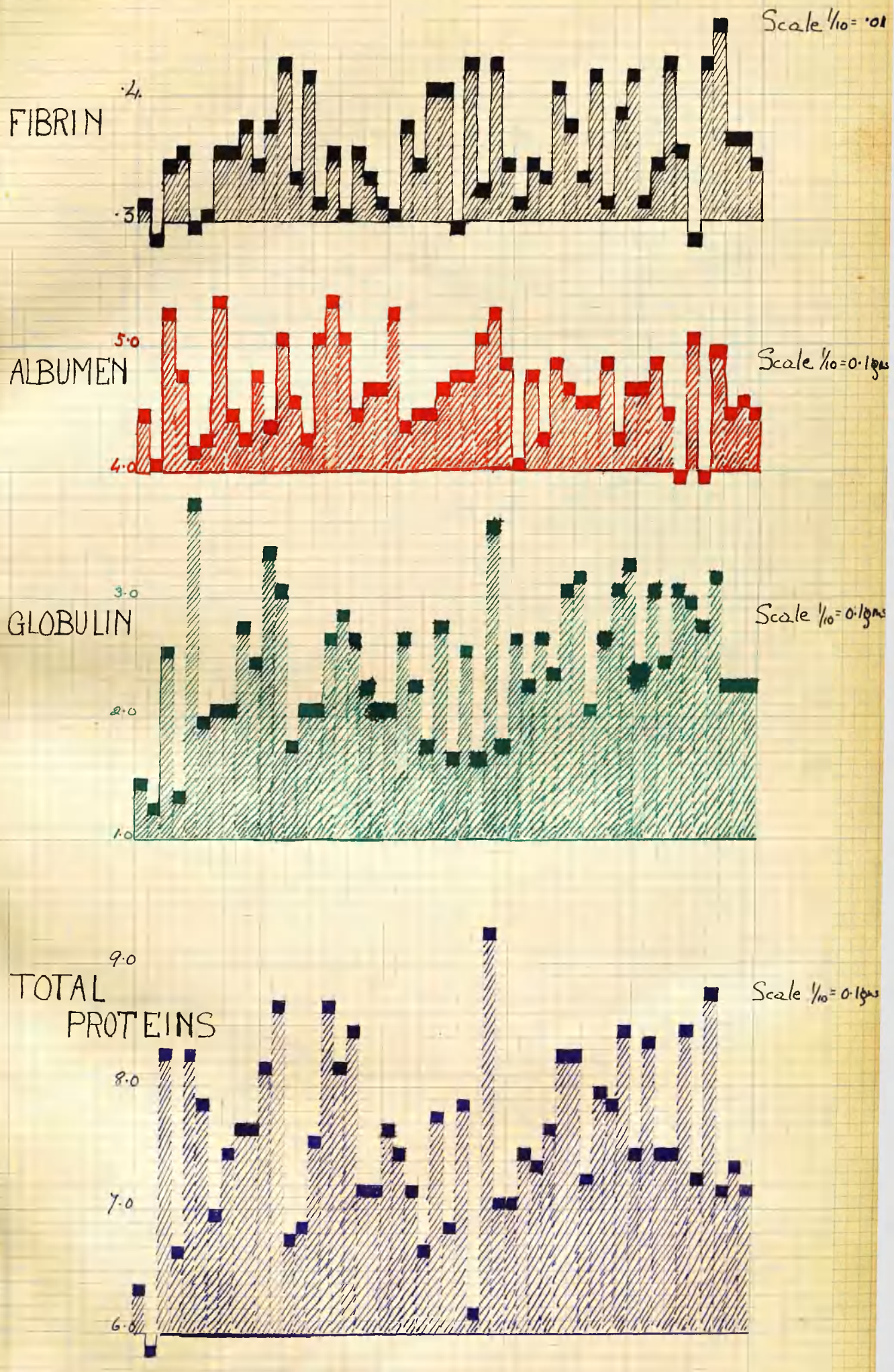
No definite relation between the constituent proteins can be discovered by studying the readings in Table I.

In a certain number of cases, a high Fibrin reading is accompanied by a high Globulin reading (e.g. Nos 12, 25, 27, 29, 40) though this is inconstant. No definite relation can be established between the Fibrin and Albumen readings. The importance of the Albumen/Globulin ratio has been emphasized by certain writers. In the cases under consideration the results show that there is a wide range in the normal subject. In 82% of the

control/

NORMALS

RELATION OF PLASMA PROTEINS GRAPH II



control cases the Albumen/Globulin ratio is 1.5 or more, the majority of cases falling between 1.5 and 2.0. Nor are the Albumen and Globulin figures complementary to each other, a high reading in one being often associated with a high reading in the other. (e.g. Nos 12, 29, 40) rather than with a complementary decrease.

The Total Protein readings vary considerably and as the Globulin range is wider than that of the other constituents, the Total figures bear a certain irregular relation to the Globulin readings.

The relation of the various constituents to each other are represented graphically in the accompanying chart (Graph II). Note in the fibrin graph 1 small square = 0.01 gms. and in the other graphs, one small square = 0.10 gms.

Other results obtained by the Colorimetric Method.

In his original article Hsien Wu gives examples of five normal cases in whom the plasma proteins were estimated by the Colorimetric Method.(7) His findings are as follows:-

Fibrin.	Albumen.	Globulin.	Total Protein.
-	4.55 gms.	1.95 gms.	6.50 gms.
-	4.80 gms.	1.75 gms.	6.55 gms.
=	5.28 gms.	2.23 gms.	7.51 gms.
(0.222 gms.)	4.75 gms.	1.87 gms.	6.62 gms.
-	4.89 gms.	2.65 gms.	7.52 gms.

When this table is compared with the findings in the present series, it will be seen at once that the only Fibrin figure available is much below any of the normal readings/

readings in Table I. The Globulin and Total Protein figures are slightly lower than the average in this series but it must be taken into account that in Wu's cases the fibrin figure is not included in the total. The Albumen results are similar in both investigations. Coetzee,(2) employing the same technique, found the following figures in normal non-pregnant women: Fibrin = 0.32 gms. Albumen = 5.27 gms., Globulin = 2.46 gms. and he states that in males the Fibrin and Globulin are slightly lower and the Albumen is slightly higher. This statement is supported by Salvesan(1) who, also employing Wu's method, found that in males Albumen = 4.44 gms., Globulin = 2.58 gms. whereas in females Albumen = 4.35 gms. and Globulin = 2.68 gms. This difference between the sexes, as previously noted, has not been confirmed in the present series.

The investigators quoted above do not supply any figures for the amount of fibrin present, but Harwitz(4) states that normally 0.3 to 0.4 gms. of fibrin per 100 cc. is present in the plasma and he considers that this is so constant that any diminution in the amount may be considered indicative of hepatic inefficiency. These figures are similar to those in the present series.

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SECTION B.

I. ERYSIPELAS.

Type of Case investigated.

Thirty five specimens of blood were examined, all except Nos. 26, 27, 29, 31, 32, 34 and 35, being withdrawn in the acute phase of the disease. These have been roughly classified as "severe" and"moderately severe". The "severe" cases (Nos. 1-12 and 25-29) all showed, in addition to pronounced local inflammation, symptoms of acute constitutional disturbance - e.g. initial rigor, high temperature (usually rising to 103^{0}-104^{0} during the course of the disease) headache, sickness and delirium. The "moderately severe" cases (Nos. 13-24 and 30-35) were those in which the local infection was unaccompanied by constitutional disturbance, other than slight pyrexia, headache and malaise. All were facial in type except case No. 21 in which the infection arose in a chronic varicose ulcer of the leg. Case No. I was a diabetic patient with a fasting blood sugar of .181 on admission and case No. 8 suffered from chronic nephritis and advanced arterio sclerosis (it may be remarked that in this case the albumen is above rather than below normal, despite the fact that the kidney efficiency was impaired). Certain other cases developed various complications (i.e. case No. 5 developed a fatal cellulitis of the face and case No. 23 a periarticular abscess of the shoulder) but in these cases the estimations were carried out before the onset of these conditions.

(Table - next page).

ERYSIPELAS. TABLE III.

"Severe."

No.	Fibrin	Albumen.	Globulin.	Total	Albumen/Globulin	No.	Fibrin	Albumen.	Globulin.	Total	Albumen/Globulin.
1	1.312	4.185	4.204	9.701	0.9	7	1.312	6.308	3.981	10.601	1.6
2	0.874	5.440	3.861	10.175	1.4	8	0.728	4.946	1.720	7.394	2.8
3	0.984	4.534	3.176	8.604	1.4	9	0.596	5.440	4.124	10.160	1.3
4	0.728	4.185	3.880	8.793	1.0	10	0.690	5.182	4.654	10.526	1.1
5	0.570	4.564	3.362	8.496	1.3	11	0.771	5.420	4.124	10.315	1.3
6	0.820	4.630	3.274	8.724	1.4	12	0.690	4.630	3.088	8.408	1.4

"Severe" Cases.

Table III shows the findings in twelve severe cases. The greatest deviation from normal is in the fibrin content which in every instance is above normal. The maximum fibrin (1.312 gms per 100 cc) is more than twice the maximum reading in the control series and is only equalled by a case of pneumonia. The Coefficient of Variation is almost 3 times as great as in the normal cases. The Albumen content is only slightly increased. The mean is a little higher than in the normal series and in five cases the reading exceeds 5 gms per 100 cc, but in all the estimations the readings fall within normal limits. The Globulin is increased in all cases except No. 8 so that the Albumen/Globulin ratio is below normal. As both Fibrin and Globulin are increased, and as in many cases the Albumen figure is above the normal average, the Total Protein readings are high, no less than 5 cases giving an amount over 10 gms per 100 cc.

"Moderately Severe." TABLE IV.

No.	Fibrin	Albumen.	Globulin.	Total	Albumen/Globulin	No.	Fibrin	Albumen.	Globulin.	Total	Albumen/Globulin.
13	0.504	4.732	3.088	8.324	1.5	19	0.690	4.185	3.685	8.560	1.1
14	0.820	4.441	4.784	10.045	0.9	20	0.596	5.308	3.986	9.890	1.3
15	0.728	4.946	2.794	8.468	1.7	21	0.504	4.837	4.408	9.749	1.0
16	0.570	4.946	4.971	10.487	0.9	22	0.505	4.837	4.154	9.496	1.1
17	0.570	4.946	2.293	7.809	2.1	23	0.468	4.946	2.946	8.360	1.6
18	0.656	4.441	4.062	9.159	1.0	24	0.624	4.630	3.820	9.074	1.2

"Moderately Severe" Cases.

Table IV shows the results in twelve moderately severe cases (Nos. 13-24). In these the rise in the Fibrin content is not so great as in the acute cases although it is consistently above the normal maximum. The Albumen exceeds 5 gms. per 100 cc. only in one case and shows a lower average than in the acute cases. The Globulin readings maintain a high level, the average Globulin being slightly higher than in the acute cases. The A/G ratio is lower than in the acute cases and definitely below the average normal. The average Total Protein readings reach almost as high a level as the Total Protein readings in the acute cases, though in only one case is the quantity more than 10 gms. per 100 cc.

Abstract of findings in Erysipelas. TABLE V.

Severe.	No. of Cases.	Mean.	Standard Deviation.	Coefficient of variation.	Range.
Fibrin	12	0.832 ± .0456	.234	28.150	0.570 - 1.312
Albumen		4.872 ± .089	.457	9.382	4.185 - 5.440
Globulin		3.620 ± .143	.736	20.345	3.720 - 4.654
Total Proteins		9.324 ± .198	1.016	10.840	7.394 -10.601
Moderate	12				
Fibrin		0.603 ± .020	.101	16.720	0.504 - 0.820
Albumen		4.766 ± .057	.293	6.149	4.441 - 5.308
Globulin		3.749 ± .153	.788	21.034	2.293 - 4.971
Total Proteins		9.881 ± .152	.783	8.595	7.809 -10.487

(Table - next page).

Course of the Disease. TABLE VI.

Case	No.	Day.	Fibrin	Albumen	Globulin	Total	A/G .
(i)	25	7th	0.874	4.732	3.375	8.981	1.3
"Severe"	26	14th	0.624	4.946	4.320	9.890	1.1
	27	25th	0.385	4.630	2.840	7.855	1.6
(ii)	28	4th	0.624	4.624	3.274	8.522	1.4
"Severe"	29	7th	0.656	4.736	2.994	8.386	1.5
	30	5th	0.524	4.732	4.515	9.771	1.0
(iii)	31	11th	0.546	4.720	2.653	7.919	1.7
"Moderately Severe"	32	27th	0.437	4.630	2.994	7.061	1.5
	33	2nd	0.328	4.441	2.463	7.232	1.7
(iv)	34	5th	0.423	4.630	2.433	7.486	1.9
"Moderately Severe"	35	14th	0.328	4.732	2.339	7.399	2.0

Course of the Disease.

Table VI gives the figures obtained in a series of estimations carried out in four patients during the course of the disease (Nos. 25-35). Two "severe" cases of Erysipelas and two "moderate" cases were selected. The first estimation was carried out during the acute stage of the disease, the second after the temperature had fallen and had remained normal for twenty four hours; in three cases a third estimation was carried out during the late stage of convalescence. These results are illustrated by the accompanying graphs.

(Note: in these and all subsequent graphs the Fibrin is represented by a continuous black line, Albumen by a continuous red line, Globulin by a continuous green line and the Total Protein by a continuous violet line. The scale for the Total Protein reading is in the right hand margin.

Scale:- 1 small square = 0.01 gms in the Fibrin reading and 0.1 gms in the Albumen, Globulin and Total Protein readings.)

In/

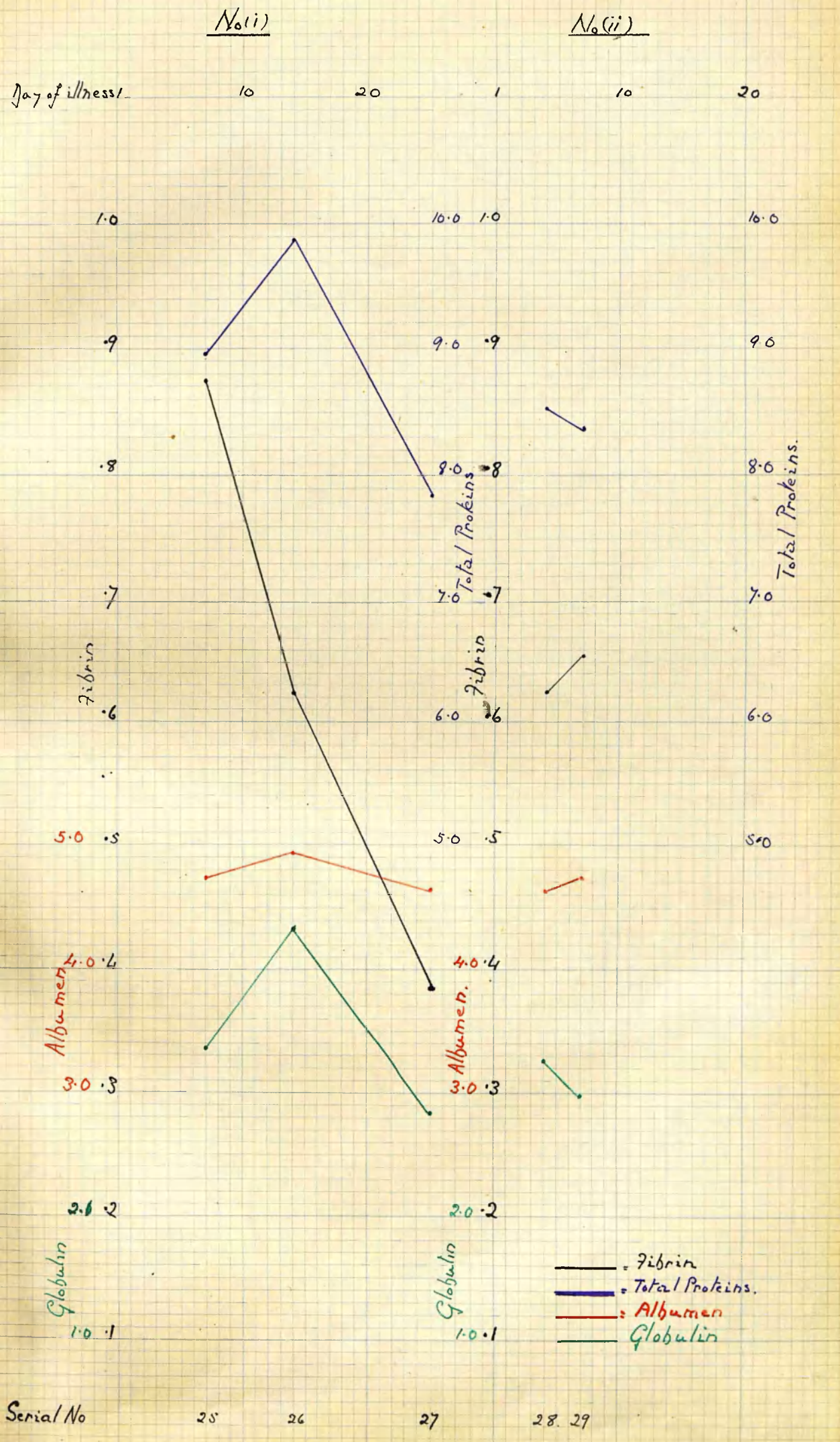
In the first "severe" case, Graph III (i) fibrin is markedly increased by the seventh day of illness and thereafter falls rapidly from 0.874 gms. per 100 cc. to 0.624 gms. per 100 cc. on the fourteenth day and to 0.385 gms. per 100 cc. on the twenty fifth day of illness. In the second "severe" case, Graph III (ii) in whom only two estimations were made, a slight rise in fibrin is seen between the fourth and seventh days of illness. The Albumen shows a slight rise, in both cases between the first and second estimations in the first case a slight decrease follows between the fourteenth and twenty fifth day (Nos. 26 and 27). In the first case the Globulin shows a well marked initial rise from the seventh to the fourteenth day and a subsequent equally definite drop; in the second case the Globulin shows a slight diminution between the first and second estimations. In both cases the Total Protein curve follows that of the Globulin almost exactly.

The third in the series, Graph IV (iii) that of a moderate case, shows a slight increase in fibrin on the fifth day of illness followed by a further rise on the eleventh day, and a subsequent decrease reaching normal by the twenty fifth day. The Globulin and Total Proteins fall steadily after the first estimation though the Globulin rises again slightly between the eleventh and twenty fifth days. The Albumen remains almost level. In the fourth case, Graph IV (iv) no deviation from normal is seen except in the fibrin curve which shows a slight rise between the second and fifth days of illness, followed by a drop to normal by the fourteenth day.

Conclusions./

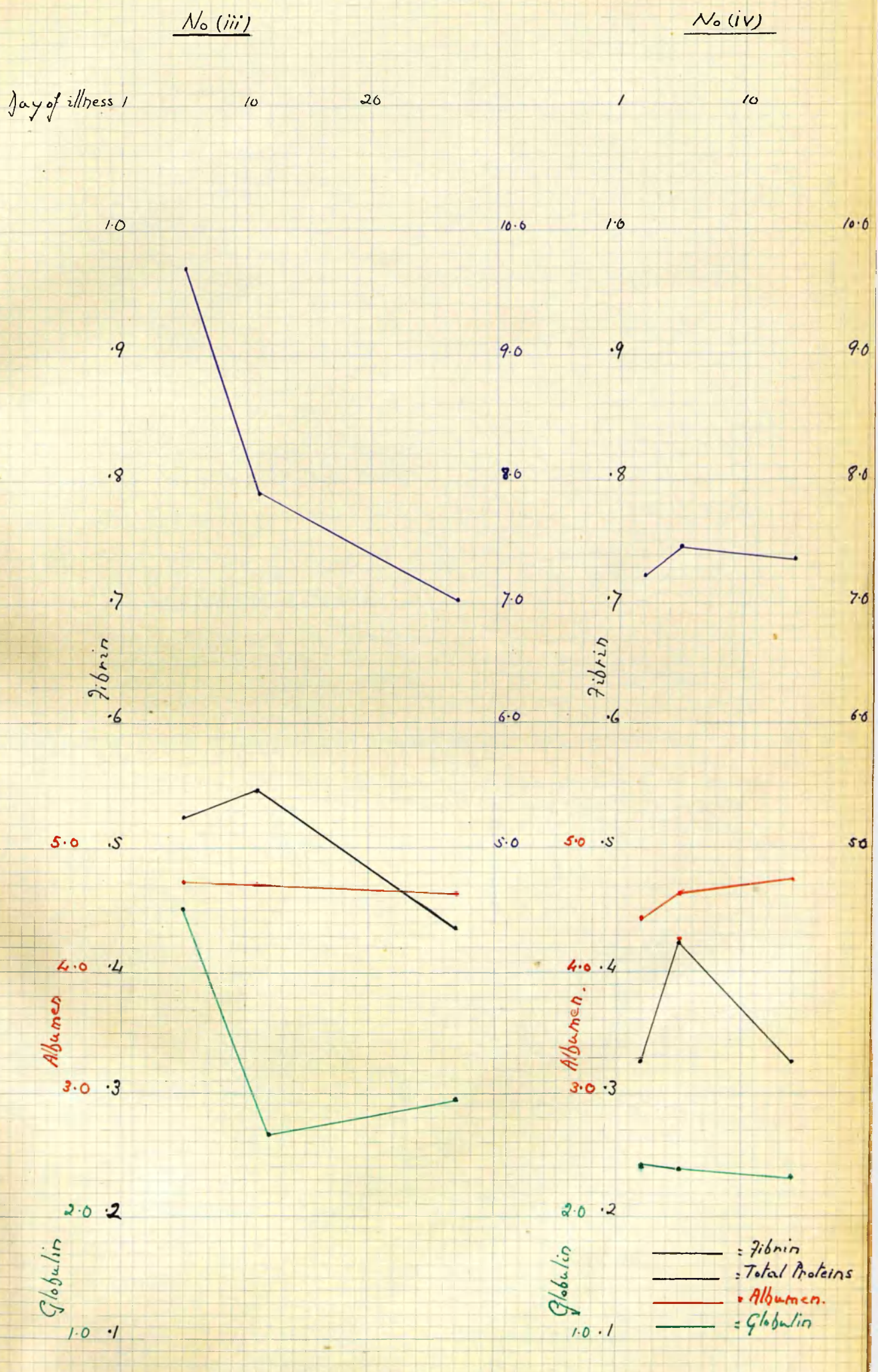
ERYSIPELAS

GRAPH III



ERYSIPELAS

GRAPH IV



Conclusions.

(1) In all cases the amount of Fibrin is increased.

(2) This increase is more pronounced in cases with severe toxaemia but is also present in the milder cases.

(3) The Coefficient of Variation for the Fibrin readings is considerably higher in the "severe" cases than in the "moderate" cases and in both it is very much greater than in the control series.

(4) The Fibrin probably reaches its maximum at the height of the disease and regains normal by the time that the patient is convalescent.

(5) The Albumen is slightly increased but all the readings are within normal limits.

(6) The Coefficient of Variation for the Albumen readings is definitely higher in the severe cases. In the severe cases the figure is greater than in the normal cases and in the moderate cases it falls below normal.

(7) The Globulin readings are increased in the acute stage.

(8) This increase is present both in the severe and in the moderate cases. The Mean Globulin is slightly higher in the moderate cases.

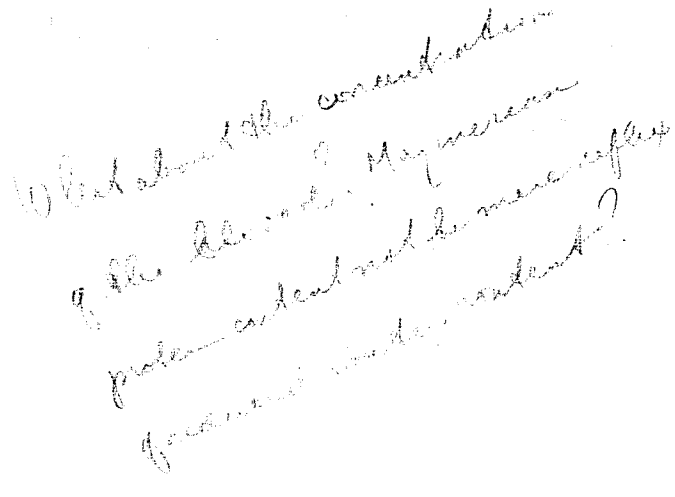
(9) The Coefficient of Variation in the Globulin readings is slightly higher in the moderate cases and in both severe and moderate cases it is rather less than normal.

(10) The Total Proteins are increased in the acute stage.

(11) On the whole the increase is greatest in the severe cases but the high Globulin readings in the moderate cases maintains the Total readings at a high level throughout the entire series.

(12) The Coefficient of Variation in the Total Protein readings is greater in the severe cases.

(13) The Albumen/Globulin ratio is lower than normal but rises during the course of the disease.



II SCARLET FEVER.

Type of Case investigated.

Thirty three estimations were made in patients suffering from Scarlet Fever. In the first twenty cases (Table VII and Table VIII) the estimations were made during the acute period of the illness, usually on the third or fourth day after the onset of symptoms. Eight of these cases were "severe" and twelve were "moderately severe". The remaining thirteen estimations were carried out on five patients at intervals during the disease; of these, two were "severe" and three were "moderately severe". With the exception of Nos. 9, 10, 11 and 13 and the cases in Table X all the patients were children between the ages of 7 and 15 years . No. 9 and Nos. 32 and 33 were two adult women in whom scarlet fever occurred during the first week of the puerperium; neither showed any evidence of pelvic infection but in the second case, when the second estimation was made (No. 33) the patient was suffering from mastitis and it is probable that the presence of this septic focus accounts for the fact that the Fibrin reading had not returned to normal by the end of the second week of illness.

SCARLET FEVER TABLE VII.

"Severe"

No.	Fibrin	Albumen	Globulin	Total	Albumen Globulin	No.	Fibrin	Albumen	Globulin	Total	Albumen Globulin
1.	0.728	3.958	3.347	8.033	1.1	5	0.426	4.185	1.856	6.467	2.2
2.	0.625	4.837	3.073	8.535	1.5	6	0.528	4.591	1.609	6.728	2.8
3.	0.642	4.107	2.246	6.995	1.8	7	0.364	4.302	2.623	7.289	1.6
4.	0.570	5.062	2.874	8.506	1.7	8	0.485	5.084	2.874	8.443	1.7

"Severe" Cases.

All the cases in Table VII were severe and showed considerable prostration, a brilliant rash, severe angina and a temperature over 103°. All were given scarlet fever antitoxic serum on admission to Hospital and the blood was withdrawn/

withdrawn from twelve to twenty four hours later. Case No. 8 was complicated by septic symptoms. In three of these cases (Nos. 5, 7, and 8) the Fibrin reading is hardly above normal though in the remaining five a definite increase is present. In the first case the Albumen reading falls below the lowest reading obtained in the control series and in cases No. 3 and No.5 the readings are also low. The Globulin is within normal limits in every case and in only two is the amount greater than the normal average (Nos. 1 and 2). The Total Protein is slightly increased in four cases only. The Albumen/Globulin ratio with one exception, exceeds 1.5.

SCARLET FEVER — TABLE VIII.

"Moderately Severe".

Fibrin.	Albumen.	Globulin.	Total.	Albumen/Globulin	No.	Fibrin.	Albumen.	Globulin	Total.	Albumen/Globulin
).656	3.627	2.449	6.732	1.4	15	0.560	4.302	3.082	7.944	1.3
).596	4.185	3.699	8.480	1.1	16	0.532	4.185	2.922	7.639	1.4
).468	5.052	2.187	7.707	2.3	17	0.606	4.630	2.589	7.823	1.7
).385	4.534	2.775	7.694	1.6	18	0.642	4.946	3.175	8.763	1.5
).524	4.268	3.423	8.215	1.2	19	0.472	4.477	2.734	7.683	1.6
).528	4.534	1.973	7.035	2.2	20	0.560	4.567	2.540	7.667	1.7

"Moderately Severe" Cases.

Results similar to those obtained in Table VII are found in the more moderate cases. In the greater number the Fibrin shows a definite increase though in three cases only does the quantity present rise above .60 gms. per 100 cc. The Albumen is less than normal in one case, but is otherwise unaffected and the Globulin and Total Protein figures show no characteristic changes. The Albumen/Globulin ratio is variable.

The effect of the injection of Antitoxic Serum.

The injection of antitoxic serum does not appear to modify the readings to an appreciable extent, the cases treated by serum being indistinguishable from those which

were/

were left untreated. This point will be discussed later in the appropriate section.

Abstract of findings in Scarlet Fever. TABLE IX.

	No. of Cases	Mean.	Standard Deviation.	Coefficient of Variation.	Range.
Fibrin	20	0.545 ± .014	.090	16.603	0.364 - 0.728gms
Albumen	"	4.472 ± .057	.378	8.464	3.627 - 5.062gms
Globulin	"	2.702 ± .080	.529	19.614	1.609 - 3.699gms
Total Proteins	"	7.719 ± .099	.654	8.478	6.467 - 8.763gms

SCARLET FEVER. TABLE X.

Course of Disease.

	No.	Day.	Fibrin.	Albumen.	Globulin.	Total.	Albumen/Globulin.
(i)	21	5th.	0.468	4.107	3.398	7.973	1.2
"Severe"	22	8th.	0.504	4.534	3.002	8.040	1.5
	23	17th.	0.397	4.692	2.068	7.157	2.2
	24	4th.	0.524	4.441	2.062	7.027	2.1
(ii)	25	9th.	0.468	4.441	2.922	7.831	1.5
"Severe"	26	15th.	0.423	4.441	2.463	7.327	1.8
(iii)	27	4th.	0.353	4.353	2.544	7.267	1.7
Moderate	28	9th.	0.354	4.630	3.088	8.072	1.4
	29	3rd.	0.452	4.630	1.885	6.967	2.4
(iv)	30	6th.	0.504	5.062	1.888	7.454	2.6
Moderate	31	16th.	0.385	4.732	2.653	7.770	1.7
(v)	32	3rd.	0.524	4.268	2.349	7.141	1.8
Moderate	33	14th.	0.468	4.630	2.433	7.531	1.9

Course of the Disease.

The course of the disease was studied in five cases, 2 of which were "severe" and 3 of which were "moderate". Graph No. V (i) (Table X Nos. 21, 22 and 23) shows the behaviour of the plasma proteins in a severe case treated by antitoxin 24 hours before the first estimation was made. On the 5th day of illness, when the blood was withdrawn, the patient's temperature was still over 103° and she was much prostrated. The graph shows that the Fibrin is slightly increased in the first estimation and that it increases slightly between the 5th and 8th days of illness and is normal by the 18th day. The Albumen rises between the first and second estimation but thereafter remains almost level; the Globulin, slightly above normal in the first two estimations, falls rapidly in convalescence. The Total Proteins show a similar slight increase and subsequent fall.

Graph No. V (ii) (Nos. 24, 25 and 26) illustrate the second "severe" case. In it the Fibrin shows a moderately increase on the fourth day of illness but by the 9th day the amount is hardly above normal and on the 15th day the figure is within normal limits. The Globulin and Total Proteins show a rise between the 4th and 9th days; the Albumen remains constant.

The remaining three graphs Graph VI (iii) and (iv) and Graph VII (v) illustrate the curves in mild cases and show that in all cases the rise in Fibrin, which is never pronounced, is of short duration. The Albumen, Globulin and Total Proteins rise slightly in all cases between the first and second estimations. No. VI (iv) in which a third estimation was made, shows that the globulin rises further between the second and third estimation and that the Albumen falls slightly.

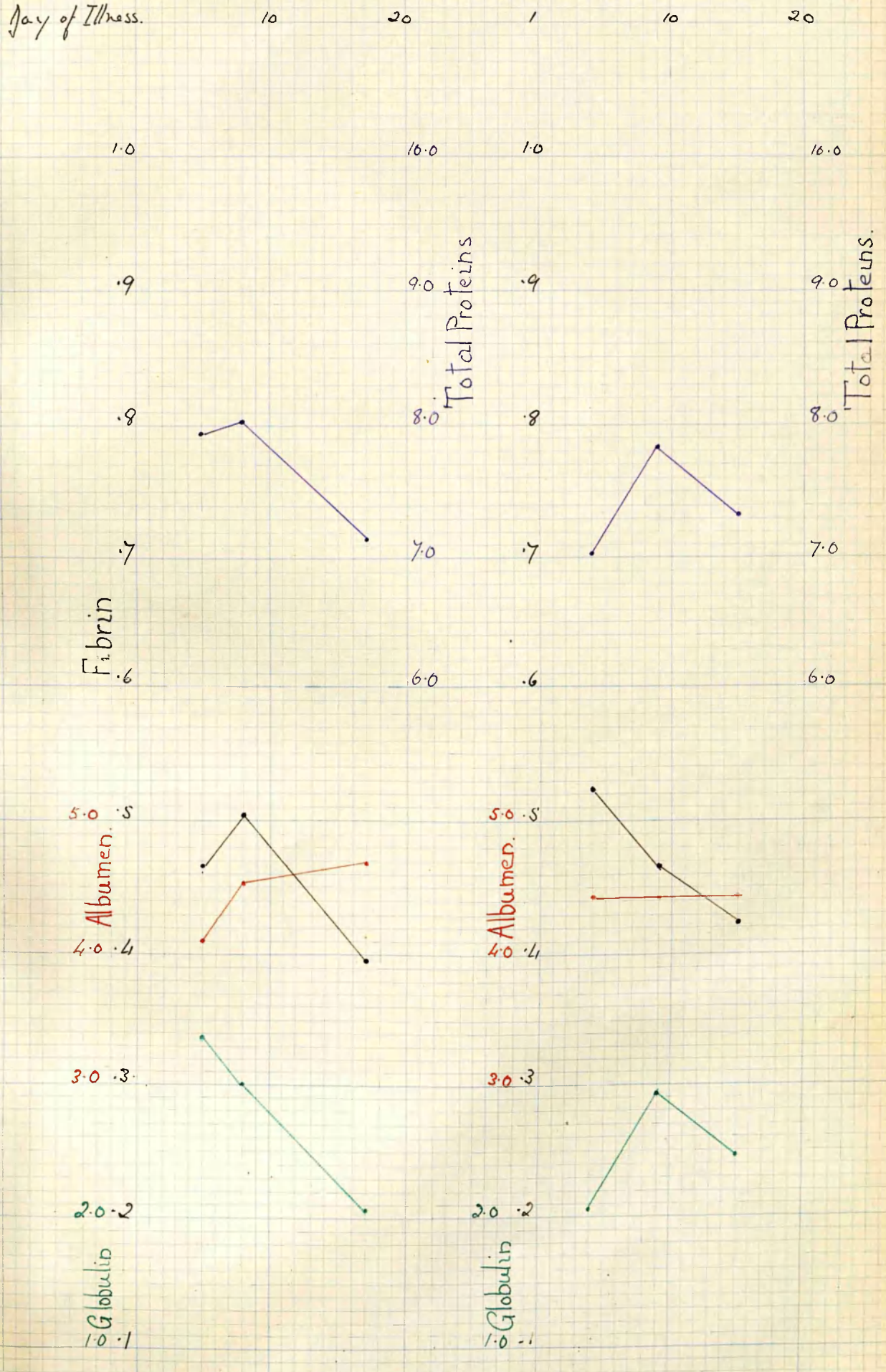
Conclusions./

SCARLET-FEVER.

GRAPH V

No (i)

No (ii)



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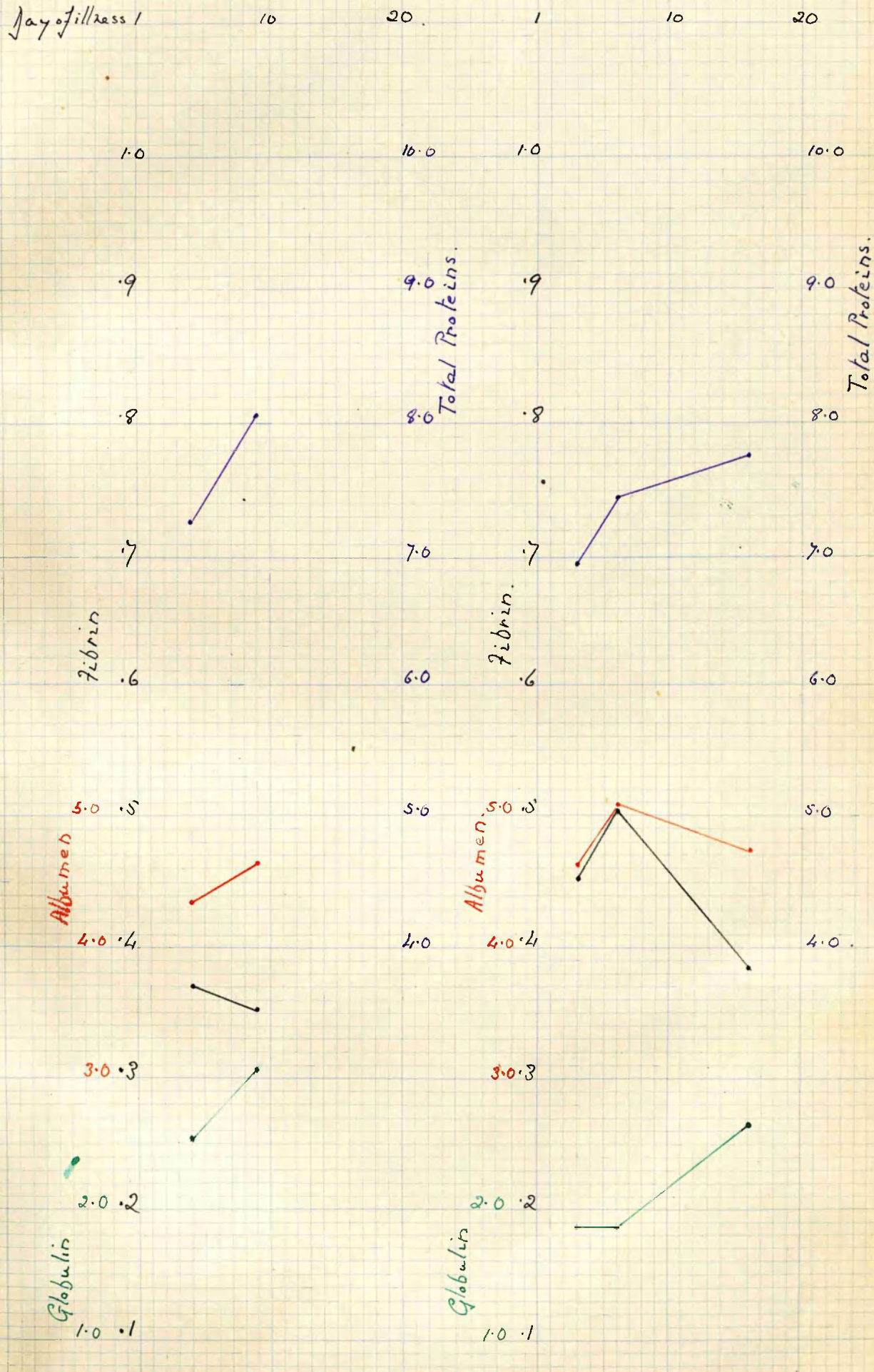
SCARLET-FEVER

GRAPH VI

No (iii)

No (iv)



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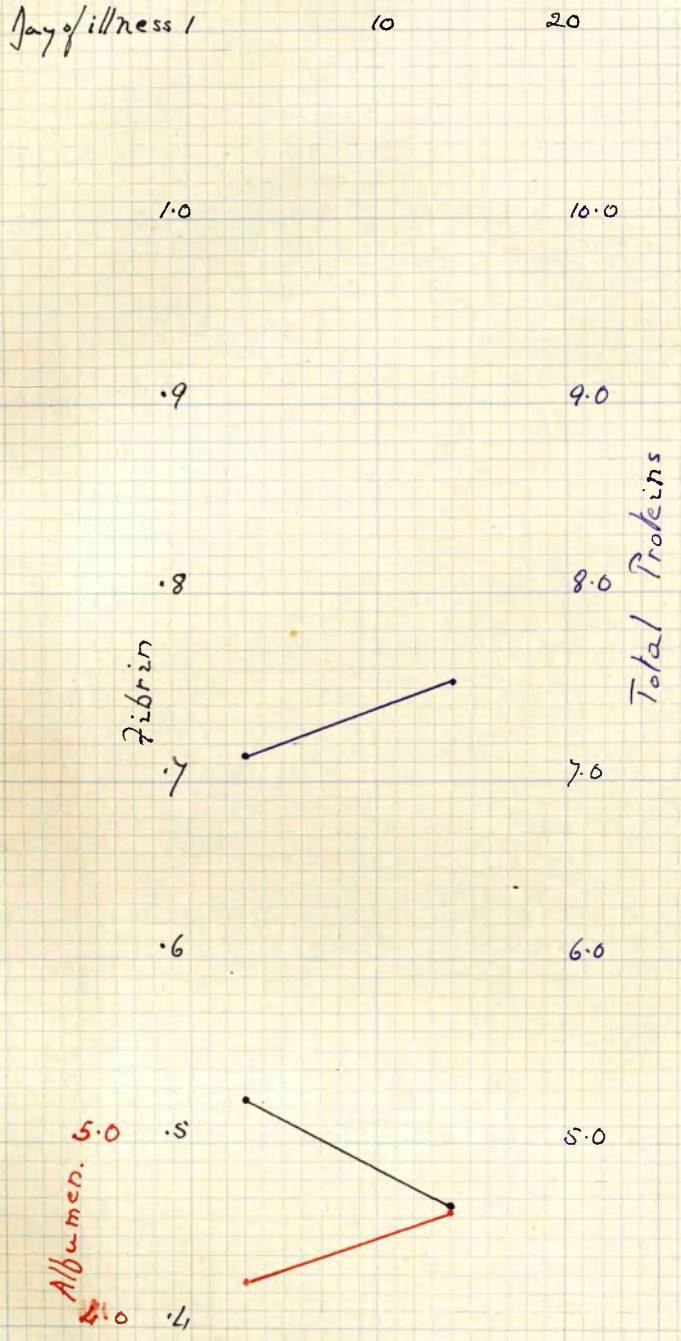
SCARLET-FEVER. GRAPH VII

No (V)



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Conclusions.

(1) There is a moderate but almost constant rise in Fibrin.

(2) This does not appear to depend upon the degree of toxaemia present, nor on the severity of the local symptoms and is practically unaffected by the occurrence of septic complications.

(3) The Coefficient of Variation is similar to that in moderate cases of Erysipelas and is greater than normal.

(4) The Fibrin which may rise between the onset of the disease and the end of the first week of illness probably returns rapidly to normal.

(5) The Albumen is slightly below the normal mean reading and may fall below the normal minimum. In some cases a slight increase is present during the course of the disease.

(6) The Coefficient of Variation falls between that in the severe and that in the moderate cases of Erysipelas and is above normal.

(7) The Globulin is always within normal limits and shows no constant curve during the course of the disease.

(8) The Coefficient of Variation is less than in the normal cases.

(9) The Total Proteins are also little affected, though they may be slightly increased.

(10) The Coefficient of Variation for the Total Proteins is similar to the figures found in Moderate Erysipelas and is slightly below the normal.

(11) The Albumen/Globulin ratio is normal, the majority of cases being above 1.5.

Comparison between Erysipelas and Scarlet Fever.

Cases of severe Scarlet Fever accompanied by a marked degree of toxaemia and pronounced local symptoms do not show such definite alterations in the plasma proteins as is present in severe cases of Erysipelas. Even the moderate cases of Erysipelas show a higher average reading in the Fibrin and Globulin constituents. From this it would appear that different infections, even when caused by closely allied organisms, do not produce the same reaction in the plasma proteins.

In this connection it may be noted that H. Wu found the following readings in a case of streptococcal septicaemia Albumen = 2.76 gms., Globulin 2.80 gms., and Total Proteins = 5.56 gms./

= 5.56 gms. per 100 cc. The Albumen/Globulin ratio = .9. In the two streptococcal diseases under consideration this pronounced diminution in Albumen and Total Proteins has not been found.

III. PNEUMONIA.

Type of Case Investigated.

The blood in pneumonia was examined in forty one cases. Table XI shows the results in 20 cases estimated during the precritical stage of the illness. All were uncomplicated cases of Lobar pneumonia, with the exception of Nos. 1, 17 and 19. In case No. 1 pneumonia was the terminal event in diabetis mellitus (The blood sugar was .212 on admission and Rothera's test was strongly positive in the urine) and in case No. 17 the disease was superimposed on a chronic bronchitis with a failing cardiac compensation. In case No. 19, a child of 10 years, the blood was examined on the 14th day of continued fever, both lungs being in turn affected. The remaining 21 estimations were carried out in 7 cases, at intervals during their illness.

PNEUMONIA. TABLE XI.

No.	Fibrin	Albumen.	Globulin.	Total	Albumen Globulin	No.	Fibrin	Albumen	Globulin	Total	Albumen Globulin.
1	1.312	4.185	4.204	9.701	.9	11	0.830	4.692	4.783	10.305	.9
2	0.880	5.440	3.134	9.454	1.7	12	0.596	4.107	3.758	8.461	1.0
3	0.874	4.477	2.843	8.194	1.5	13	0.750	4.268	4.006	9.024	1.0
4	0.880	4.268	4.006	9.154	1.0	14	0.771	4.477	3.927	9.175	1.1
5	0.546	5.308	3.259	9.113	1.6	15	0.895	4.946	4.061	9.902	1.2
6	0.820	4.268	2.087	7.175	2.0	16	0.800	4.185	2.425	7.410	1.7
7	1.093	4.530	2.935	8.558	1.5	17	0.771	4.732	2.493	7.996	1.8
8	0.830	4.992	4.871	10.693	1.0	18	0.874	4.946	3.593	9.413	1.3
9	0.624	4.030	3.302	7.956	1.2	19	0.596	4.353	2.141	7.090	2.0
10	0.656	3.819	2.916	7.391	1.3	20	0.781	4.883	3.268	8.932	1.4

Case 1-20.

The most striking feature in Table XI is the marked increase in Fibrin in almost all cases, comparable to that in severe Erysipelas. In two cases the figure exceeds 1 gm. per 100 cc.

The/

The Albumen readings show wide variations (a maximum of 5.440 gms. per 100 cc. and a minimum of 3.819 gms. per 100 cc.) but the average is normal. The amount of Globulin is increased in about three fourths of the cases and in six cases the quantity has risen above 4 gms. per 100 cc. There is however no constant relation between the Fibrin and Globulin figures - e.g. case No. 7 gives a very high Fibrin reading (1.093 gms. per 100 cc. with a normal Globulin reading (2.935 gms. per 100 cc.) and cases Nos. 2 and 4 have an identical amount of Fibrin give readings of 3.134 gms. of Globulin per 100 cc. and 4.006 gms. per 100 cc., respectively. The Albumen/Globulin ratio is inconstant ranging between .9 and 2.0 but in the majority of cases it is less than 1.5 and the average is only 1.3. As the Fibrin and in most cases the Globulin also, is increased, the Total Proteins reading is high, about three fourths of the cases estimated being above the average normal. In half of the cases the total is over 9 gms. per 100 cc. and in two cases the amount exceeds 10 gms. per 100 cc.

Abstract of Findings in Pneumonia. TABLE XII.

	No. of cases.	Mean.	Standard Deviation.	Coefficient of Variation	Range.
rin	20	0.809 ± .026	.170	21.180	0.546 - 1.312
umen	"	4.545 ± .064	.427	9.399	3.819 - 5.440
bulin	"	3.401 ± .118	.782	23.057	2.087 - 4.871
tal Proteins	"	8.755 ± .152	1.006	11.488	7.092 -10.305

PNEUMONIA: COURSE OF THE DISEASE. TABLE XIII.

Case.	No.	Day.	Fibrin.	Albumen.	Globulin.	Total.	Albumen / Globulin.
(i)	21	5th	0.570	4.441	1.937	6.937	2.2
	22	9th	0.481	4.781	2.339	7.601	2.0
	23	20th	0.364	5.308	1.134	6.806	4.6
(ii)	24	4th	0.820	4.732	2.994	8.546	1.5
	25	8th	0.690	4.477	2.335	7.502	1.4
(iii)	26	4th	0.771	4.732	1.427	6.930	3.3
	27	8th	0.704	4.534	1.609	6.847	2.8
	28	20th	0.385	4.692	2.747	7.827	1.7
(iv)	29	5th	0.880	4.732	4.261	9.873	1.1
	30	9th	0.397	4.534	2.376	7.307	1.9
	31	15th	0.385	4.532	3.759	8.678	1.2
(v)	32	2nd	0.570	-	-	-	-
	33	4th	0.820	4.477	2.463	7.760	1.8
	34	8th	0.728	4.353	3.170	8.251	1.3
	35	15th	0.410	4.532	2.102	8.046	2.1
(vi)	36	2nd	0.820	4.946	3.593	9.359	1.3
	37	5th	0.704	4.692	2.014	7.410	2.3
	38	7th	0.704	4.946	1.720	7.370	2.8
	39	16th	0.423	4.732	1.791	6.946	2.6
(vii)	40	5th	0.874	4.946	3.593	9.413	1.3
	41	10th	0.570	5.062	1.880	7.512	2.6

The Course of the Disease.

The variations in the plasma proteins, during the course of the disease were studied in 7 cases. In 5 of these, the first estimations were made on the 4th or 5th day of illness, but in two cases specimens were available on the 2nd day.

Case (i) was a girl aged 14 years, admitted on the 4th day of the disease, acutely ill, with high pyrexia, delirium and extreme cyanosis. The percussion note was impaired at the left base, but otherwise the physical signs were negative until the 7th day of illness when definite tubular breathing was present over the left lower lobe. The temperature fell by lysis between the 7th and 9th days. The readings in these estimations were not typical of Lobar Pneumonia. The Fibrin was only slightly increased and the Globulin reading was rather less than normal in the first estimation. The Fibrin fell slightly in the subsequent estimations; the Globulin first increased but fell to a very low figure in the third estimation; the Albumen showed a rise on each occasion. The Total Proteins were low throughout. In view of the fact that the girl gave a history of a cough of several months' duration, the extreme degree of cyanosis present and the indefinite physical signs, the question of an acute tubercular infection was considered. The very low Globulin reading was, however, against this diagnosis (c.f.Pulmonary Tuberculosis) and the patient was dismissed with the lung clear after five weeks in Hospital. It is probable that ~~the~~ this was an Influenzal rather than a Pneumococcal infection (c.f. Influenza).

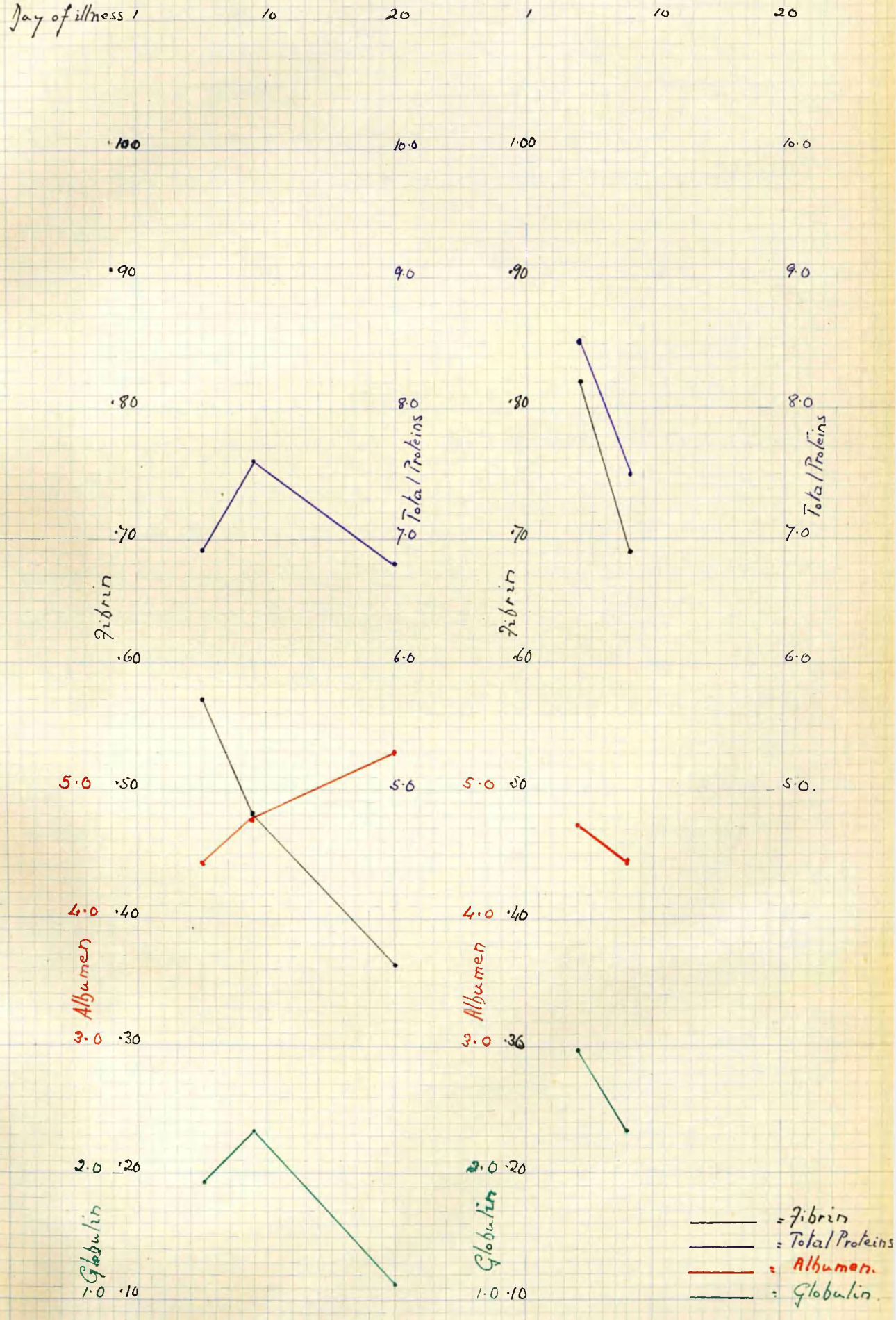
Case (ii) shows the readings in a typical case of Lobar Pneumonia in whom the crisis occurred on the 7th day. All the constituents are increased and show a decided drop after/

PNEUMONIA

GRAPH VIII

No (i)

No (ii)



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after the crisis.

Case (iii) was also typical, with the crisis on the 7th day. There is a decided rise in Fibrin in the precritical stage followed by a postcritical fall. The Globulin which is unusually low in the first estimation rises steadily in the subsequent specimens so that the Total Proteins increase rather than decrease during convalescence. The Albumen remains almost level.

Case (iv), a similar case with the crisis on the 6th day, shows a Fibrin curve similar to the preceding case. A very decided fall in Fibrin occurs between the fifth and ninth days of illness. The Globulin and Total Proteins also fall sharply but rise again in the third estimation. The Albumen is, again, practically constant.

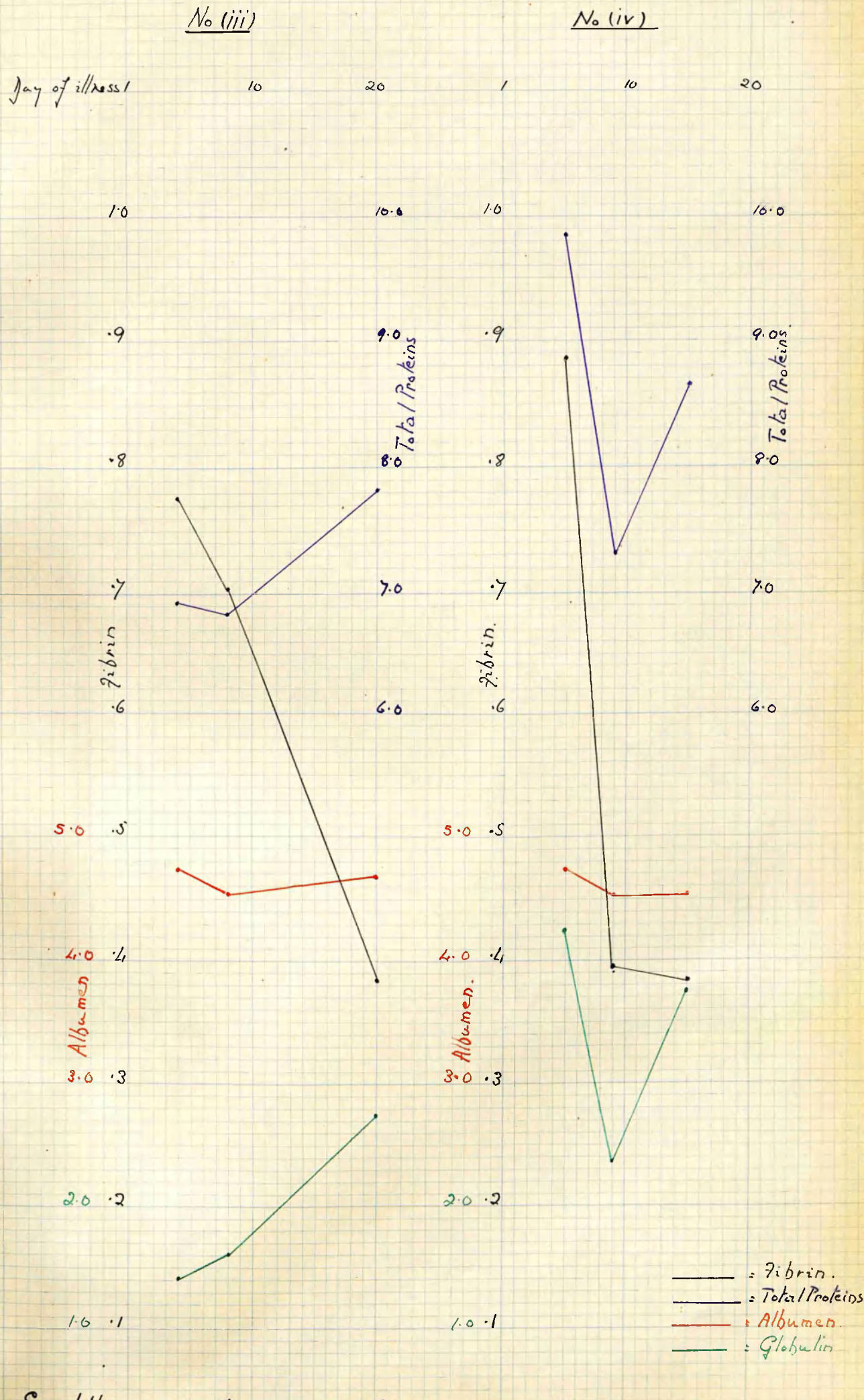
In the next two cases, a specimen was obtained as early as the second day of illness; in Case (v) the Fibrin is only 0.570 gms. per 100 cc. on the second day and rises rapidly to 0.820 gms. per 100 cc. on the fourth day. It falls slightly by the eighth day and is still slightly above normal on the fifth day. The Globulin and Total Proteins show a slight rise between the first and second specimens followed by a fall to normal. The Albumen is slightly increased during convalescence.

Case vi presented features suggestive of enteric fever. She had been "out of sorts" for some days before the onset of her illness and had been constipated. On admission she suffered from diarrhoea accompanied by abdominal pain and distension. Her temperature chart showed a fairly sharp "staircase" rise from the second to the fourth day of illness and it was only on the fourth day that definite physical signs of consolidation were detected in the lungs. The Widal test was negative and the temperature fell by crisis on the seventh day. Examination of the blood on the

second/

PNEUMONIA

GRAPH IX



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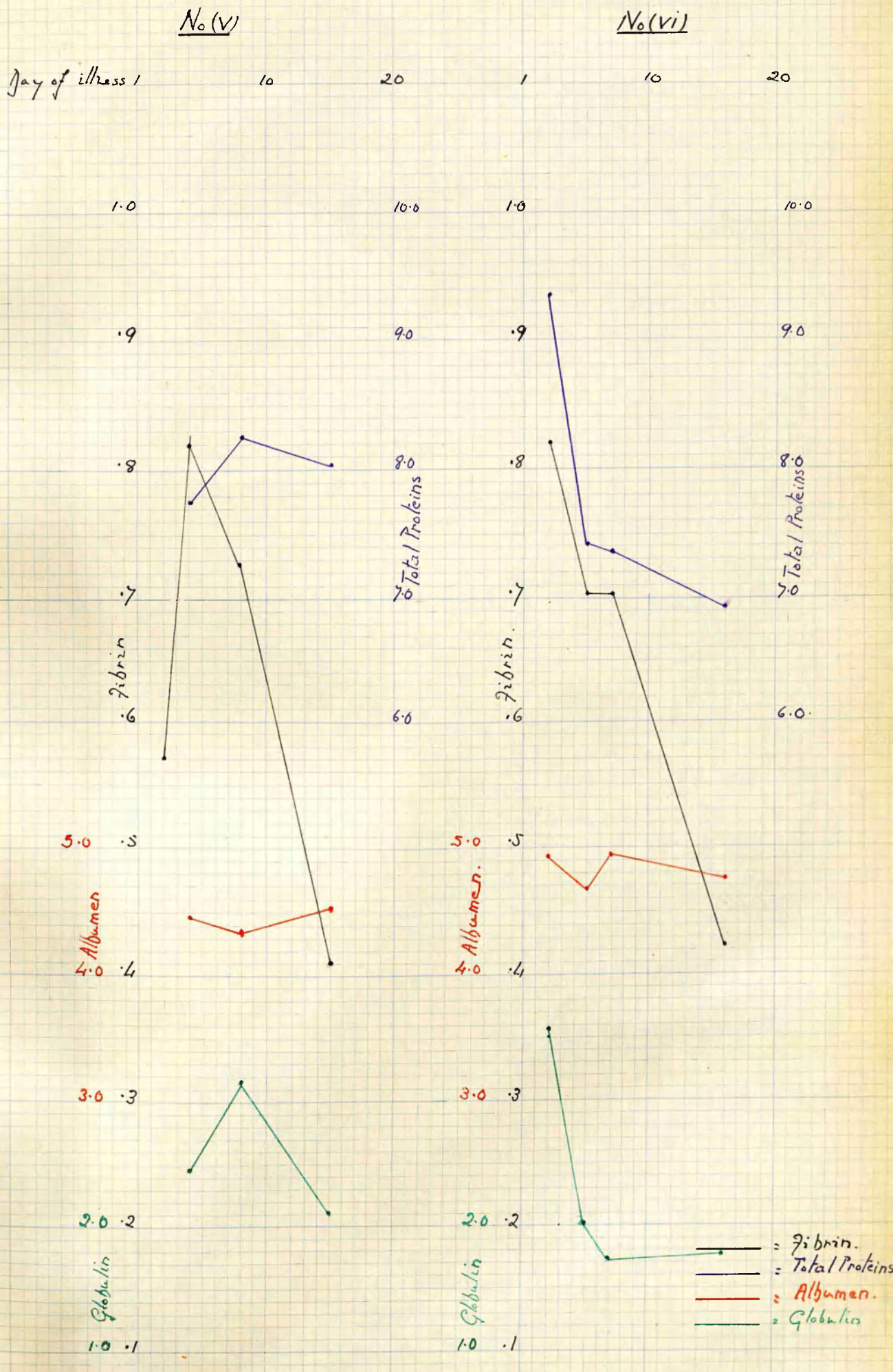
PNEUMONIA

GRAPH X.



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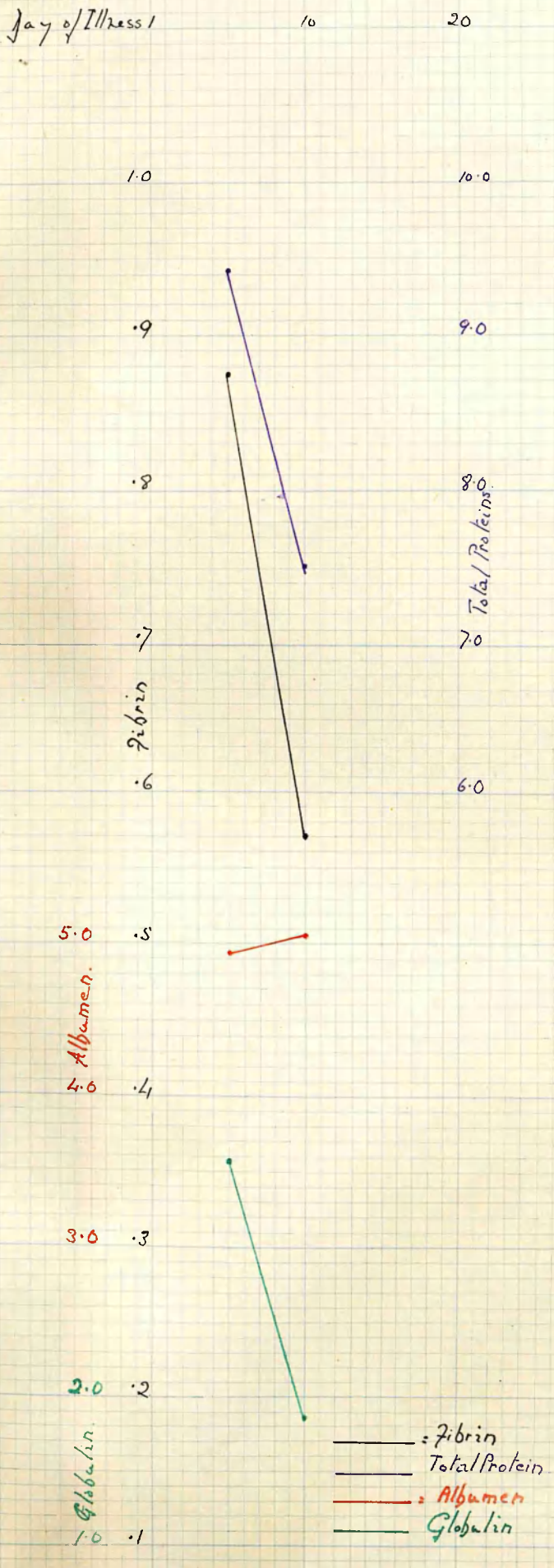
PNEUMONIA GRAPH XI

No (vii)



Serial No. 40 41

second day shows a great increase in Fibrin which drops slightly by the fifth day, remains stationary till the seventh day and is almost normal by the sixteenth day. The Globulin, increased on the second day, falls in each successive estimation and the Total Proteins follow a similar curve. The Albumen findings are irregular but the range of variation is within narrow limits. In view of the definite increase in Fibrin, a feature, as will be demonstrated later, that is not present in enteric fever, it seemed probable as early as the second day - i.e, before the physical signs developed, that this case was one of pneumonia rather than one of enteric fever.

The remaining case (vii) gives a marked increase in Fibrin, Globulin and Total Proteins in the pre-critical estimation, followed by a rapid drop after the crisis. The Albumen is almost constant.

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CONCLUSIONS.

1. The Fibrin content is increased and may be much above normal.

2. It is probable that the maximum is attained early in the illness, that it may begin to fall before the crisis is reached and that thereafter it falls rapidly so that it regains normal by the third or fourth week of illness. The amount is certainly greater in the acute inflammatory period than in the stage of resolution.

3. The Coefficient of Variation for the Fibrin figures is considerably above normal.

4. The Albumen readings are variable, always within normal limits and show little variation during the course of the illness.

5. The Coefficient of Variation for the Albumen readings is also greater than normal.

6. The Globulin is usually increased in the acute stage although this is not so universally true as in cases of Pulmonary Tuberculosis. Its behaviour is not constant during the course of the disease, but in several of the cases stidied, the later readings fall below normal.

7. The Coefficient of Variation for the Globulin readings is high.

8. The Total Proteins are normally increased, the increase varying/

varying largely with the Globulin content.

9. The Coefficient of variation for the Total Proteins is also higher than normal.

10. The Albumen/Globulin ratio is variable, but in three fourths of the cases it is 1.5 or under.

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IV. OTHER INFECTIONS OF THE RESPIRATORY TRACT.

Influenza. TABLE XIV.

No.	Fibrin.	Albumen.	Globulin.	Total	Albumen/Globulin
1	0.312	5.308	1.534	7.154	3.4
2	0.771	3.627	1.682	6.080	2.1
3	0.892	4.353	2.544	7.789	1.7
4	0.624	4.185	2.162	6.971	1.9
5	0.820	4.353	2.444	7.617	1.7
6	0.642	4.185	2.699	7.526	1.5
7	0.820	4.692	2.994	8.506	1.5

Bronchiectasis.

No.	Fibrin.	Albumen.	Globulin.	Total.	Albumen/Globulin.
1	0.771	4.404	4.550	9.705	.9

Influenza.

The blood of seven cases of Influenza complicated by bronchopneumonia was examined and the results are shown in Table XIV. All these cases occurred during the epidemic of March, 1926.

The first example gives a normal Fibrin reading, but all the subsequent specimens show an increase comparable to that present in Lobar Pneumonia. The Globulin on the other hand is not increased and in two cases is well below the average normal. In one case the Albumen content falls definitely below the minimum normal reading; the others are within normal limits. The Total Proteins do not show the marked increase that is seen in pneumococcal infections. The Albumen/Globulin ratio is 1.5 and over.

ABSTRACT OF FINDINGS IN INFLUENZA. TABLE XV.

	No. of Cases.	Mean.	Range.
Fibrin	7	0.697	0.312 - 0.892
Albumen		4.530	3.627 - 5.308
Globulin		2.294	1.534 - 2.994
Total Proteins		7.377	6.080 - 8.506

Conclusions.

1. The Fibrin is almost invariably increased.
2. The Albumen is normal.
3. The Globulin reading is not increased and may even fall below the normal mean.
4. The Total Proteins are not increased.
5. The Albumen/Globulin ratio is 1.5 or over.

Bronchiectasis.

One case of Bronchiectasis in the terminal stage was also examined. In it, both Fibrin and Globulin are increased so that the Total Proteins are high. The Albumen/Globulin ratio is low. These findings are similar to those in cases of Lobar Pneumonia or of advanced Phthisis.

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V. TUBERCULOSIS.

Type of Case investigated.

This series includes twenty cases of Pulmonary Tuberculosis, two cases of Tuberculous Meningitis, one case of Acute Miliary Tuberculosis and two cases of Pleurisy, almost certainly of Tuberculous origin.

The cases of Pulmonary Disease are classified as "Acute" and "Chronic". The Acute cases were all far advanced in the disease, and showed emaciation, pyrexia and extensive physical signs in the lungs. The more chronic cases were those in whom although definite lesions were present in the lungs, there was little or no pyrexia. For the most part the latter class were not confined to bed.

PULMONARY TUBERCULOSIS. (Acute) TABLE XVI.

No.	Fibrin.	Albumen.	Globulin.	Total.	Albumen / Globulin.
1	0.524	4.268	2.220	7.012	1.9
2	0.880	4.441	3.175	8.496	1.3
3	0.820	4.534	4.443	9.797	1.0
4	0.596	4.185	2.699	7.480	1.5
5	0.656	4.534	1.609	6.799	2.8
6	0.728	4.534	4.443	9.705	1.0
7	0.656	4.732	4.261	9.649	1.1
8	0.654	4.185	5.020	9.859	.8
9	0.704	4.534	4.443	9.681	1.0
10	0.642	4.107	4.371	9.120	.9
11	0.370	4.992	4.871	10.233	1.0
12	0.524	4.185	2.699	7.408	1.5

Acute Pulmonary Tuberculosis.

The "Acute" cases with one exception show an increase in fibrin. This increase is not so pronounced as in Pneumonia or severe Erysipelas, but is greater than in Scarlet Fever. The average Albumen content is normal and the readings do not exceed the normal limits. The Globulin reading is above normal average in all but two cases (Nos 1 and 5) and in seven of the twelve cases the amount present is over 4 gms. per 100 cc.

In the greater number of cases therefore the Total Proteins are increased and the Albumen/Globulin ratio is less than 1.5

PULMONARY TUBERCULOSIS.(Chronic) TABLE XVII.

No.	Fibrin.	Albumen.	Globulin.	Total.	Albumen / Globulin
13	0.437	4.185	4.082	8.704	1.0
14	0.660	4.268	3.082	8.010	1.3
15	0.596	3.886	3.603	8.085	1.0
16	0.656	4.353	3.725	8.734	1.1
17	0.524	4.837	4.154	9.515	1.1
18	0.560	4.107	4.155	8.822	.9
19	0.524	5.440	1.834	7.798	2.9
20	0.452	4.837	3.686	8.975	1.3
21	0.504	3.886	2.977	7.367	1.3
22	0.528	4.185	3.572	8.285	1.1
23	0.468	4.268	2.922	7.658	1.4
24	0.570	5.182	4.320	10.672	1.1

Chronic Phthisis.

The "Chronic" cases also show an increase in Fibrin, although the readings do not attain as high a level as in the acute cases. In two cases the Albumen reading is less than 4 gms. per 100 cc., a possible indication of early renal/

renal damage, but the average Albumen content is slightly higher than in the Acute cases. The increase in Globulin is also present in the chronic cases, and though the readings do not reach as high a figure as those in Table XVI, the Albumen/Globulin ratio is very slightly lower. The Total Protein is increased in almost all cases.

ABSTRACT OF FINDINGS IN PULMONARY TUBERCULOSIS.

TABLE XVIII.

	No. of Cases.	Mean.	Standard Deviation.	Coefficient of variation.	Range.
(a) Acute.	12				
Fibrin.		0.711 ± .026	.131	20.303	0.370-0.880
Albumen		4.435 ± .052	.267	6.030	4.107-4.992
Globulin		3.687 ± .214	1.097	29.761	1.609-5.020
Total Proteins		8.769 ± .236	1.213	13.843	6.799-10.233
(b) Chronic	12				
Fibrin		0.498 ± .013	.068	12.729	0.437-0.660
Albumen		4.452 ± .095	.489	10.993	3.886-5.440
Globulin		3.509 ± .132	.686	19.387	1.834-4.320
Total Proteins		8.502 + .147	.755	8.885	7.367-10.072

NON PULMONARY TUBERCULOSIS. TABLE XIX.

No.	Localization.	Fibrin.	Albumen.	Globulin.	Total.	Albumen / Globulin.
25	Meninges	0.350	4.030	3.643	8.023	1.1
26	"	0.452	4.107	3.572	8.131	1.1
27	Generalized	0.452	4.790	4.413	9.655	1.0
28	Pleura	0.596	4.441	3.263	8.300	1.3
29	"	0.598	4.946	4.315	9.859	1.1

Non Pulmonary Tuberculosis.

Cases Nos. 25 and 26 were both cases of Tuberculous Meningitis occurring in adults. In neither was there evidence of gross tubercular disease in the lungs or elsewhere. Case No.26 shows a slight increase in Fibrin but in the other case the Fibrin is unaffected. The increase in Globulin, characteristic of the pulmonary cases, is present in both cases of meningitis and the Albumen readings are below the normal average. The Albumen/Globulin ratio therefore is low. The Total Proteins are moderately increased.

Case No.27 was one of Acute Miliary Tuberculosis occurring in a child of 9 years, who was admitted to Hospital in the second week of illness, certified as Typhoid Fever. The Widal reaction was negative and the diagnosis of generalized tuberculosis was confirmed at autopsy. In this case the Fibrin is only slightly above normal, but the Globulin is very much increased so that, although the Albumen is above the normal average, the Albumen/Globulin ratio is low. The Total Proteins figure is high. If these findings be compared with those in the first two weeks of Enteric Fever, it will be found that in the latter disease, the Fibrin reading is usually below normal and that in no case is there so great an increase in Globulin or so high a Total Proteins figure nor is the Albumen/Globulin ratio so low. These findings therefore were strongly in favour of the case being one of Tuberculosis rather than of Enteric Fever.

Cases Nos.28 and 29 both suffered from Pleurisy with a small amount of effusion and both were almost certainly Tuberculous in type. Both show a moderate increase in Fibrin, a definite increase in Globulin, a high Total Protein and a low Albumen/Globulin ratio.

Conclusions.

1. The Fibrin is increased in all the cases of intrapulmonary disease, in both the acute and chronic form; it is only slightly increased in the cases of Meningitis and in the case of Generalized Tuberculosis; the cases of Pleurisy occupy an intermediate position.

2. The Coefficient of Variation for the Fibrin readings is very much higher in the acute than in the chronic cases and in both it is greater than normal.

3. The Albumen shows little deviation from normal though in a number of cases it is slightly below the normal mean.

4. The Coefficient of Variation for the Albumen readings is higher in the chronic than in the acute cases.

5. The Globulin is increased in three fourths of the cases of pulmonary and in all the cases of extra-pulmonary disease. In half the cases the reading is above 4 gms. per 100 cc.. This is the most characteristic feature in the specimens examined.

6. The Coefficient of Variation for the Globulin readings is considerably greater than normal in the acute cases and slightly less than normal in the chronic cases.

7. The Total Proteins are increased.

8. The Coefficient of Variation, as in the Globulin readings, is above normal in the acute and below normal in the chronic series.

9. The Albumen/Globulin ratio is low. With only three exceptions, it is less than 1.5.

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VI. TYPHUS FEVER.

(These specimens were made available by the courtesy of the staff of Belvidere Hospital).

The course of the disease was studied in four cases. All the cases were acutely ill and all were females. The Weil-Felix reaction was positive. The first specimens of blood were withdrawn in the acute pre-critical stage of the illness, the second specimens on the fourth or fifth day after the crisis and the final specimens at the close of the sixth week when the patients were convalescent.

TYPHUS FEVER.

Course of Disease. TABLE XX.

	No.	Day.	Fibrin.	Albumen.	Globulin.	Total.	Albumen / Globulin.
(i)	1	10th	0.291	4.268	2.623	7.182	1.6
	2.	39th	0.410	4.946	2.980	7.336	1.6
(ii)	3	12th	0.364	4.946	2.192	7.504	2.2
	4	19th	0.385	5.182	2.763	8.330	1.8
	5	41st	0.364	5.182	3.160	8.706	1.6
(iii)	6	16th	0.133	4.441	2.060	6.634	2.1
	7	20th	0.452	4.732	2.994	7.178	1.5
	8	40th	0.397	4.732	3.375	8.504	1.4
(iv)	9	15th	0.114	4.837	2.546	7.497	1.8
	10	20th	0.546	5.182	3.160	8.888	1.6
	11	41st	0.423	5.062	3.268	8.753	1.5

Pre-critical Stage.

The striking feature in the estimations made in the acute stage is the low fibrin content. Cases (iii) and (iv) give the lowest readings in all the diseases studied, case (i) is below normal and case (ii) is about the average normal level./

level. The Globulin readings are normal and no abnormality is noted in the Albumen. The Albumen/Globulin ratio is above 1.5 in all four cases.

Post-Critical Stage.

Immediately after the crisis the Fibrin content rises to a point rather above normal. This rise is very obvious in Cases Nos. (iii) and (iv) but is present in a lesser degree in Case No.(ii). (No second specimen was available in Case No.(i).) There is also a definite increase both in Albumen and Globulin,so that the Total Proteins show a sharp rise. The Albumen/Globulin ratio figure falls in all these cases. This sudden alteration in the plasma constituents has only been noted in this disease.

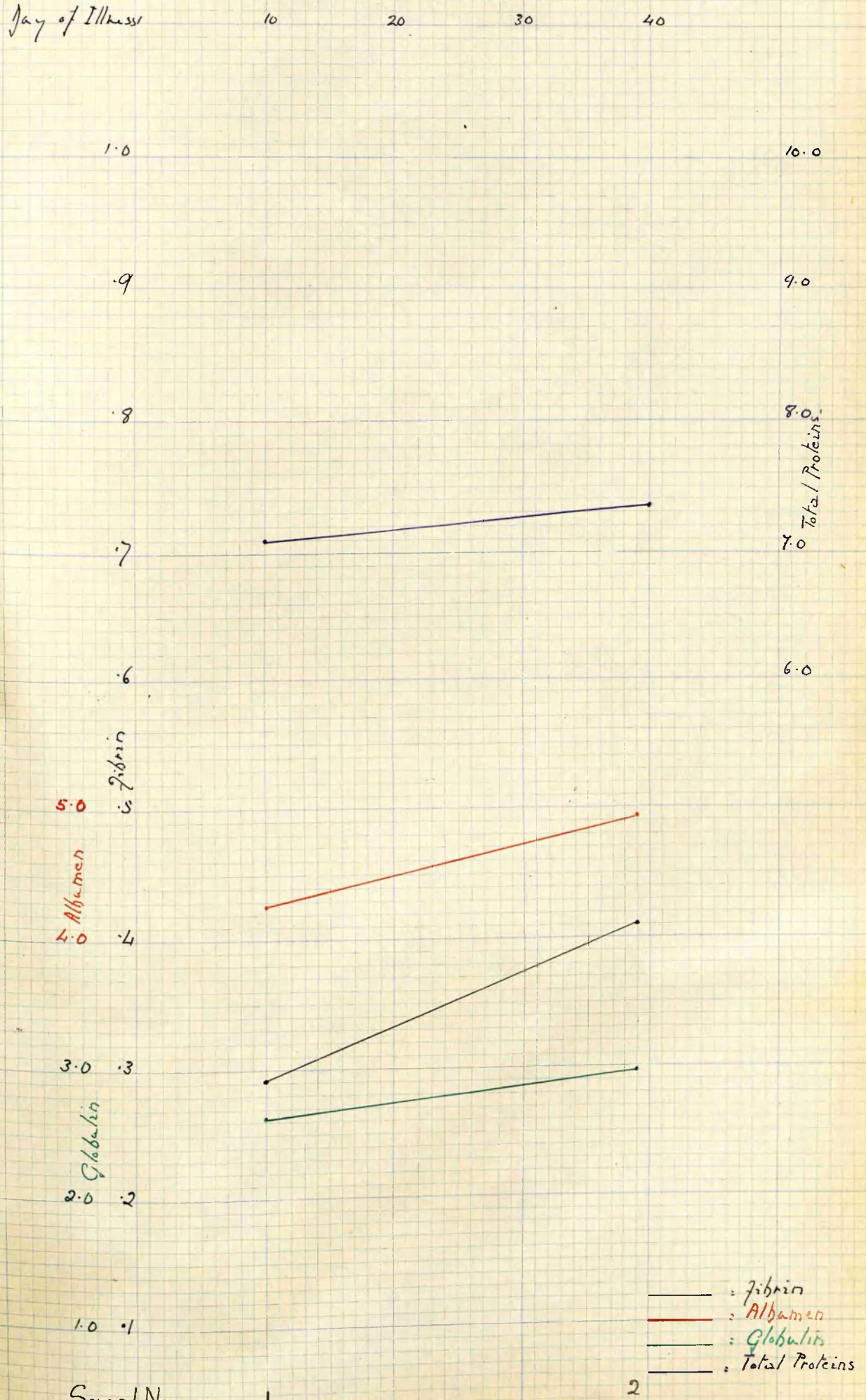
Convalescent Stage.

In the third estimation, carried out when the patients were entirely convalescent, the Fibrin has dropped to normal. The Globulin readings have risen slightly and the Albumen readings maintain their level so that the Total Proteins are further increased in three cases and remains above the average normal in the remaining case. The Albumen/Globulin ratio falls slightly.

TYPHUS FEVER

No (1)

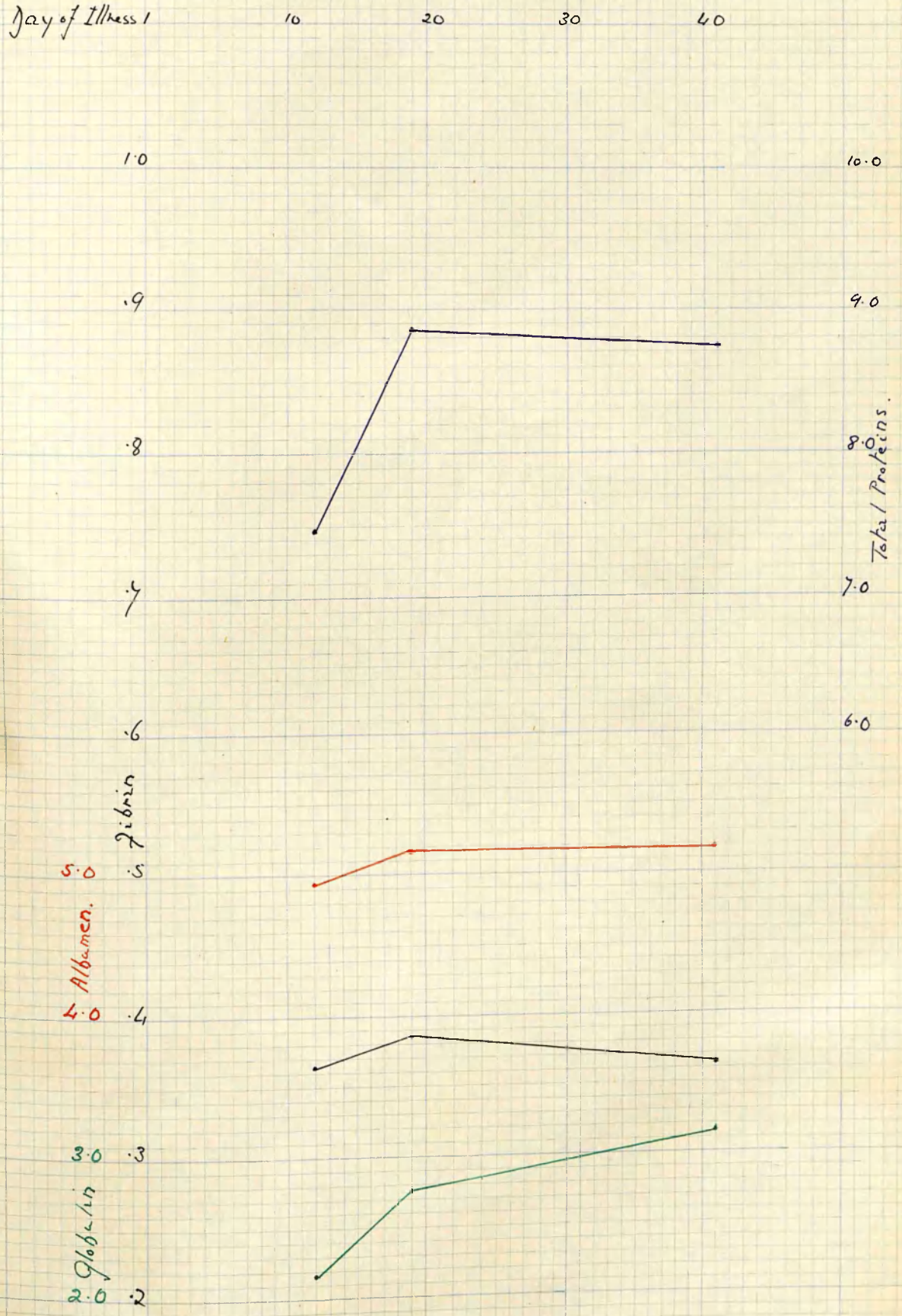
GRAPH XII



TYPHUS FEVER

GRAPH XIII

No (ii).



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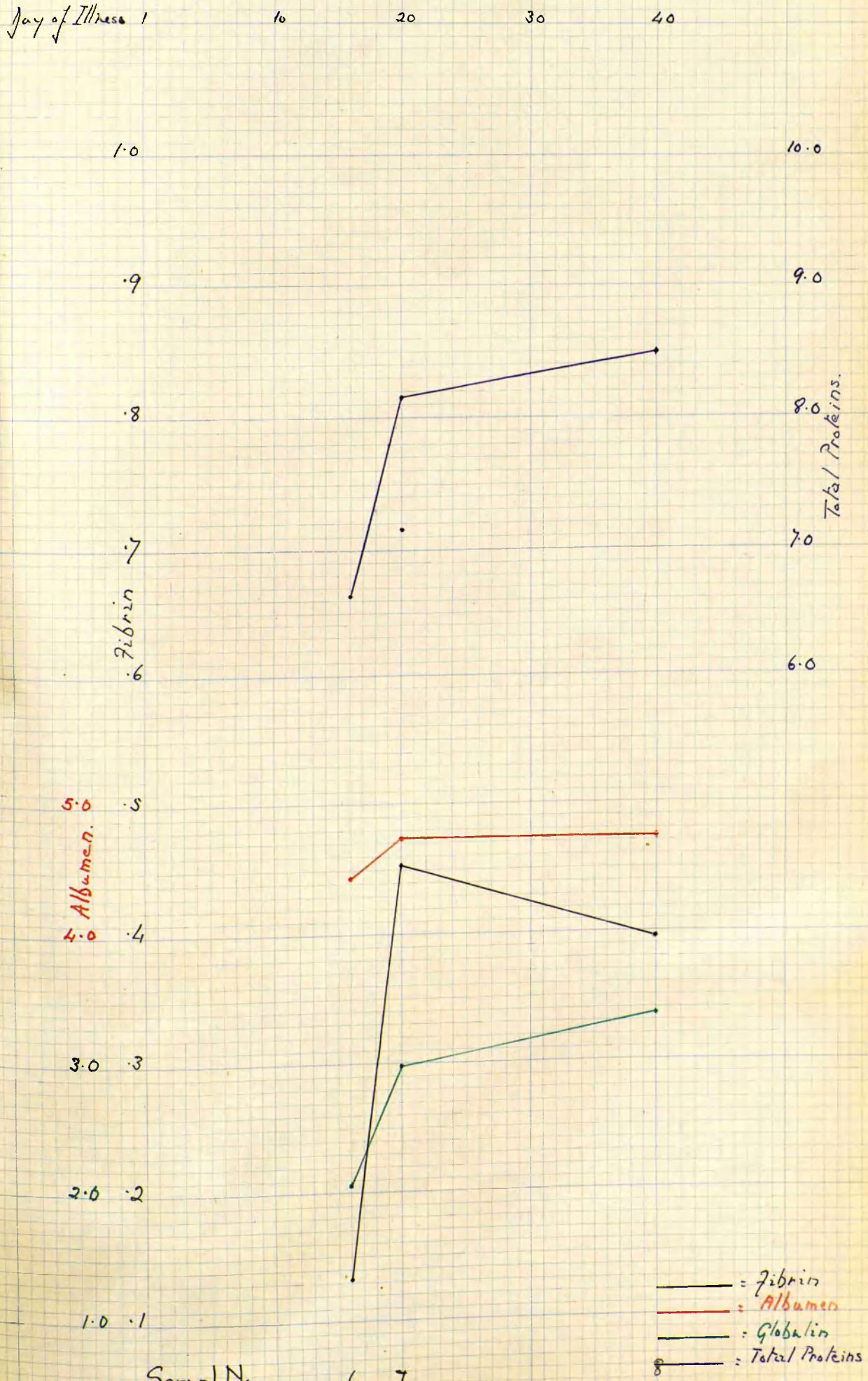
TYPHUS FEVER

GRAPH XIV

No (iii)

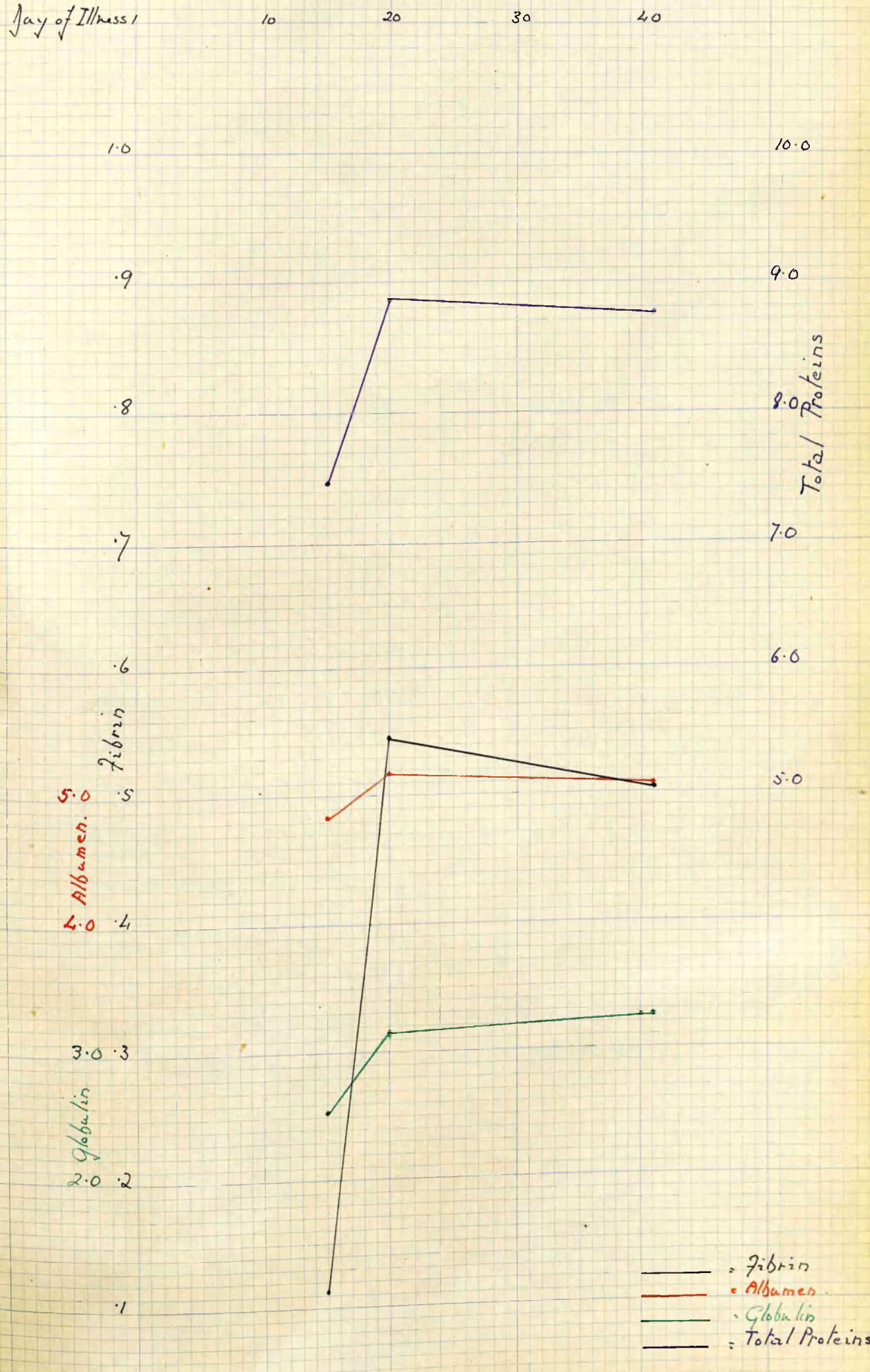


Serial No 6 7

TYPHUS-FEVER

GRAPH XV.

No. (iv)



Serial No 9 10 11

ABSTRACT OF FINDINGS IN TYPHUS FEVER. TABLE XXI.

	Mean.	Range.
Pre-critical stage		
Fibrin	0.225	0.114 - 0.364
Albumen	4.623	4.268 - 4.946
Globulin	2.355	2.060 - 2.628
Total Proteins	7.204	6.713 - 7.504
Albumen / Globulin	1.62	1.6 - 2.2
Post Critical stage.		
Fibrin	0.461	0.385 - 0.546
Albumen	5.032	4.732 - 5.182
Globulin	2.972	2.763 - 3.160
Total Proteins	8.132	7.178 - 8.888
Albumen / Globulin	1.63	1.5 - 1.8
Convalescent stage		
Fibrin	0.398	0.364 - 0.423
Albumen	4.980	4.732 - 5.182
Globulin	3.195	2.980 - 3.375
Total Protein	8.323	7.336 - 8.753
Albumen / Globulin	1.52	1.4 - 1.6

Conclusions.

1. In the pre-critical stage the Fibrin is normal or diminished. The Albumen and Globulin are normal and the Total Proteins are slightly below the normal mean.

2/

2. In the post-critical stage, all the constituents are increased. The Fibrin in particular, may show a sharp rise.

3. In the convalescent stage, the Fibrin returns to normal but the Globulin, Albumen and Total Proteins remain high.

4. The Albumen/Globulin ratio remains fairly stable, but a slight fall occurs during the course of the disease.

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VII. TYPHOID FEVER. TABLE XXII.

No.	Week of Illness.	Fibrin.	Albumen.	Globulin.	Total.	Albumen / Globulin
1.	2nd	0.285	4.837	3.061	8.183	1.5
2	2nd	0.267	4.477	2.376	7.120	1.8
3	2nd	0.437	4.946	1.968	7.351	2.5
4	3rd	0.656	4.534	3.176	8.366	1.4
5	6th	0.423	4.837	3.175	8.435	1.5

Table XXII shows the findings in five cases of Typhoid fever. In three of these the blood was examined in the second week, in one in the third week and in one in the sixth week of illness. All the patients were acutely ill and in all cases B.typhosus was agglutinated by their serum. In the three specimens examined in the second week of illness, the Fibrin is slightly below normal in two and is not raised above normal limits in the third case, but it is definitely increased in the specimen examined in the third week. In the case estimated in the sixth week, it has fallen again to normal. The Albumen shows no deviation from normal throughout but the Globulin and Total Protein figures are rather higher in the later than in the earlier estimations. From these five cases it seemed probable that the plasma proteins, more especially the Fibrin, vary considerably during the course of the disease, so that in the cases that were investigated subsequently, several estimations were carried out on each patient, at intervals during the illness. Six patients were examined, on whom nineteen estimations were made, giving in all a total of twenty-four cases of Typhoid Fever. In addition two estimations were made in a patient suffering from Typhoid and Bronchiectasis.

TYPHOID FEVER. TABLE XXIII.

Course of the Disease.

Case.	No.	Day of illness.	Fibrin.	Albumen.	Globulin.	Total.	Albumen / Globulin
(i)	6	19	0.397	5.182	2.577	8.156	2.0
	7	27	0.397	4.946	2.453	7.796	2.0
	8	39	0.452	4.441	1.595	6.488	2.7
	9	46	0.385	4.353	2.018	6.756	2.1
(ii)	10	23	0.142	4.268	3.606	7.416	1.4
	11	31	0.279	4.992	2.293	7.564	2.1
	12	44	0.546	4.946	2.794	7.286	1.7
	13	51	0.704	4.308	2.534	7.546	1.7
	14	91	0.397	4.534	3.176	8.107	1.4
(iii)	15	14	0.148	4.692	2.820	7.660	1.6
	16	21	0.273	4.353	1.676	6.302	2.5
	17	36	0.437	4.268	3.609	8.314	1.1
	18	60	0.437	5.080	3.501	9.039	1.4
(iv)	19	25	0.524	4.353	2.843	7.720	1.5
	20	40	0.560	4.534	2.347	7.441	1.9
(v)	21	15	0.481	4.591	2.202	7.274	2.0
	22	24	0.475	4.185	2.495	7.105	1.7
(vi)	23	20	0.410	4.732	2.493	7.635	1.8
	24	29	0.528	4.534	3.362	8.424	1.3
			TYPHOID + BRONCHIECTASIS.				
(i)	1	?14	0.704	4.534	2.922	8.160	1.5
	2	?30	0.504	4.185	3.170	7.859	1.3

Course of the Disease.

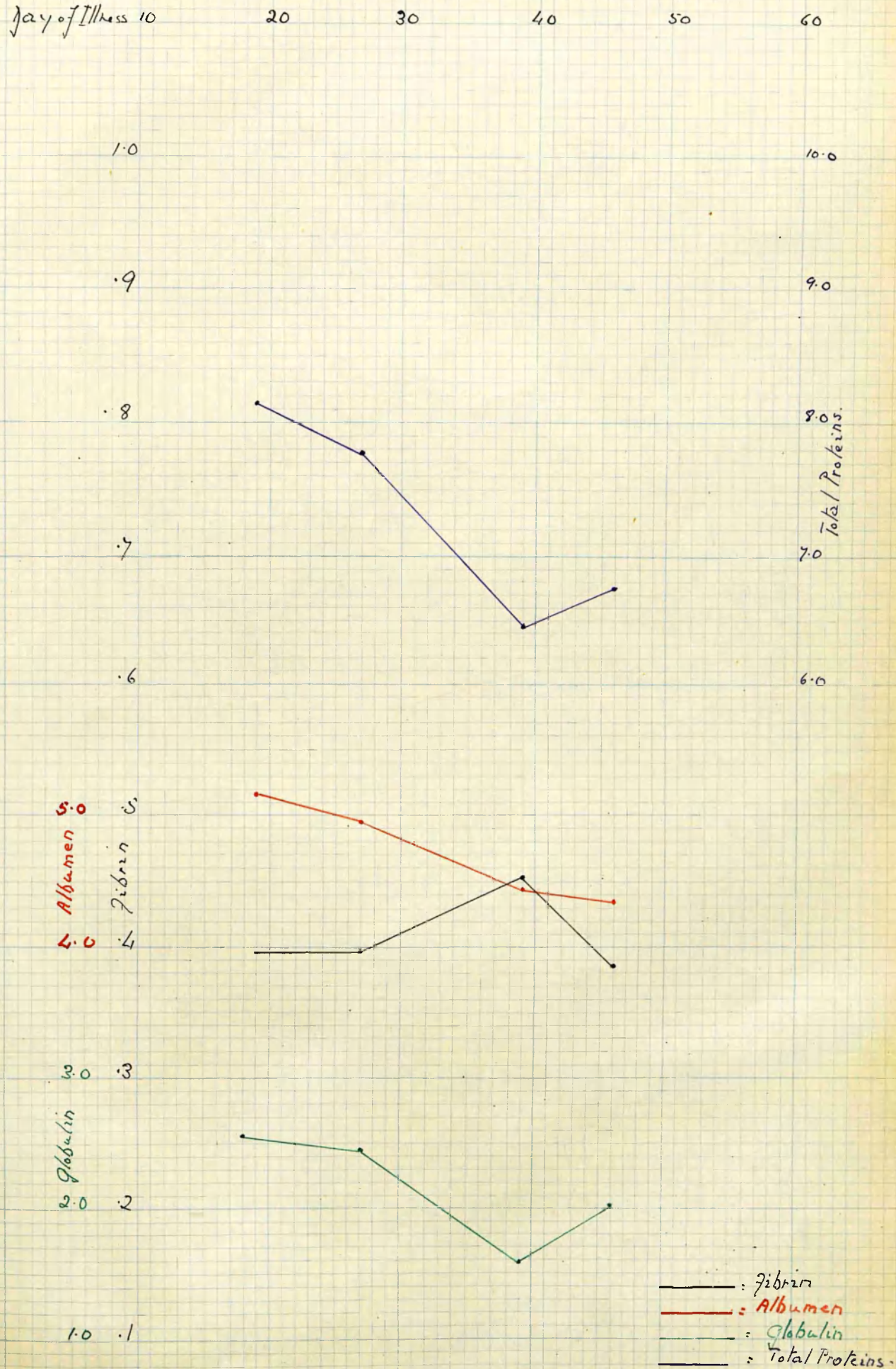
Case (i) Table XXIII (Graph XVI) was a male patient, very acutely ill. who made a slow recovery, his convalescence being prolonged for some weeks after the final estimation was made. In his case, the fibrin shows little variation from normal beyond a slight rise in the fifth week. The Albumen shows a slight decrease during the course of the illness and the Globulin is diminished in the fifth week though it rises again in the sixth. The Total Proteins remain within normal limits. In this case the blood findings were normal before convalescence was established.

The next case (ii) (Graph XVII) was also seriously ill and remained in the typhoid state during the second, third and fourth weeks of illness. In her case the first fibrin reading is considerably below normal. In the three subsequent examinations, made in the third, fifth and seventh weeks respectively, the fibrin rises steadily, reaching its maximum reading (o.704 gms. per 100 cc.) on the forty-eighth day of illness. This estimation (Serial No.13) was made on the fourth day of a relapse and it is to be noted that the steady rise in fibrin is unaffected by a recrudescence of symptoms similar to those present when the patient was admitted, when the fibrin only amounted to 0.142 gms. per 100 cc. The Albumen rises slightly between the first and second estimations and falls subsequently. The Globulin and Total Proteins are increased in the early stages, fall rapidly and then rise again slowly during convalescence.

The next three cases were all less severe and presented no unusual clinical features. Graph XVIII shows a fibrin curve which, starting below normal in the second week, rises gradually to the fifth week and thereafter remains almost level. The next case (Graph XIX) shows a slight rise from the fourth to the sixth week, but in the fifth case (Graph XX) the fibrin shows an increase in the second week (0.481 gms/100 cc.) and a fall in the fourth week,

TYPHOID FEVER
No (1)

GRAPH XVI



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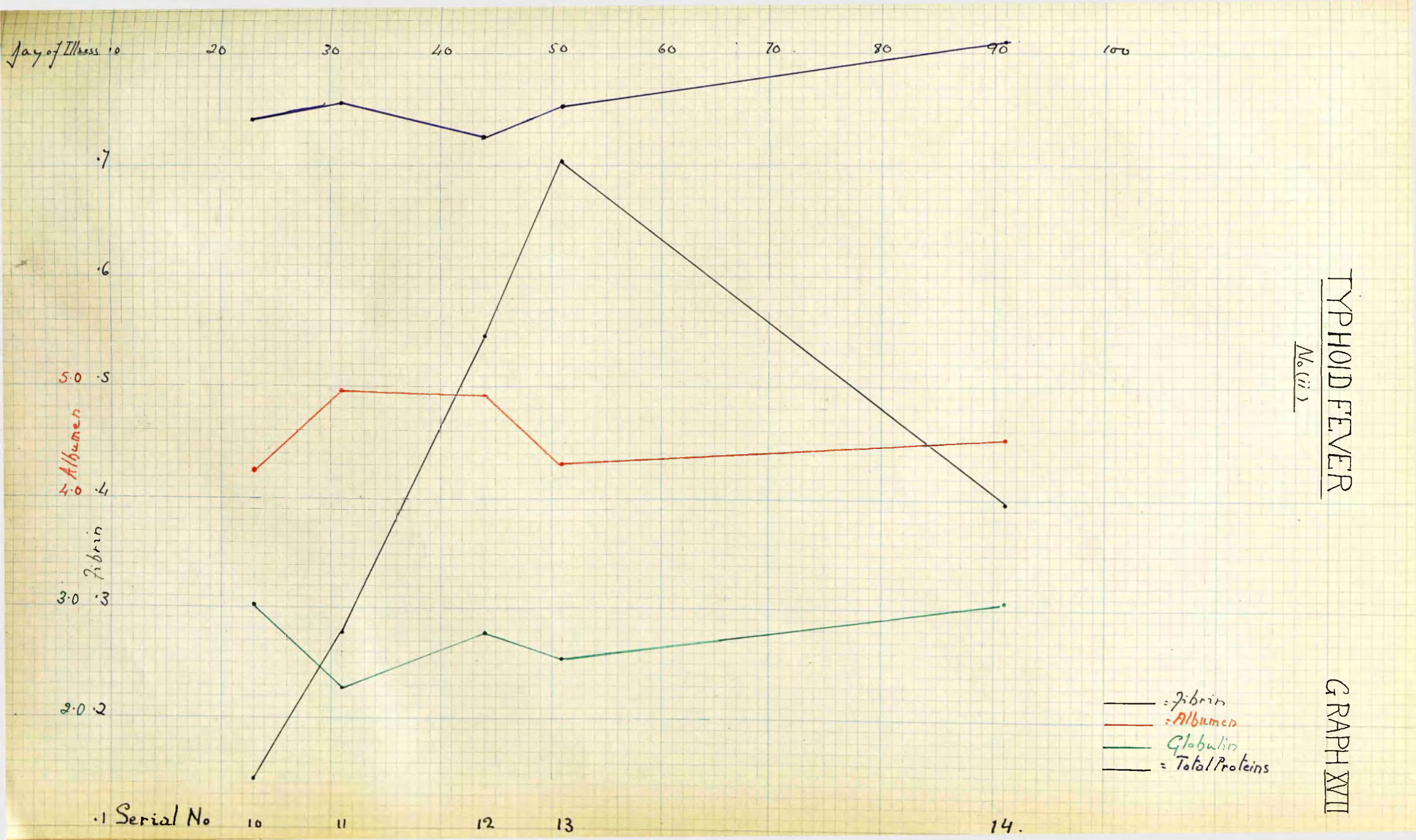


TYPHOID FEVER

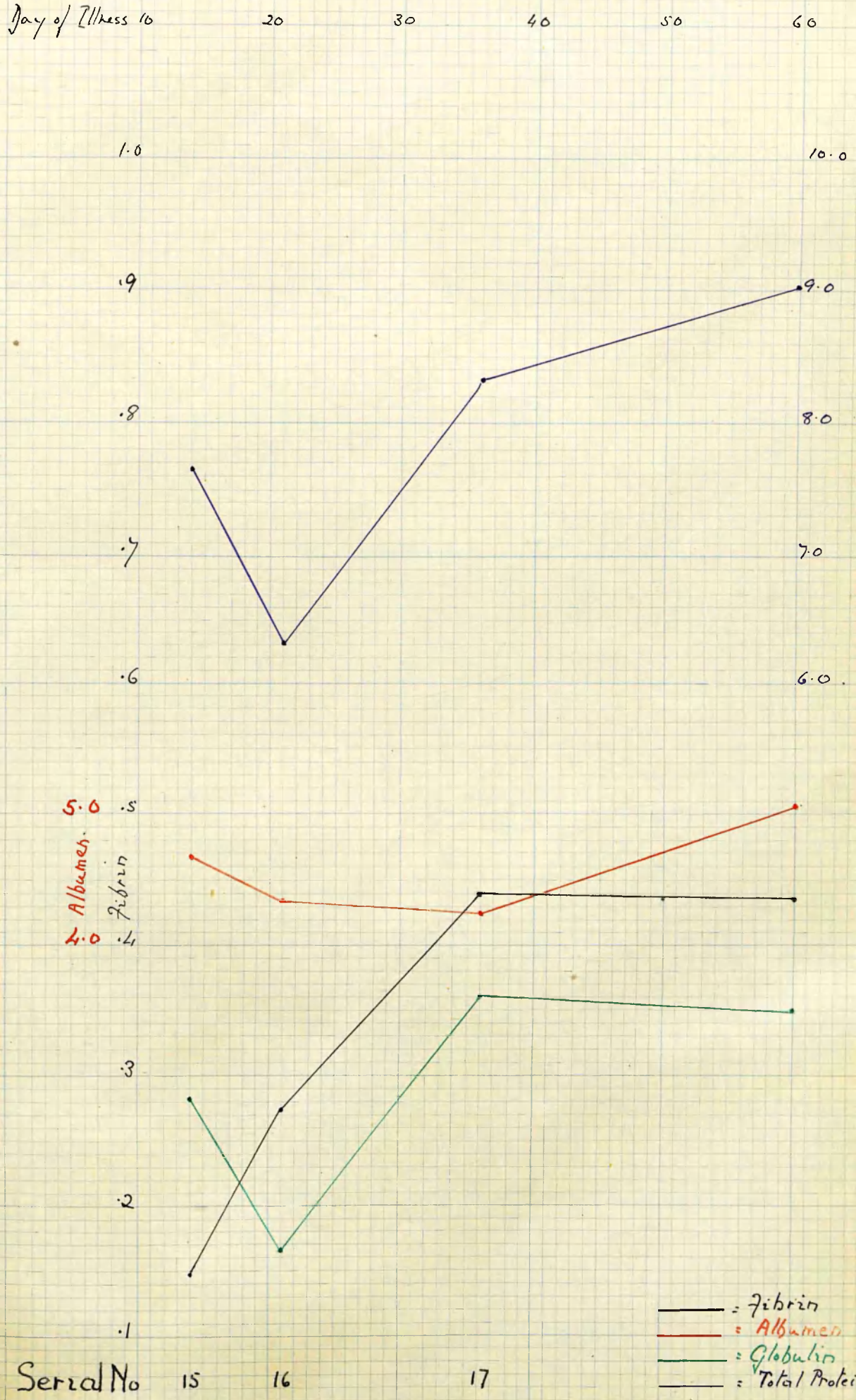
No (ii)

GRAPH XVII

TYPHOID-FEVER

No (iii)

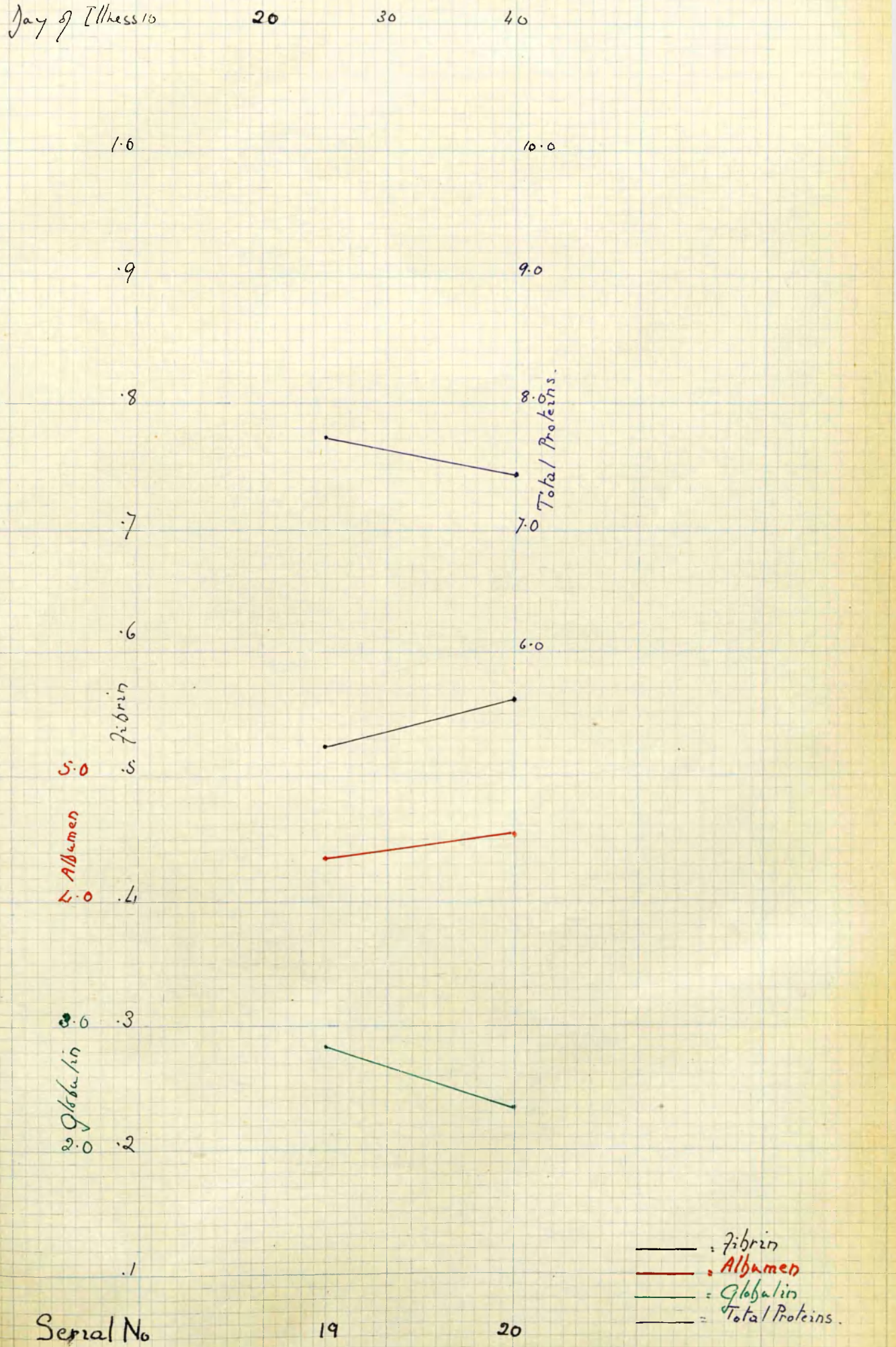
GRAPH XVIII



TYPHOID FEVER

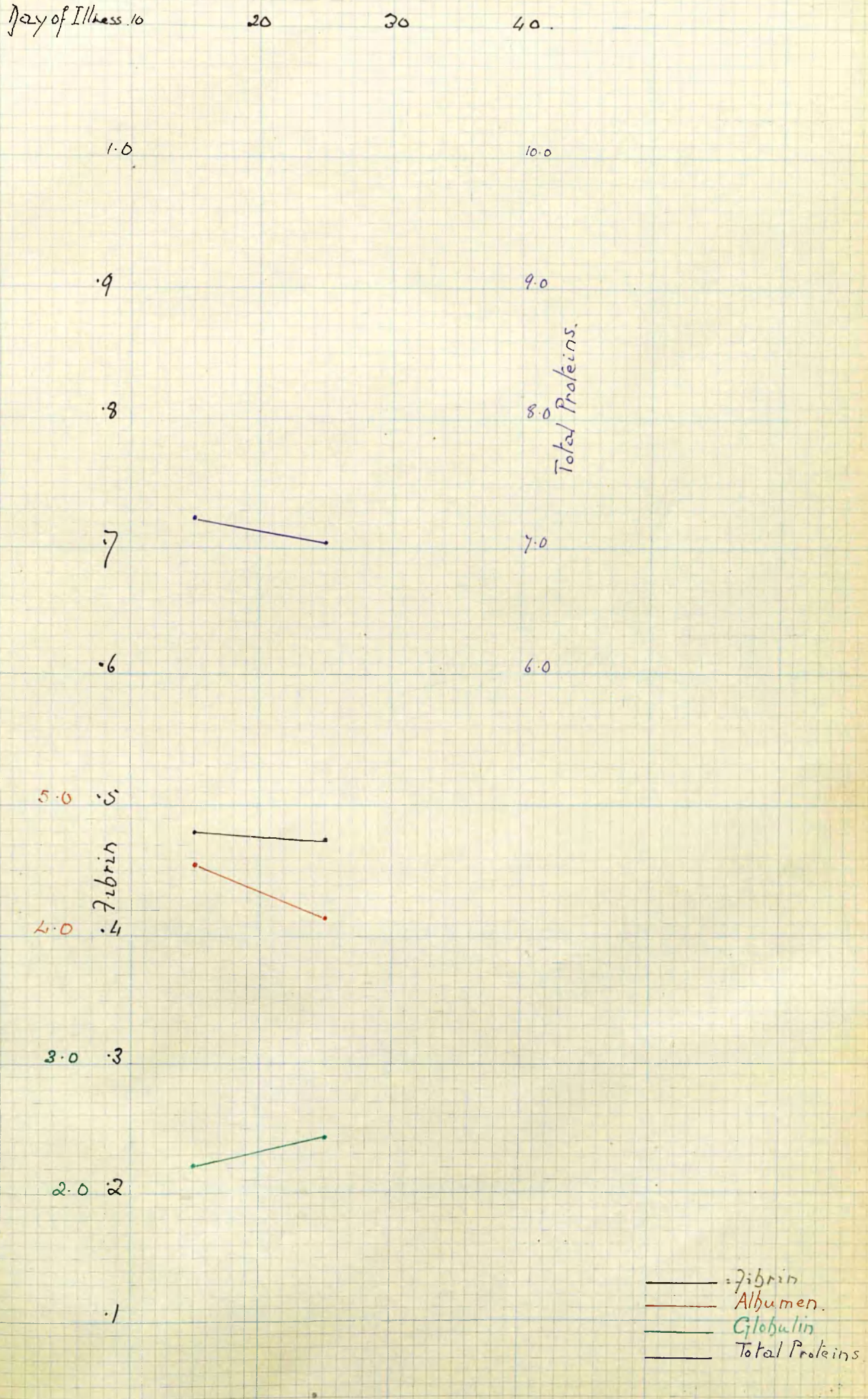
GRAPH XIX.

No (iv)



TYPHOID FEVER
No(v)

GRAPH XX.



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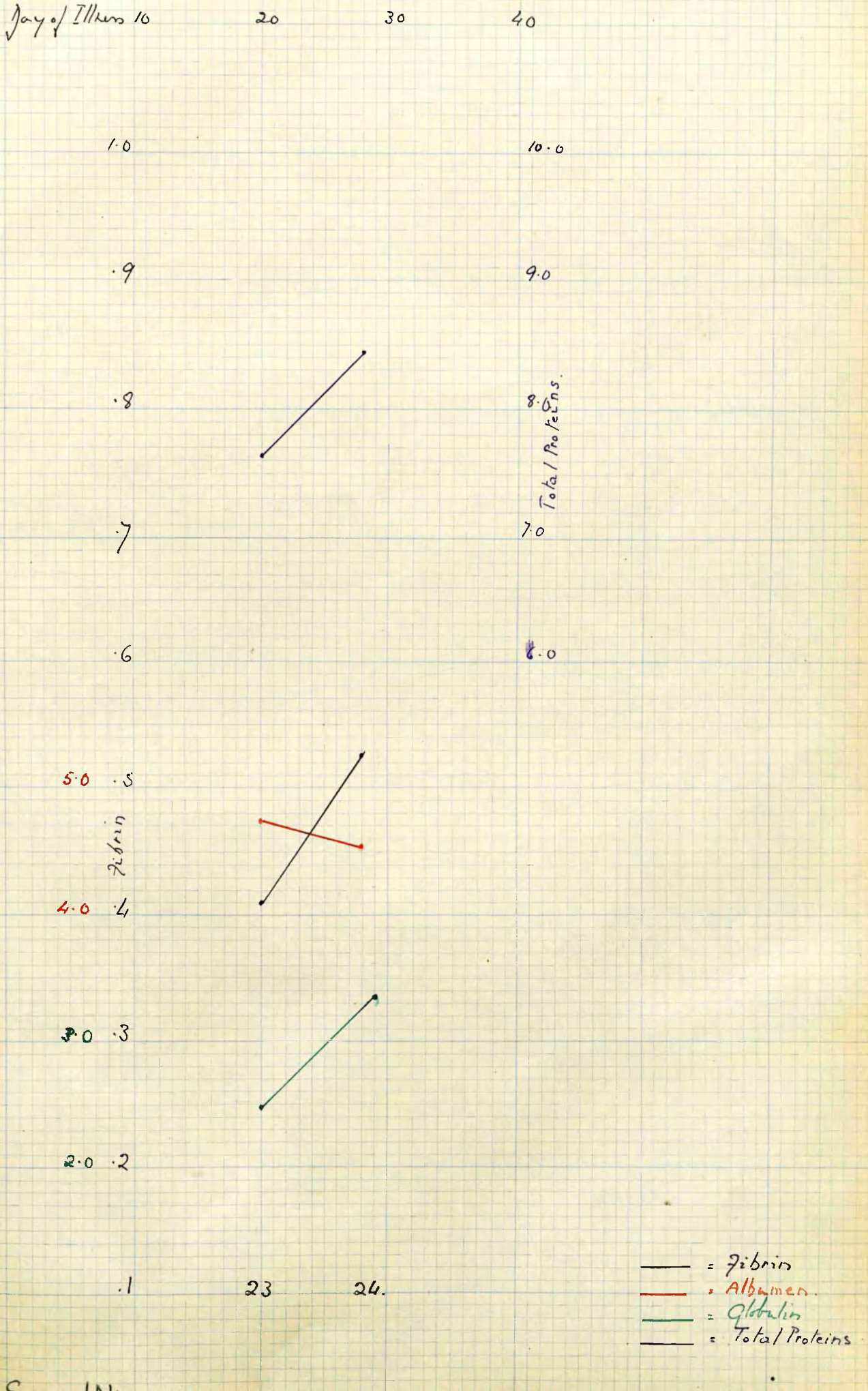
TYPHOID FEVER

GRAPH XXI.

No (vi)



Serial No.

(0.475 gms./100 cc.) The other constituents do not vary widely and the readings are all within normal limits.

Case (vi) (Graph XXI) was a young woman in whom typhoid fever was complicated by an acute gonococcal infection. She died in the typhoid state in the fourth week of illness. In this case the Fibrin is normal in the third week and rises slightly before death. The Globulin and Total Proteins show a similar slight increase.

In the case in which typhoid was superimposed on a chronic and extensive Bronchiectasis, the findings are similar to those found in the uncomplicated Bronchiectasis (c.f. Respiratory Diseases) i.e. increased Fibrin, a Globulin reading above the average mean reading and a normal Albumen.

ABSTRCT OF FINDINGS IN TYPHOID FEVER.

TABLE XXIV.

1st and 2nd weeks of Illness.	Mean.	Range.
1st and 2nd weeks of Illness.		
Fibrin	0.293	0.142 - 0.481
Albumen	4.635	4.268 - 4.946
Globulin	2.738	1.968 - 4.006
Total Proteins	7.667	7.120 - 8.416
Albumen / Globulin	1.75	1.5 - 2.8
3rd and 4th weeks of illness		
Fibrin	0.445	0.273 - 0.656
Albumen	4.598	4.185 - 5.182
Globulin	2.538	1.676 - 3.362
Total Proteins	7.586	6.302 - 8.424
Albumen / Globulin	1.73	1.3 - 2.5
5th,6th,7th weeks of illness.		
Fibrin	0.501	0.385 - 0.704
Albumen	4.526	4.268 - 4.946
Globulin	2.581	1.595 - 3.609
Total Proteins	7.452	6.488 - 8.435
Albumen / Globulin	1.90	1.1 - 2.7

IX. PARATYPHOID (B) FEVER. TABLE XXV.

No.	Day of Illness.	Fibrin.	Albumen.	Globulin.	Total.	Albumen / Globulin.
1	2nd	0.262	5.062	3.375	8.699	1.5
2	2nd	0.328	4.732	2.753	7.813	1.7
3	2nd	0.385	3.958	2.785	7.128	1.4
4	3rd	0.656	4.946	3.377	8.979	1.4
5	3rd	0.437	3.886	2.977	7.300	1.3
6	5th	0.481	4.946	3.377	8.804	1.4

Paratyphoid (B) Fever.

Results similar to those in infections by B.Typhosus are obtained in cases infected by B.Paratyphosus B., although in the latter disease the fibrin variations do not show so wide a range as in Typhoid Fever.

Table XXV contains the findings in six estimations, three of which were made in the second, two in the third and one in the fifth week of illness. This last case (No.5.) suffered from a mild degree of jaundice at the time when the estimation was made. Of the three early cases, one gives a definitely diminished fibrin reading and in both the other cases no increase is present. Of the two specimens withdrawn in the third week one shows a definite increase in fibrin and in the other the amount is above the normal average. In the case examined in the fifth week the fibrin is again slightly increased. No consistent changes can be distinguished in the other constituent proteins. In two cases the Albumen is below normal.

PARATYPHOID FEVER. TABLE XXVI.

Course of the Disease.

Case	No.	Day of Illness.	Fibrin.	Albumen.	Globulin.	Total.	Albumen / Globulin
(i)	7	9	0.385	4.441	2.463	7.289	1.8
	8	13	0.481	4.107	2.685	7.273	1.5
	9	33	0.504	5.062	3.069	8.635	1.3
(ii)	10	15	0.389	4.353	3.530	8.530	1.2
	11	30	0.624	5.060	4.214	9.898	1.2
	12	41	0.524	-	-	-	-

Course of the Disease.

This was studied in two mild cases in one of whom three complete estimations and in one of whom two complete estimations and one fibrin estimation were made. Both were mild cases and both were dismissed well by the end of the dixth week.

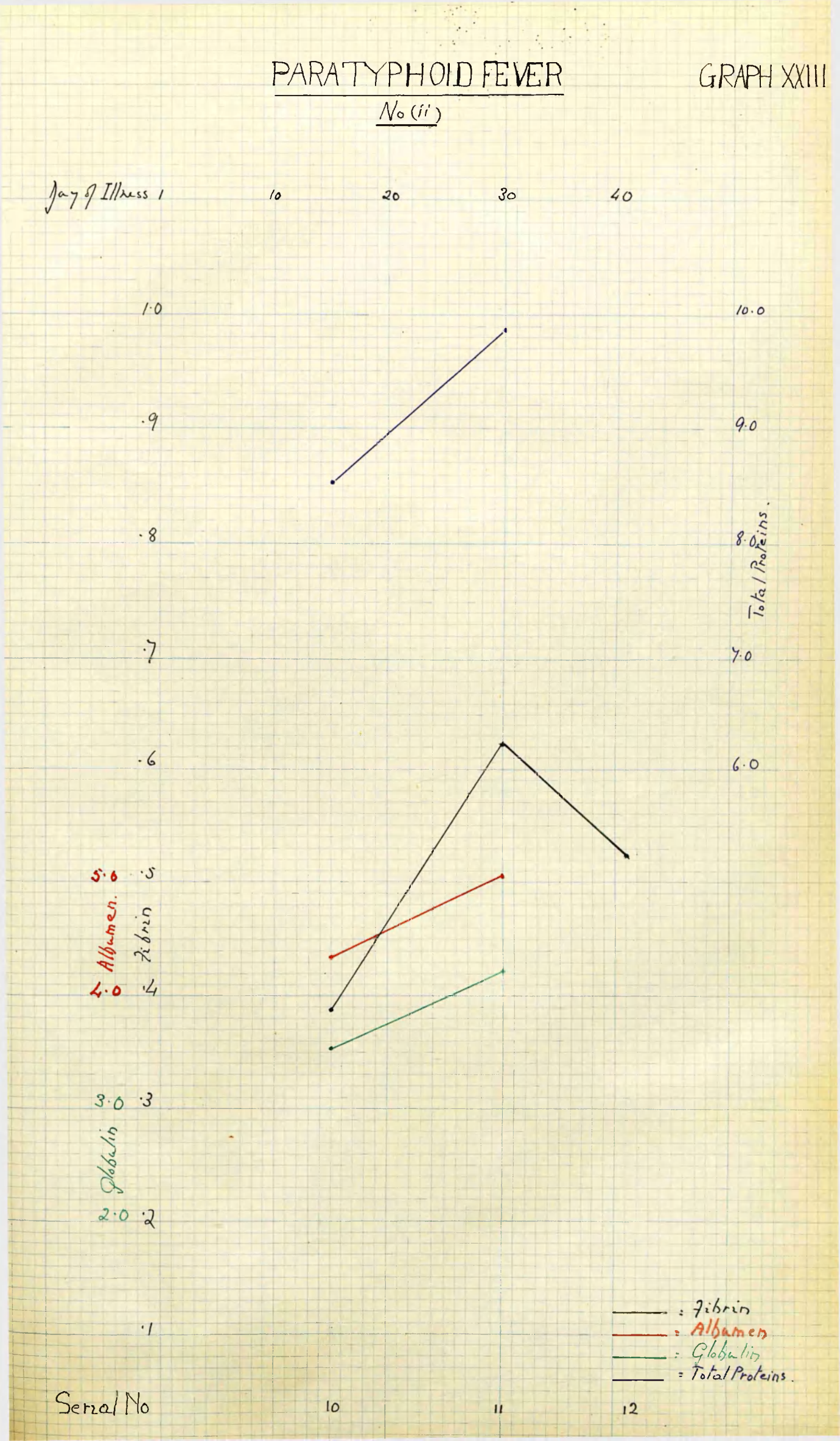
In both cases the fibrin reading is normal in the first specimen, withdrawn in the early stage of the illness and in both it is slightly increased in the third and fourth weeks. In the first case a further slight rise is present in the fifth week; in the second case in the sixth week, the amount has fallen slightly, though it is still definitely above nor normal. In the second case, the Globulin and Total Proteins are increased in amount in both the estimations made; in the first case the Albumen Globulin and Total Proteins are increased in convalescence.

The variations in Paratyphoid fever are summarized in Table XXVII.

PARATYPHOID FEVER

GRAPH XXIII

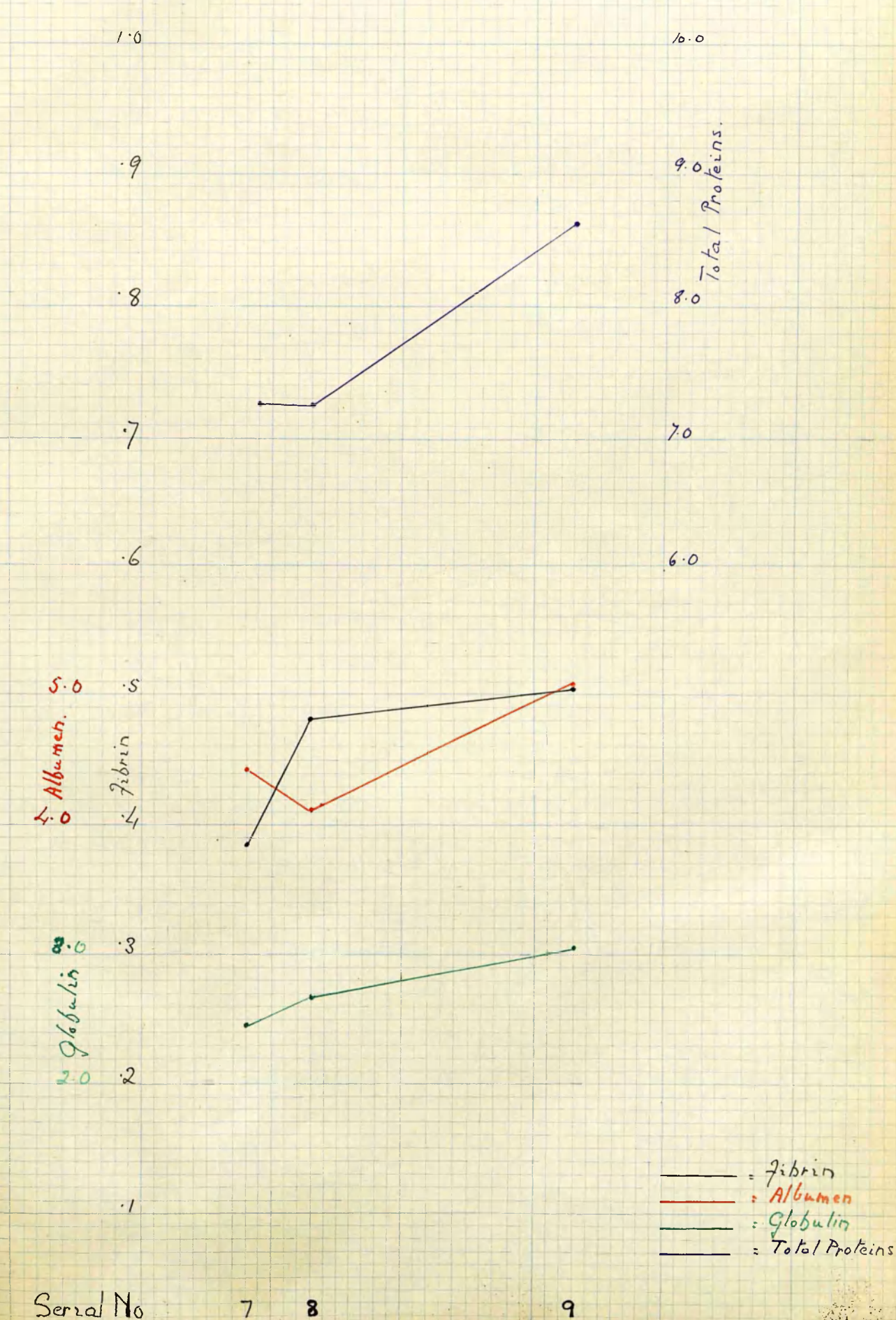
No (ii)



PARATYPHOID FEVER

GRAPH XXII

No. 1)



ABSTRACT OF FINDINGS IN PARATYPHOID FEVER. TABLE XXVII.

	Mean.	Range.
1st and 2nd weeks of illness.		
Fibrin.	0.349	0.262 - 0.389
Albumen	4.509	3.958 - 5.062
Globulin	2.981	2.463 - 3.530
Total Proteins	7.693	7.128 - 8.699
Albumen / Globulin	1.52	1.2 - 1.8
3rd and 4th weeks of illness.		
Fibrin	0.549	0.437 - 0.656
Albumen	4.499	3.886 - 5.060
Globulin	3.310	2.685 - 4.214
Total Proteins	8.362	7.273 - 9.898
Albumen / Globulin	1.35	1.2 - 1.5
5th and 6th weeks of illness.		
Fibrin	0.503	0.481 - 0.524
Albumen	5.004	4.946 - 5.062
Globulin	3.223	3.069 - 3.377
Total Proteins	8.714	8.635 - 8.804
Albumen / Globulin	1.35	1.3 - 1.4

Conclusions.

Typhoid and Paratyphoid Fevers.

1. The fibrin in the early stages of the disease, i.e. up to the third week of illness is definitely low, in many cases actually below and never appreciably above normal limits. The changes are more marked in B.Typhosus infections than in cases due to B.Paratyphosus B.

2. The fibrin increases in the third and fourth weeks to a point above normal. In mild cases it is probable that it falls thereafter but in severe cases a further increase occurs in the later weeks of illness and the reading only returns to normal after prolonged convalescence. It is noteworthy that the increase coincides with the period in which thrombosis is most likely to complicate the course of the disease.

3. The Albumen findings are variable, the average amount showing a slight fall during the course of the disease.

4/

4. The Globulin is little affected, a few cases show a slight increase during the later weeks. This rise is present in both cases of Paratyphoid in which more than one estimation was made.

5. The Mean Globulin in Paratyphoid is slightly higher than in Typhoid, at all stages of the disease.

6. The ratio of Albumen/Globulin is inconstant, normally above 1.5. This figure is lower in Paratyphoid than in Typhoid.

7. The Total Proteins are invariably within normal limits.

8. The total figure is definitely higher in Paratyphoid than in Typhoid and in the former the readings are higher in the convalescent phase than in the early stages.

The diagnostic value of the Fibrin variations will be discussed later.

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X. MISCELLANEOUS INFECTIONS. TABLE XXVIII.

No.	Disease.	Fibrin.	Albumen.	Globulin.	Total.	Albumen / Globulin
1	Diphtheria	0.528	5.084	1.762	7.374	2.8
2	"	0.532	4.650	3.088	8.270	1.5
3	"	0.528	4.732	3.020	8.280	1.5
4	"	0.472	4.353	2.041	6.866	2.1
5	Herpes Ophthalmicus	0.874	4.441	3.263	8.578	1.3
6	"	0.570	3.627	3.290	7.487	1.1
7	Secondary Syphilis	0.656	5.360	2.841	8.857	1.8
8	Spirochaetal Jaundice	0.468	4.534	4.443	9.441	1.0
9	Encephalitis Lethargica	0.305	4.353	2.544	7.202	1.7
10	Cerebrospinal Fever	0.133	4.650	2.847	7.630	1.6
11	Exophthalmic Goitre	0.485	3.298	1.904	5.687	1.7
12	Ulcerative Colitis.	0.690	4.387	3.725	8.802	1.1
13	Enteritic	0.546	4.692	2.162	7.400	2.1
14	Pyelitis(coliform bacilli)	0.426	4.837	3.268	8.531	1.4

Miscellaneous Infections.

This series includes four cases of Diphtheria, two cases of Herpes Ophthalmicus (one associated with Syphilis), one case of Secondary Syphilis and one case each of Spirochaetal Jaundice, Exophthalmic Goitre, Cerebrospinal Meningitis, Encephalitis Lethargica, Ulcerative colitis, Enteritis and Pyelitis.

Diphtheria.

All four cases were adult females and showed typical throat lesions though none showed symptoms of marked toxaemia. The throat cultures were positive for Klebs-Loeffler bacillus. The readings are those obtained in any mild infection and are very similar to those found in Scarlet Fever. In all, four cases the Fibrin content is moderately increased; in two cases the Globulin is rather

above/

above and in two cases rather below the average normal; the Albumen in 3 cases is slightly above average normal but in all cases is within normal limits.

Herpes Ophthalmicus.

Two cases were examined; both were adult females and both were certified as Erysipelas, the presence of vesicles and of well-marked erythema over the affected area, producing a superficial resemblance to that disease. Case 5 gives readings typical of any acute inflammatory condition, i.e. increased Fibrin, increased Globulin and an Albumen reading within normal limits. The Albumen: Globulin ratio = 1.38. Case 6 gave a ++ Wassermann Reaction though she did not show any evidence of active Syphilis. In this case there was a slight increase of Fibrin and an increase in Globulin similar to that in Case 5, though the Albumen is definitely diminished, No albuminuria was present.

Albumen:Globulin ratio = 1.1

Secondary Syphilis.

The patient was an adult female married three months before, who gave a history of sore throat, slight temperature and general malaise and who showed a characteristic syphilitic rash. The Wassermann Reaction was + +.

The Fibrin content is increased and is considerably above that in Case 6 as was to be expected in the acute stage of the disease; but in this case the Globulin is not raised above the average normal and the Albumen reading instead of being diminished is high so that the Albumen/Globulin ratio becomes 1.8. These two cases of syphilis (Nos.6 & 7) may be compared with two cases reported by Wu, (7) in which he gives the results of the Albumen and Globulin estimations:-

Albumen.	Globulin.	Total.	Albumen/Globulin
4.63 gms.	3.41 gms.	8.04	1.3
4.95 gms.	4.41 gms.	4.37	1.1

In these cases the high Globulin reading with a low Albumen/Globulin ratio, is similar to the findings in Case 6, though in Wu's cases the Total Proteins reach a higher figure.

Spirochaetal jaundice.

This specimen of blood was obtained from a male adult who was admitted to the Glasgow Royal Infirmary, acutely ill with high pyrexia, vomiting, rigors and jaundice. The disease was rapidly fatal. Spirochaetes were isolated from the blood. This specimen shows a slight increase in fibrin and a marked increase in Globulin, the Albumen reading remaining normal: the total Proteins are increased. Similar readings are seen in a case of paratyphoid fever complicated by a mild degree of jaundice. (Table XXV. No.5.) in which Fibrin = .481 gms. Globulin=3.377, Albumen=4.946 gms. and Total Proteins=8.804 gms. In both these cases the hepatic efficiency must have been impaired and yet in both the Fibrin is slightly increased rather than diminished. This is in accordance with the findings of Coetzee(9) (Proc: Roy.Soc. Med. 1925) who states that a reduction in fibrin need not necessarily occur even if the liver function is impaired and who instances three cases of cirrhosis of the liver in which the fibrin reached .50 gms/100 cc. On the other hand he states that in severe toxaemias of pregnancy, more especially in eclampsia, in which considerable liver damage is present, the Globulin was reduced in amount. In both these cases, more especially in the case of spirochaetal jaundice, the Globulin is increased.

Encephalitis Lethargica.

One case was examined. This was a girl aged 18 years, who was admitted in a semi-stuperous condition in the second week of illness. She had no pyrexia and her only symptom was drowsiness followed by mental deterioration.

The/

The blood was examined soon after admission and was found normal in all its readings.

Cerebro-spinal Meningitis.

One case was examined. This was a girl of 8 years who died within a week of the onset of symptoms. The blood was withdrawn on the day before death and the patient had had several doses of antimeningococcic serum intrathecally and intramuscularly. The fibrin reading is exceptionally low - the lowest in any disease except Typhus in the acute stage. If the injection of foreign protein has a toxic action on the plasma, producing a breaking down of the constituent proteins, it is possible that this diminution in fibrin is due to the repeated injection of serum rather than to the disease. As previously noted no diminution of the protein constituents occurred in cases of scarlet fever treated with antitoxin, but it should be borne in mind that no case of Scarlet Fever received more than one injection whereas in the present casr the serum had been injected repeatedly and in greater bulk (vide infra; Section C. Relation of Plasma Proteins to the injection of Serum).

Exophthalmic Goitre.

This was a female patient aged 44 years, with an exophthalmic goitre of some four years' duration. She was admitted with evidence of failing cardiac compensation including albumenuria and oedema of the legs, and died with signs of hypostatic pneumonia. Two points are of interest. In the first place, in contrast with a true Lobar or Influenzal Pneumonia, the fibrin in this case is only slightly above normal. Secondly both the Albumen and Globulin are low and the Total is the lowest found in any case in the present series. It has been shown that the serum dilution is less in oedematous cardiac patients than in oedematous nephritic patients. (16) In the present case it was demonstrated by post mortem examination that a chronic interstitial nephritis was present. This is in accordance with the low Albumen and low Total Protein figures obtained.

Ulcerative Colitis.

This was a woman of 44 years, who was admitted in an advanced state of weakness in the fifth week of illness and who died shortly after admission. The condition had been diagnosed as Typhoid but Widal's reaction was negative on three occasions. There was no clinical evidence of a malignant condition of the bowel nor of abdominal Tuberculosis, but as autopsy was refused neither condition can be absolutely excluded. The blood findings certainly are compatible with those in other types of Tuberculosis and an increase in Globulin has also been described in cases of carcinoma. Irregular pyrexia was present throughout the illness and the patient passed frequent small motions containing mucus, pus and some blood. Death was due to exhaustion. In this case the Fibrin is increased and the Globulin is above the normal average.

Enteritis.

This patient was also certified as Typhoid fever and was admitted with slight temperature, loose stools and abdominal pain and tenderness. The Widal test was negative and the patient was convalescent in a few days. The blood was examined on the fifth day of illness. The Fibrin shows a moderate increase and the Albumen and Globulin are normal. As no case of Typhoid or Paratyphoid shows an increase in Fibrin in the early weeks of illness, it is possible in this case to exclude either infection from the Fibrin reading alone.

Pyelitis.

This patient, an adult woman, suffered from pyrexia, acute lumbar pain with tenderness over the right kidney. The urine contained abundant pus and coliform organisms. The Fibrin and Globulin readings are slightly above normal and the Total Protein is increased.

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SECTION C.

Summary, Conclusions and General Discussion.

Comparison of Results in the various Infections.

For purposes of comparison the findings in the preceding sections are arranged in three tables. The first recapitulates the figures obtained in the control cases. The second comprises those diseases in which a sufficient number of observations were made to justify the calculation of the Standard Deviation and Coefficient of Variation of each constituent, (i.e. Erysipelas severe and moderate, Scarlet Fever, Pneumonia and Acute and Chronic Pulmonary Tuberculosis). The third includes those diseases in which although fewer estimations were made, it is possible to arrive at definite conclusions regarding the behaviour of the plasma proteins (i.e. Influenza, Diphtheria, Typhoid and Paratyphoid fevers and Typhus Fever). In this series the number of cases is so small (for example, Typhus Fever in which four examples only were available in the acute stage) that it is perhaps hardly permissible to compare such results with other diseases in which twenty or more specimens were examined, but the findings in these cases seem to be sufficiently distinctive to warrant their inclusion in the tables.

The contrasting features in the various infections are readily seen in the accompanying graph (No.XXIV) in which the highest, lowest and mean readings of each constituent protein are plotted and joined by a vertical line which therefore represents the range of the protein in that disease. The scale and colours employed are the same as in the preceding graphs.

NORMAL CONTROLS.

TABLE XXIX.

	No.of Cases.	Mean.	Standard Deviation.	Coefficient of variation.	Range.
Fibrin	50	0.366 ± 0.004	.043	9.194	0.298-0.468
Albumen		4.745 ± 0.035	.370	7.796	4.030-5.440
Globulin		2.560 ± 0.053	.559	21.822	1.431-3.804
Total Proteins		7.671 ± 0.066	.692	9.022	5.914-9.347

COMPARISON OF RESULTS.

TABLE XXX.

Disease.	No.of cases.	Mean.	Standard Deviation.	Coefficient of variation.	Range.
Erysipelas(severe)	12				
Fibrin		0.882 ± 0.046	.234	28.150	0.570-1.312
Albumen		4.872 ± 0.089	.457	9.382	4.185-5.440
Globulin		3.620 ± 0.143	.736	20.345	1.720-4.654
Total Proteins		9.324 ± 0.198	1.016	10.840	7.394-10.601
Erysipelas (moderate)	12				
Fibrin		0.603 ± 0.020	.101	16.720	0.504-0.820
Albumen		4.766 ± 0.057	.293	6.149	4.441-5.308
Globulin		3.749 ± 0.153	.788	21.034	2.293-4.971
Total Proteins.		9.881 ± 0.152	.783	8.595	7.809-10.487
Scarlet Fever.	20				
Fibrin		0.545 ± 0.014	.090	16.603	0.364-0.728
Albumen		4.472 ± 0.057	.378	8.463	3.627-5.062
Globulin		2.702 ± 0.080	.529	19.614	1.609-3.699
Total Proteins		7.719 ± 0.099	.654	8.478	6.467-8.763
Pneumonia	20				
Fibrin		0.809 ± 0.026	.170	21.180	0.546-1.312
Albumen		4.545 ± 0.064	.427	9.399	3.819-5.440
Globulin		3.401 ± 0.118	.782	23.057	2.087-4.871
Total Proteins		8.755 ± 0.152	1.006	11.488	7.092-10.305
Pulmonary Tuberculosis. (acute)	12				
Fibrin		0.711 ± 0.026	.131	20.303	0.370-0.880
Albumen		4.435 ± 0.052	.267	6.030	4.107-4.992
Globulin		3.687 ± 0.214	1.097	29.761	1.609-5.020
Total Proteins		8.769 ± 0.236	1.213	13.843	6.799-10.233
Pulmonary Tuberculosis (chronic)	12				
Fibrin		0.498 ± 0.013	.068	12.729	0.437-0.660
Albumen		4.452 ± 0.095	.489	10.993	3.886-5.440
Globulin		3.509 ± 0.132	.680	19.387	1.834-4.320
Total Proteins		0.502 ± 0.147	.755	8.885	7.367-10.072

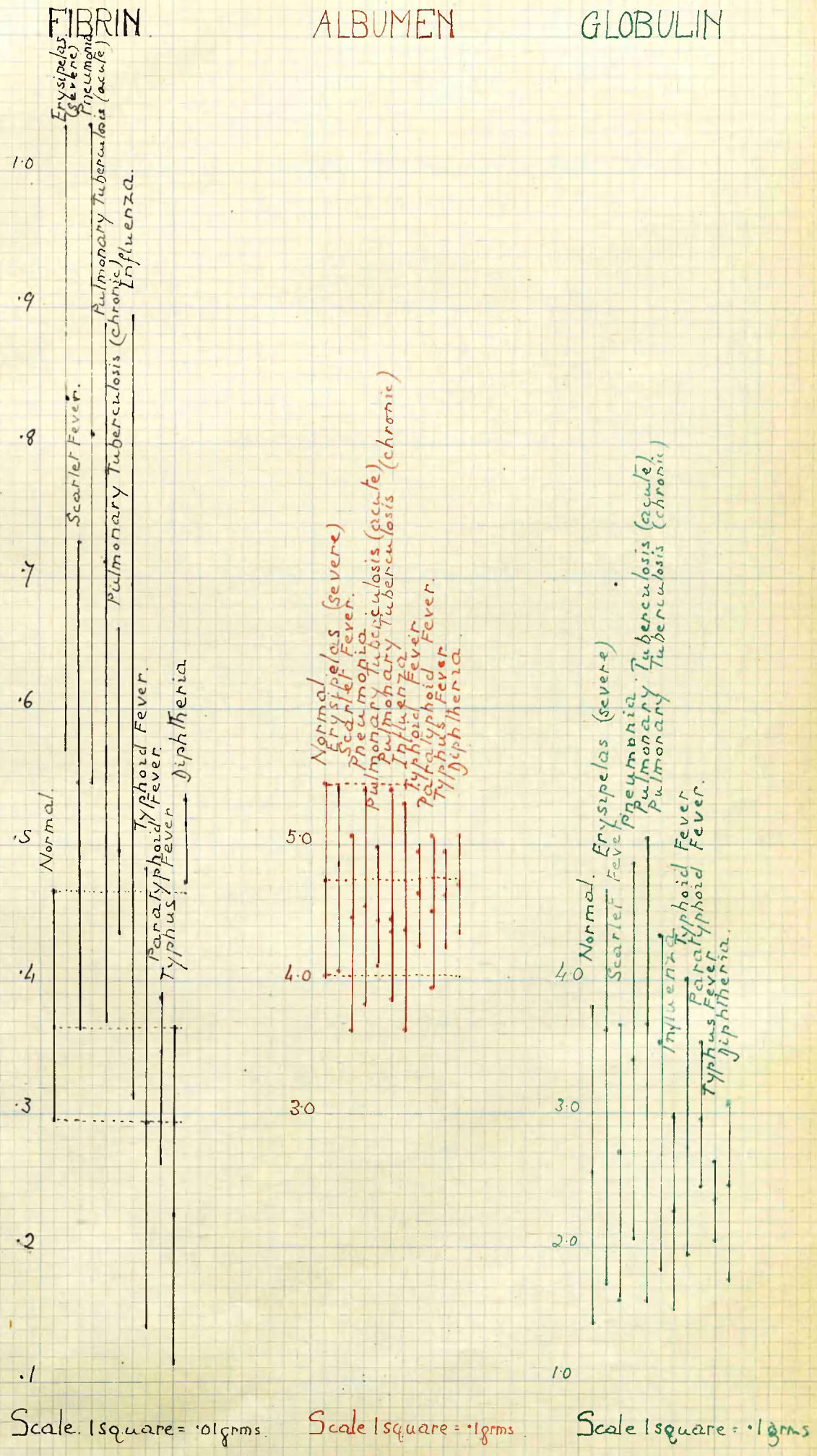
COMPARISON OF RESULTS. TABLE XXXI.

	No. of cases.	Mean.	Range.
Influenza.	7		
Fibrin		0.697	0.312 - 0.892
Albumen		4.386	3.627 - 5.308
Globulin		2.294	1.534 - 2.992
Total Proteins		7.377	6.080 - 8.506
Typhoid Fever	7		
Fibrin		0.293	0.142 - 0.481
Albumen		4.635	4.268 - 4.946
Globulin		2.738	1.968 - 4.006
Total Proteins		7.667	7.120 - 8.416
Paratyphoid Fever	5		
Fibrin		0.349	0.262 - 0.389
Albumen		4.509	3.958 - 5.062
Globulin		2.981	2.463 - 3.530
Total Proteins		7.693	7.128 - 8.699
Typhoid Fever	4		
Fibrin		0.225	0.114 - 0.364
Albumen		4.623	4.268 - 4.946
Globulin		2.355	2.060 - 2.623
Total Proteins		7.204	6.713 - 7.504
Diphtheria	4		
Fibrin		0.515	0.472 - 0.532
Albumen		4.702	4.353 - 5.084
Globulin		2.477	1.762 - 3.088
Total Proteins		7.697	6.866 - 8.280

Note.

The cases of Typhoid and Paratyphoid fever quoted in this table are those in which the blood was estimated in the first and second weeks of illness. The cases of Typhoid Fever are those in whom the blood was examined in the pre-critical stage.

RANGE OF PLASMA PROTEINS GRAPH XXIV



Fibrin.

All the diseases investigated except Paratyphoid, show a wider range between the minimum and maximum readings than appear in the normal cases. The highest readings are found in Erysipelas, Pneumonia (equal) Influenza, acute Pulmonary Tuberculosis. Scarlet Fever, Diphtheria and Chronic Pulmonary Tuberculosis in this order: the lowest readings are obtained in Typhus, Typhoid and Paratyphoid fevers. In Erysipelas, Pneumonia and Diphtheria all the readings are above normal limits and in Scarlet Fever, Influenza and Tuberculosis the maximum and mean readings exceed normal. In these three diseases, the minimum readings are within the normal range. In Tuberculosis, the minimum readings are also within the normal range; in Scarlet Fever the minimum coincides with the mean normal; and in Influenza the minimum amount falls below the normal mean. In Typhus, Typhoid and Paratyphoid the minimum readings are considerably below normal and in Typhoid the mean reading is also below the normal minimum. The highest reading is also below the normal minimum. The highest reading in Typhoid, on the other hand, is very slightly above normal.

It appears, therefore, that in these three diseases, the fibrin content is either normal or less than normal whereas in the other infections it is increased, the increase varying in each disease and reaching its maximum in Erysipelas and Pneumonia. The range varies widely in the different diseases and is greater in the acute diseases than in the more chronic and moderate conditions. The Coefficient of Variation reaches its highest figure in severe Erysipelas (almost three times as great as in Normal cases) and in all the cases in which it is determined, it exceeds normal.

Albumen/

Albumen.

The deviation from normal is very slight. No reading exceeds the maximum found in a normal control. In Scarlet Fever, Pneumonia, Influenza, Chronic Pulmonary Tuberculosis and Paratyphoid the minimum readings are below the normal limit and in all the diseases, except Erysipelas, the mean value is below the normal mean. In Erysipelas the mean is slightly above the normal mean figure. It is possible that the slight decrease in Albumen may be due to temporary impairment of the kidney function and may be associated with the albuminuria often present in any febrile condition. It is, however, difficult to account for the increase present in Erysipelas. The Coefficient of Variation is practically normal; only in chronic Pulmonary Tuberculosis is the figure appreciably above that in normal cases.

Globulin.

In view of the fact that the Globulin readings in Normal cases show a wide range, it is difficult to estimate the value of the results obtained in the infective diseases, especially as the process employed in determining the amount present is more liable to error than that in the Fibrin and Albumen estimates. Roughly speaking, however, any reading that exceeds 3 gms. per 100 cc. may be considered abnormally high. In none of the diseases investigated has the amount fallen below the normal minimum.

In Acute Pulmonary Tuberculosis, Pneumonia and Erysipelas the maximum Globulin content is considerably above, and in chronic Pulmonary Tuberculosis and Typhoid Fever is slightly above normal limits. In these diseases and also in Scarlet Fever and Paratyphoid fever the mean Globulin reading is higher than the normal. In Typhus fever and Influenza the mean is slightly less than normal. The Coefficient of Variation in the Normal series is 21.822

which is surpassed by the figures obtained in Erysipelas, Pneumonia and Acute Pulmonary Tuberculosis.

Total Proteins.

The normal range is so wide that the majority of readings in all the diseases fall within it. In Erysipelas, Pneumonia and Acute and Chronic Phthisis the maximum and mean readings are higher than the normal maximum and mean readings respectively. In no disease is the amount less than the normal minimum.

Clinical Significance.

In most of the infections in which the blood has been examined very similar changes occur - viz., an increase in Fibrin and frequently of Globulin with a consequent rise in the Total Proteins, accompanied by a normal Albumen content. The reactions of the plasma have, therefore, little significance in the differentiation of one disease from another. It is only in Typhoid, Paratyphoid and Typhus fevers that the alteration in the Fibrin moiety is sufficiently typical to have a definite diagnostic value. In Typhoid during the first three weeks of the disease, and in the pre-critical stage of Typhus, the Fibrin is either normal or below normal in amount and the Globulin is either normal or only slightly increased. These points may be utilised in differentiating these diseases from -

1. Pneumonia.

This has already been illustrated in Table XIII. Nos. 36 - 39. The clinical features in this case, the insidious onset, staircase rise in temperature, constipation accompanied by abdominal pain and followed by diarrhoea, suggested a possible diagnosis of enteric. As early as the second day on which the patient was confined to bed, the fibrin reading was 0.820 gms. per 100 cc. From the

Fibrin/

Fibrin reading alone, in this instance, Typhoid could be excluded. In many cases the marked increase in Globulin would be additional evidence against a diagnosis of enteric. This test has the advantage of giving a reliable result at a stage of the illness when a negative Widal reaction is still of no value. Direct blood culture in bile may give a positive result in the early stages of the disease, but this requires a very much more elaborate technique than that employed in the estimation of Fibrin. The latter test has the advantage of requiring a short time only for its performance.

2. Influenza.

In this disease also, the definite increase in Fibrin would assist in the differential diagnosis, though in the case of Influenza the Globulin findings would have no confirmatory value.

3. Acute Miliary Tuberculosis.

The diagnostic value of the test in this condition has been illustrated by case No.27. Table XIX. In this case the Fibrin is only slightly increased (0.452 gms. per 100 cc., a reading which might occur in any of the three infections) but the Globulin reading is higher than in any case of Typhoid or Typhus fever examined. This supports the diagnosis of Tuberculosis but it cannot be considered conclusive evidence. The increase in both Fibrin and Globulin would be of value in differentiating between Typhoid infections and Pulmonary Tuberculosis.

4. Enteritis.

In the only case examined with a simple enteritis, the Fibrin showed a slight but definite increase above normal limits.

Conclusions.

When we review the results obtained, first in the series of Normal cases and secondly in the series of Pathological conditions, we arrive at the conclusion that in the Infective fevers, definite changes occur in the protein constituents of the blood plasma. These changes vary qualitatively and quantitatively in the different diseases and in certain infections the variations from normal are so constant that they may be considered typical of that condition, e.g. the increase in Fibrin and Globulin in Pneumonia or Erysipelas, the low Fibrin figure in the early stages of Typhoid infections, followed by an increase, varying in amount with the severity of the attack, or the almost invariable rise in Globulin in cases of Tuberculosis.

Of the three constituent proteins, the Fibrin is by far the most frequently and the most consistently affected. In almost all the diseases studied an increase in Fibrin is present at some stage of the disease, although, as has been previously noted, this increase may be preceded by a diminution, in the early stages. In a number of diseases the Globulin is also increased, but in other diseases in which the Fibrin may show a wide variation from normal, it appears unaffected. In none of the diseases studied was the Globulin diminished.

The Albumen on the other hand, shows very little alteration beyond a slight diminution in the mean readings in almost all the acute infections.

These changes are sufficiently constant to have a definite, though limited practical value in the differential diagnosis between certain of the infections.

GENERAL DISCUSSION.

Such therefore are the bare facts that emerged during the present investigation. The causes for the changes in the plasma are, however, difficult to determine. It would appear that the biochemical reactions in the circulating plasma, produced by an acute infection, affect the body as a whole, irrespective of the portal of entry or of the localization of the disease. The determining factor in their production must, therefore, lie with the infecting agent, which, produces a more or less specific reaction in the plasma-forming tissues of the body. If this be so, the question arises as to the relative importance of:- (a) The organism itself or possibly the nature of its protein. (b) The production of toxin by the organism. (c) The production of antitoxin by the body.

In the present state of our knowledge it is impossible to dogmatize on the part played in the production of the constituent proteins, by each of these factors. It remains, therefore, to indicate briefly the lines for further research and to emphasize certain points that seem to throw light upon the subject.

(1) Relation of the Plasma Proteins to Immunity.

From the behaviour of the Fibrin and Globulin of the plasma, it appears probable that their variations bear some relation to the phenomenon of Immunity. Comparable curves for both constituents are found in Pneumonia and Erysipelas; both Fibrin and Globulin rise on the onset of the symptoms and begin to fall rather before the onset of the crisis and reach normal by the time that convalescence is established. Both these diseases give rise to the rapid production of defensive bodies, indicated by a sharp crisis and in both the immunity is short-lived so that recurrence is/

is common.

Typhus, in which the crisis is as dramatic as in Pneumonia, also shows a definite alteration in the plasma Fibrin that synchronizes with the critical fall in temperature. In this disease, however, the curve is reversed, the pre-critical phase being associated with a low Fibrin content and the later stage with a slight increase above normal. The Globulin shows less variation but rises slightly towards convalescence. The Immunity in this case is lasting. It seems possible that the initial alteration is due to the presence of toxin which in the case of Pneumonia and Erysipelas is associated with a high Fibrin and normal Globulin, and that the subsequent rapid fall in the first two diseases and the subsequent rise in Typhus may be due to the replacement of toxin by anti-toxin. Further evidence that the plasma proteins are related to the production of Immunity is found in Typhoid and Paratyphoid fevers. In these diseases, the immunity developes more slowly and is of a more lasting nature than in Erysipelas or Pneumonia, and in both diseases there is a gradual rise in Fibrin from a point below to a point above normal, followed by a slow fall to normal and in both the Globulin tends to rise gradually during the whole course of the illness.

In view of the fact that antitoxin is supposed to be allied in structure, to the Globulins,(11) it is interesting to note that the Globulin is increased in the pre-critical stages of Erysipelas and Pneumonia and falls rapidly thereafter. In both infections the immunity is of short duration. In Typhus fever and in the majority of Typhoid infections and in three out of five cases of Scarlet Fever in which the course of the disease was studied, the Globulin rises slightly during the course of the disease and is still slightly increased when the patient is convalescent./

convalescent. In these diseases the immunity is of long duration.

Cases of Tuberculosis, all of a comparatively chronic character, in which a large amount of antitoxin is present in the circulation, show a very high Globulin reading. Influenza, on the other hand, an acute infection in which the immunity is of extremely short duration, shows no rise in Globulin above the normal figure. These facts suggest that there is a definite association between the production of antitoxin and the production of Globulin. The normal Globulin is, however, so erratic in its behaviour that no final conclusion can be drawn. The relation of such definite immunity phenomena as the Widal or WeilFelix reactions to the Fibrin and Globulin content of the plasma would be of value.

2. Relation of the Plasma Proteins to Anaphylaxis.

Unfortunately no cases of serum disease were available for examination. It would obviously be of the greatest service in determining the part played by an invading organism or by its toxin in producing alterations in the plasma, if the blood were examined in a series of cases in which the symptoms were certainly caused by anaphylaxis and not by an organism, e.g. cases of serum rashes, serum arthritis and serum adenitis. It is even possible that the plasma reactions might be of practical value in differentiating the two conditions. A further interesting study would be the condition of the plasma in cases of scarlatinal nephritis, a condition that may be included among the anaphylactic rather than among the toxic manifestations, compared with that produced by a definite toxin e.g. mercury or the toxins associated with pregnancy.

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3. Relation of the Plasma Proteins to Toxaemias of non-infective origin.

The toxaemias of pregnancy furnish examples of toxic states in which the toxin is not associated with an infecting organism. The Medical Research Council's report on the Toxaemias of Pregnancy[12] gives the following figures for the Fibrin content of the blood:-

		Maximum.	Minimum.	Mean.
1. Albumenuria.	12 cases.	.596 gms.	.211 gms.	.392 gms.
2. Toxaemia	16 cases	.546 gms.	.298 gms.	.404 gms.
3. Nephritis toxaemia.	15 cases	.546 gms.	.186 gms.	.384 gms.
4. Eclampsia	32 cases	.820 gms.	.194 gms.	.393 gms.
5. Controls	39 cases	.546 gms.	.262 gms.	.402 gms.

The controls in this series show the slight increase in Fibrin characteristic of the later stages of pregnancy. The range in each group is great, particularly in Eclampsia, so that no definite conclusions may be drawn. On the whole, it appears that the toxins present in pregnancy do not produce such typical changes as the toxins produced by the acute infections.

Relation of the Plasma Proteins to the Injection of Serum.

The action of an injected protein upon the proteins of the blood has still to be determined. Coetzee[13] has demonstrated a rise in Fibrin and Globulin following injection. In the present series, the cases treated by Scarlet fever antitoxin serum seem entirely unaffected, the cases treated with serum being indistinguishable from the untreated cases. Further, in the only example of Cerebro-spinal fever which had been treated by repeated injections (intra-thecal and intramuscular) of antimeningo-coccic serum the Fibrin is definitely low and the Globulin is normal. This suggests that the injected protein has a toxic action upon the blood proteins, producing a diminution in/the

in the Fibrin content. Such results are unexpected in view of the widespread, if somewhat empirical use of serum as a haemostatic agent in cases of haemorrhage. It appears that as the Fibrin is not increased, the effect produced by the infection of serum upon the coagulability of the blood, must be due to an increased production of thrombokinase or thrombin or one of its precursors.

As pointed out above, the existence of antitoxin in the blood may be associated with an increase in Globulin. In the Scarlet Fever cases, however, no increase in Globulin follows the introduction of antitoxin formed outside the body, ie. the production of a passive immunity is not associated with an increased Globulin, whereas in active immunity there is frequently a definite rise in Globulin. Such a rise is present in the pre-critical stage of pneumonia or in the convalescent stage of Typhus. It will be remembered that passive immunity is of short duration.

The present investigation has proved conclusively that in the healthy control the findings in the plasma are sufficiently constant to establish a definite standard and that any deviation from that standard is certainly abnormal. It has also been shown that in all the acute infections studied, changes are present that affect one or more of the constituent proteins. the Fibrin moiety being that most frequently and most consistently affected. The changes present are remarkably constant for each infection, and have therefore a definite practical value. Not only may they be employed, as they have been employed heretofore, in the study of impaired renal function or in estimating hepatic efficiency, but they may also be utilized in the differential diagnosis between certain of the infections. Furthermore, it/

it appears probable that a study of the plasma proteins in relation to Immunity, to Anaphylaxis and to certain toxic states may throw light upon the origin of the plasma changes, and, that conversely, the nature and extent of the plasma variations may be of great value in determining the origin and nature of various toxic and anaphylactic phenomena.

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