

THE VARIATION IN THE AMOUNT OF COMPLEMENT IN THE BLOOD IN SOME ACUTE INFECTIOUS DISEASES AND ITS RELATION TO THE CLINICAL FEATURES.¹

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THIS investigation upon the quantitative variations of the complement in the serum of patients suffering from enteric fever, erysipelas, diphtheria, and scarlet fever has been carried out in the laboratory of Ruchill Hospital, Glasgow.

The variation of the complement has been followed up as far as the opportunities have permitted, though when dealing with patients who are acutely ill difficulties necessarily arise in conducting complete series of blood examinations.

CONCEPTIONS OF COMPLEMENT.

As is well known, there are two classes of substances concerned in the mechanism of immunity in an organism—the specific immune body, and the less definite complement or alexin. The latter is absolutely essential to the mechanism of immunity, but with regard to its specificity some difference of opinion exists.

Muir and Browning (1908¹) define complement as that labile substance of normal serum which is taken up by the combination of an antigen and its anti-substance. Bordet (1909²) believes in the functional unity of complement, while Ehrlich (1906³) believes in a pluralistic conception of complement. The latter author believes he has demonstrated at least five different kinds of complement in goat serum. Muir and Browning (1908⁴) have shown that this difference in the molecules of complement exists, and that it depends upon a number of gradations in their affinities and action; but that there is also a certain community in the combining relationships of the complement molecules, *e.g.*, if sufficient bacteria be used along with a suitable immune body in the presence of fresh serum, the hæmolytic as well as the bacteriolytic or bacteriophilic complement is absorbed in the reaction.

In all diseases, especially acute infectious diseases, it may be assumed as probable that, in the development of immunity (resist-

¹ Received July 2, 1913.

ance), at the most active stage of the disease such different types of complement as exist in the patient may be used up by the union of the causal bacteria (antigen) and with their specific immune body.

The adoption of the hæmolytic test, *in vitro*, might suggest the criticism that only the hæmolytic portion is estimated in the reaction, were it not that, as has just been mentioned, bacteriolytic and hæmolytic complements display a common action in the presence of sufficient antigen. This condition, with reference to the bacteriolytic complement, exists in the test tube experiments, as there is always present sufficient of the antigen (ox red blood corpuscles). The hæmolytic properties of the serum may, therefore, be taken as a probable measure of the total complement content.

[METHOD BY WHICH THE SERUM HAS BEEN INVESTIGATED.

The hæmolytic effect upon ox corpuscles of fresh serum from patients in the presence of a suitable immune body (rabbit *v.* ox) has been used as an index of the amount of complement present.

Patients' serum.—The blood of the patient was withdrawn from one of the veins in front of the elbow by means of a 10 c.c. serum syringe. From 8 c.c. to 10 c.c. supplied the necessary amount of serum for each examination, namely, 4 c.c. to 5 c.c. The amount required restricted the total number of examinations which could be carried out in each case. To prevent any accidental hæmolysis, the syringe, needles, and test tubes for receiving the blood were all taken out of sterile 0.85 per cent. saline solution. The blood was allowed to stand for several hours, usually six, at room temperature, and the serum pipetted off and centrifugalised to clear it completely of red corpuscles, as the presence of even a small quantity of the latter obscures the reading, since they are not lysed during the test.

In practically every case the estimation of the hæmolytic power of the serum was made on the day upon which the blood was withdrawn. The specimens of blood were taken before the midday meal, and in this way the serum was obtained clear, or nearly so in most cases; but when this was not possible, and the serum was opalescent or turbid from the presence of chyle, the reading of the result did not appear to be materially affected, as the complete stage of hæmolysis could readily be seen in spite of the cloudiness of the solution.

Ox Corpuscles.—Ox corpuscles were used throughout as the antigen. The writer has not investigated the possibility of different samples of ox corpuscles being more readily lysed than others under the same conditions. The ox blood, which has been used during the course of the work, was obtained from a receptacle in which the defibrinated blood of several animals had been pooled, and if a difference in susceptibility to the hæmolytic action of human sera does exist, this has probably been reduced to a minimum by the mixing.

Immune Body.—The method adopted in the production of a suitable immune body and in the estimation of its dosage was that advised by Muir (1909⁵). At the end of six days after bleeding the immunised rabbits, the minimum hæmolytic dose of the immune serum was estimated. For complement, guinea-pigs' serum, which had been treated with ox corpuscles for two hours in an ice chamber to remove the natural immune body, was used. The maximum dose of the several hæmolytic sera used throughout this work was 0.001 c.c. for 1 c.c. of a 5 per cent. suspension of ox corpuscles in 0.85 per cent. saline solution.

Technique.

All the test tubes and pipettes used were taken from saline solution. A 5 per cent. suspension of washed ox corpuscles in 0·85 per cent. saline solution was used in all the tests. The red corpuscles in 5 c.c. of defibrinated ox blood were washed three times by centrifugalising, and made up to 100 c.c. with saline. To each cubic centimetre of this suspension five times the minimum hæmolytic dose of the immune body (rabbit *v.* ox) was added to sensitise the corpuscles, and this mixture incubated at 37° C. for thirty minutes or more before use.

On account of the considerable differences in the hæmolytic power of the various fresh sera, a series of twenty-four test tubes was necessary for each examination. Into each of the series of test tubes 1 c.c. of this sensitised suspension of ox corpuscles was measured, and the following quantities of the patients' serum were then added:—0·02, 0·04, 0·06, 0·08, 0·09, 0·1, 0·11, 0·12, 0·13, 0·14, 0·15, 0·16, 0·17, 0·18, 0·19, 0·2, 0·21, 0·22, 0·23, 0·24, 0·25, 0·26, 0·27, 0·28 c.c. respectively. In the case of very inactive sera the quantities were suitably modified. The test tubes were incubated at 37° C. for one hour, and shaken meanwhile at intervals of fifteen minutes. The reading was then taken. At first a second reading was also taken next day, but as the differences between the two were small this was discontinued. The hour limit was adopted throughout. The complement content of the serum was determined by the presence of complete hæmolysis, as indicated by the absolute disappearance of turbidity.

As a source of error the presence of a natural immune body in human serum against ox corpuscles was investigated. Numerous estimations were made of the natural hæmolytic power of fresh human serum, and this was always found to be relatively slight. The amount of natural immune body found was so small that its removal by treatment of the sera at 0° C. with fresh ox corpuscles was not considered necessary. It has not been possible, because of the rate of deterioration of the complement, to store all the samples of serum obtained from the patients during the whole period of illness when the estimations were being made, in order that all might be tested under exactly the same conditions; but the precautions observed, namely, the time of collection and examination of the blood, the constant amount of immune body used for sensitising the ox corpuscles, the fact that the ox corpuscles were from several animals, and the fixed period of incubation for the test series all tend to a uniformity of results.

Method of recording the Results.

In taking the observations the amount of serum required to effect complete hæmolysis was recorded, but as this is evidently proportional to the reciprocal of the amount of complement contained in the serum, the results have been calculated on the latter basis. For example, if two sera be taken, and if of one the amount required to produce hæmolysis is 0·2 c.c., and of the other 0·05 c.c., then the amounts of complement present in the two sera are evidently in the proportion of 5 to 20. The reciprocal for each amount of serum used has been calculated.

COMPLEMENT IN NORMAL SERUM.

As a standard of comparison between the amount of complement in the serum in health and in disease, about forty examinations were made on normal sera. In the first place, the writer's serum was

examined for daily variations in relation to meals, and the results are recorded in Table I.

TABLE I.

Hour.	Complete Hæmolysis produced by	Reciprocal for Complement.
10 a.m.—Serum clear . . .	0·25 c.c.	4·00
1 p.m.—Serum opalescent . .	0·23 „	4·34
5.30 p.m.—Serum turbid . . .	0·23 „	4·34
8.30 p.m.—Serum turbid . . .	0·23 „	4·34

It was not possible to make a similar investigation of the hæmolytic power of the complement in any other individual's serum, as from 8 to 10 c.c. of blood were required to furnish sufficient serum for each examination. From the results obtained (Table I.) it seems reasonable to infer that variations in the amount of complement in the serum from hour to hour are not marked, nor does the presence of the products of absorption of food appear to influence, to any great extent, the complement value. On another occasion the writer examined his serum at intervals of two days throughout a period of six days (Table II.).

TABLE II.

Examination.	Production of Complete Hæmolysis.	Reciprocal representing Complement.
1st examination . . .	0·23 c.c. produced complete hæmolysis	4·34
2nd „ . . .	0·18 c.c. „ „ „	5·55
3rd „ . . .	0·23 c.c. „ „ „	4·34

Again a fairly uniform result was obtained. In this instance the variation, although somewhat marked, is very much smaller than that observed during the course of some acute diseases.

Similar examinations were made of the serum of a number of healthy adults and of others who had long been convalescent. The results are given in Table III. :—

TABLE III.

Healthy Adults.			Convalescents.		
Case.	Serum.	Complement.	Case.	Serum.	Complement.
1. . {	(a) 0·18 c.c.	(a) 5·55	1. . .	0·24 c.c.	4·16
2. . .	(b) 0·17 „	(b) 5·88	2. . .	0·19 „	5·26
3. . .	0·17 „	5·88	4. . .	0·18 „	5·55
4. . .	0·18 „	5·55	5. . .	0·22 „	4·54
5. . .	0·23 „	4·34	6. . .	0·28 „	3·57
6. . .	0·28 „	3·57	7. . {	(a) 0·20 „	(a) 5·00
7. . .	0·20 „	5·00	8. . .	(b) 0·20 „	(b) 5·00
8. . {	0·30 „	3·83	9. . .	0·20 „	5·00
9. . .	(a) 0·22 „	(a) 4·54	10. . .	0·20 „	5·00
10. . .	(b) 0·28 „	(b) 3·57			
11. . .	0·21 „	4·76			
12. . .	0·17 „	5·88			
	0·18 „ +	5·55			
	0·21 „ +	4·76			

"Serum" = Amount of serum required to produce complete hæmolysis of 1 c.c. sensitised ox corpuscles.
 "Complement" = Represented by the reciprocal of the amount of serum required to produce complete hæmolysis of the test amount of sensitised ox corpuscles.
Note.—In all other Tables "Serum" and "Complement" have this meaning.

It is seen from the results that the amount of fresh normal serum, which is capable of completely hæmolysing 1 c.c. of sensitised ox corpuscles in one hour, varied between 0·17 c.c. and 0·28 c.c., giving the reciprocal figures for complement 5·88 and 3·57 units respectively. The mean of all the complement figures obtained from these examinations of the serum of healthy adults and convalescents is 4·84, and in subsequent parts of this paper this is referred to as the normal average amount of complement.

CONSIDERATION OF SOME SPECIAL POINTS.

A. Complement and Age.

In the sections which follow dealing with acute infectious diseases various ages are represented. The influence of this factor upon the quantity of complement present in the serum, and upon the variations in its amount during the course of disease, has consequently to be considered. The figures chosen as most likely to throw light upon this point are those representing the greatest amount of complement present during the acute stage of the various diseases, and the amount present towards the end of convalescence in all the patients examined,—the latter quantity probably approaching most nearly the normal of each case. A careful analysis of these figures does not dis-

close any definite relation between age and the amount of complement observed at any of the periods selected.

B. Complement in the Individual.

There are very considerable differences in the amount of complement present in the individuals examined, both in the acute stage of the illness and in convalescence. These differences are much more marked in the acute stage of the fever. They exist in varying degrees during convalescence, but the majority of the figures are fairly close together and show little variation from the mean. In some cases, however, a very considerable departure from the mean both in excess and deficit occurs, but the number of individuals showing this phenomenon forms only a small proportion of the whole. In interpreting the observations, each case must, therefore, be taken to afford its own criterion. In some, in which a small amount of complement was found during the course of the illness, a like deficiency continued during convalescence; in others the amount was large throughout. Illustrative cases of each of these may be given in Table IV.

TABLE IV.

Disease.	Greatest Amount of Complement during Fever.	Amount of Complement in Convalescence.
Case 16.—Enteric fever . . .	12·42 units	7·14
Case 10.—Scarlet fever . . .	10·00 „	8·33
Case 17.—Diphtheria . . .	2·17 „	3·33
Case 12.—Diphtheria . . .	0·00 „	0·00

OBSERVATIONS IN PARTICULAR DISEASES.

A. ENTERIC FEVER.

This disease affords very favourable opportunities for the study of variations in the amount of complement, and the correlation of such with the clinical appearances illustrated by the different types of cases. It may reasonably be inferred that immune body is probably smaller in amount when prostration and toxæmia are most marked than when recovery is taking place. This cannot be measured by the agglutinating power of a typhoid serum, because agglutination may be well marked during the worst period of the disease or even prior to death. Thus the formation of agglutinin alone does not bring about the establishment of immunity in enteric fever. Specific immune body or bodies requiring the presence of complement are necessary

for the complete destruction of the typhoid bacillus. The more immune body present the greater will be the amount of complement required in order that the former may be used to greatest advantage. The presence of the infecting agent in the body stimulates the production of both antibody and complement, but the response in each case is not the same. The intermediary body and complement are independent of one another.

Investigations have been carried out in forty cases of enteric fever. In thirty-two of these, examinations of the serum were made at varying intervals throughout the whole period during which the patients were in hospital. The cases have been considered in the following groups:—

(A.) Uncomplicated cases.

(B.) Cases complicated with relapses, thrombosis, and secondary infections.

(C.) Fatal cases.

GROUP A.—Uncomplicated Cases.

Clinically the patients in this group resembled one another in that the appearance of enteric fever as manifested by all were typical; marked differences in the degree of illness, however, existed. The diagnosis in each case was made from clinical evidence, corroborated by the Widal reaction; while in many cases the *B. typhosus* was isolated from the blood, fæces, or urine. It will make for an easier understanding if the variations in the amount of complement are described in reference to a special case which seemed to supply the type. Case 1 fulfils the condition.

This patient was admitted to hospital on the eighth day of illness, suffering from a severe attack of enteric fever. The temperature remained constant about 102° F., until the twentieth day of illness, when it became remittent; reaching normal only on the twenty-seventh day. The patient was markedly prostrate. Improvement was associated with the remissions of temperature. Convalescence was uninterrupted. The complement, or that amount of it estimated by the hæmolytic test, was found to be most abundant during the period of fever, 10·00 units being present. What changes may have taken place during the intervals between the examinations cannot of course be stated, but the general course of the variations showed that there was a steady decline in the amount from the end of the period of pyrexia until shortly before the patient was dismissed, well, when the complement figure was 3·57 units. (See figures in Appendix A, Case 1.)

Thus in a favourable case, such as this Case 1, when infection is being successfully overcome as shown by the improvement in the patient's general condition, complement decreases in amount. This suggests that when immune body is being produced the complement is fixed, and so there is less available for the hæmolytic test *in vitro*. As already remarked, though complement may be diverse in character, yet it is none the less true that the fall in the amount of complement is probably explained by the appearance of immune bodies.

Sixteen cases, including that just recorded (Cases 1 to 16)

showed the same general phenomena. From this it seems reasonable to conclude that the immune body was lacking during the period of fever. As soon as it was produced in sufficient quantity, as evidenced by the favourable clinical course of the fever, the complement diminished in amount. The complement fluctuations in the various cases, however, did not agree in all particulars. The diminution did not always happen at the same period. It occurred almost immediately after the temperature became normal in two cases (5 and 16). In three cases (2, 4, and 15) the diminution was most apparent a week after the disappearance of the fever. In six cases (1, 3, 6, 7, 10, and 11) it was most marked at the end of the second week; in two cases (8 and 14) at the end of the third week, and in the remaining three cases (9, 12, and 13) about the end of the fourth or fifth weeks. These dates are only approximate, as the intervals at which the examinations of the serum were carried out varied in length. There is sufficient variation, however, to show that the establishment of immunity does not take place at any fixed time. This is in accordance with what is known clinically regarding the appearance of the tongue in some cases during convalescence from enteric fever, and also with the manner in which typical rose spots may appear within the first fortnight or three weeks after the temperature has reached normal.

The questions now arise as to whether the mildness or the severity of the attack and the length of the fever have any relation to the time at which the complement shows a diminution in amount. (See Table V.)

TABLE V.—*The relation between the Type of Attack and the Period at which Complement falls in Amount.*

Case.	Type of Illness.	Approximate Duration of Fever.	Approximate Period after End of Fever at which Complement is diminished.	Greatest Amount of Complement during Fever, and Day upon which Observation was made.
1	Severe	26 days	16 days after end of fever	10·00 units on the 11th day.
2	"	27 "	9 "	8·33 " 12th "
3	"	28 " (?)	16 "	8·33 " 21st " (?)
4	Moderate	22 "	9 "	6·66 " 21st "
5	Severe	23 "	End of fever	16·66 " 13th "
6	"	26 "	18 days after end of fever	16·66 " 23rd "
7	"	17 " (?)	14 "	7·69 " 18th " (?)
8	Very severe	52 "	21 "	6·66 " 41st "
9	Severe	34 "	28 "	9·09 " 24th "
10	"	39 "	14 "	12·50 " 28th "
11	"	28 "	18 "	8·33 " 28th "
12	"	52 "	28 "	12·50 " 20th "
13	Moderate	25 "	34 "	5·26 " 12th "
14	"	39 "	22 "	5·00 " 20th "
15	"	13 "	9 "	6·66 " 10th "
16	Severe	17 "	End of fever	12·42 " 14th "

In four patients, who were moderately ill (Cases 4, 15, 14, and 13), the fall in complement was most apparent—one week, one week,

three weeks, and five weeks, respectively, after the temperature had settled. In the other twelve cases of this group, all of which were acutely ill, this occurred between the end of the fever and five weeks afterwards. Therefore no definite statement can be made from this analysis as to the time at which complement is distinctly diminished, and, indirectly, it follows that the period at which an optimum amount of immune body is present probably varies irrespective of the severity of the attack.

Diminution of Complement in relation to the Length of the Fever.

The duration of the fever differed very markedly in the sixteen cases which are being considered. Between an abortive attack, lasting thirteen days (Case 15), and an attack which was prolonged to the fifty-second day (Case 8) various periods of fever are represented. In five cases (15, 16, 4, 5, and 2), in which the fever lasted thirteen days, seventeen days, three weeks, three weeks, and four weeks, respectively, a marked fall in complement was observed either at the end of the fever or some time during the first week of convalescence. In the other eleven cases, most of which suffered from a fever lasting four weeks or more, the diminution in complement, as far as is shown by the examinations made, occurred at times varying between two and four, or perhaps five weeks after the pyrexia had subsided.

From this observation it may be deduced that the shorter the period of the fever the earlier is a distinct fall in the amount of complement noted, and the longer the fever the longer after its termination is complete immunity established.

The Quantity of the Complement during the Fever in relation to the Severity of the Attack.

It will be seen from Table V. that the greatest quantity of complement present in the cases of Group A during the pyrexia varied between 5 and 16 units. Those cases in which the highest complement figure was between 8 units and 16 were acutely ill. In one, however (Case 8), who was extremely ill, and at one period in the typhoid state, the complement figure at its highest was only 7 units. This represented a comparatively inactive type of serum, and when taken in conjunction with the clinical facts seemed to indicate that in addition to a failure or slow production of immune body, complement was similarly affected, or that only a weak type of complement was present.

The other four cases (4, 13, 14, and 15), in which complement even when greatest in amount was only between 7 units and 5, were all moderately ill. The low complement figure and the comparative mildness of the attack in each, even although the fever was prolonged in one of them (Case 14) to thirty-nine days, seem to indicate that in these cases a considerable amount of immune body was produced fairly early in the fever, and that this was probably sufficient to

mitigate the symptoms, but not great enough to end the fever. In other words, the immunity factors were nearly balanced throughout the illness. From these observations it would appear that the quantity of complement present in certain cases of enteric fever bears some relation to the type of illness.

Irregularities in the Production of the Complement.

Irregularity of the course of complement was seen in some cases, particularly in four (Cases 9, 10, 11, and 12). They resembled one another clinically, and the fever lasted four weeks or longer. The temperature curve in the first three of these showed a break, as if the fever were subsiding about the twenty-first day. A recrudescence, however, occurred in each, lasting for a week or longer. In the remaining case (Case 12) the pyretic period, although prolonged, showed no interruption. In the first three cases the complement, which was less in amount before or at the period of the break, increased during the final part of the fever, and diminished as convalescence was established. The relatively low complement figure observed at these periods, when compared with what was found in preceding cases, and during the final phase of the fever in the cases under consideration, may mean that immune body was present fixing complement, but not in sufficient amount to end the fever at that time. In the remaining case (Case 12) something of the same kind seems to have occurred, although there was no break in the temperature or other clinical indication that the end of the fever was approaching.

The variation of the complement in these cases suggests that there may be two phases of the primary fever represented, and that the part corresponding to the secondary increase in the complement may be regarded in the nature of an exacerbation or recrudescence of the primary fever. If this is so, then these cases form a link between uncomplicated enteric fever and that associated with the relapses. In this connection the following quotation of Murchison's (1884'), based on clinical observation, is of interest:—"Relapses must not be confounded with the recrudescences which are common during the stage of ulceration. It is possible, however, that a true relapse may occasionally overlap the primary attack without any apyretic interval, and that this may be the explanation of certain cases of enteric fever which are unusually protracted." Similar cases will be referred to in the next group (B).

The two remaining cases of Group A. (Cases 17 and 18) were exceptional in that complement was much greater in amount during convalescence than at the time of the fever. In one of the cases already considered (Case 16) something of the same kind regarding complement occurred during convalescence, but not nearly so markedly. No explanation is offered for this difference.

GROUP B.—Enteric Fever with Complications, Relapses, Thrombosis, and Secondary Infections.

Eleven cases constitute this group. Of these, seven suffered from relapse, two from thrombosis of the saphenous vein, and two were associated with other types of infection, namely, erysipelas and pneumonia.

Before discussing the special phenomena of relapse, it is to be noted that in five of these cases (20, 21, 22, 25, and 26) complement behaved during the primary fever in a manner similar to that described in four cases (9 to 12) in the previous group. As before suggested, the temporary diminution probably indicates an unsuccessful attempt at this point to establish immunity. The differentiation between the primary fever and the recrudescence was best seen in the first three cases of this series, while an overlapping of the two phases of the fever was more marked in the remaining two. The temperature curves of these cases illustrated the gradation of a true relapse from the recrudescence which overlaps, or is tacked on to, the primary fever in some cases. The complement estimations were not sufficiently complete to throw further light on this hypothesis, although the nature of the complement variations obtained in two of the cases (Cases 21 and 26) points to the probable presence of a considerable amount of immune body at the period at which the lysis was interrupted.

Relapses.

With special regard to the cases in which relapses occurred, it may be stated that the phenomena followed a course such as would be expected from what has already been said in connection with uncomplicated cases. A review of the behaviour of the complement in all of this group in which examinations were made at sufficient intervals, shows that it was more abundant during the relapse than during the afebrile interval or convalescence.

In one case (Case 19), where a fairly complete record of the amount of complement in the primary fever and the relapse was made, the complement variations followed closely the course of the fever in both stages of the disease, there being a reduction during the apyretic interval and a uniformly small amount of complement present throughout convalescence. In all, except two cases (Cases 24 and 25), in which the records are incomplete, the fall in the amount of complement occurred within a week after the relapse, thus differing to some extent from what was found in uncomplicated cases. This observation seems to indicate that immune body is produced more rapidly during the relapse, and that recovery takes place sooner than from an initial fever, as is indeed also noted clinically.

In general, the course of the relapse is associated with the

presence of a considerable amount of complement, and this holds in some cases when the patients are acutely ill, but, as in all other immunity phenomena, variations in the amount of antibodies occur in this class of cases. This variation is represented by those cases in which what might be called acute relapses occurred. In one, the amount of complement present was very considerable; in the other two, though considerably higher than in the apyretic stage, yet it never reached much above twice the amount normally present in the serum of these patients.

Enteric Fever associated with a Secondary Infection.

Two cases were observed (Cases 26 and 27). In the first (Case 26) the illness was severe and prolonged. It was complicated by erysipelas of the face, and subsequent suppuration of the scalp, neck, and thigh. Complement declined in amount from the time of the primary fever until convalescence was completely established, being between 10 and 11 units during the pyretic period, and as low as 3 units when the patient was about to be dismissed, after being ill for 132 days. This conforms to what has already been described in the majority of the cases examined. At the beginning of the attack of erysipelas only five units were found present, but during the prolonged period of suppuration an increase to 10 units was observed, and thereafter when healing was in progress a final diminution occurred. The second (Case 27) was admitted to hospital suffering from lobar pneumonia. Enteric fever developed fourteen days later. Although complement was relatively small in amount throughout the illness, it was a little more abundant during the attack of enteric fever than at the time of complete convalescence. No observations were made during the attack of pneumonia. These two patients resemble each other in that they suffered from two types of infection, and that the power of production of complement appeared to be impaired at the time the second infection began. Müller (1909⁹) quotes experiments made by Schultze and Scheller, and Wassermann, who found that after one type of infection in which complement has been used up this substance is not rapidly regenerated if a secondary infection with another type of organism occurs. This explanation may be applied to the two cases under consideration regarding the relative failure of complement production at the beginning of the attack of erysipelas in the one, and of enteric fever in the other; but further evidence is required on this point.

Enteric Fever complicated with Thrombosis.

Two cases complicated with thrombosis of the saphenous vein were observed (Cases 27 and 29). The course of the variations of complement as a whole in both conforms with that found in the earlier cases described in this section; but as far as the observations show, no

marked variation in the amount of complement occurred during the time thrombosis was present.

A Case complicated with Pleurisy and Pneumonia.

The outstanding feature in this case (Case 30) was the very marked rise in the amount of complement between the first two examinations made on the 17th and 20th days of illness. A rise from 6·89 to 20·00 units occurred. This corresponds with the beginning of pleurisy and pneumonia. During this period complement remained relatively increased. Cystitis was also present, though the date of origin was somewhat obscure. There may have been a recrudescence of the enteric fever at the same time, but this could not be corroborated clinically. When convalescence was established the quantity of complement decreased. The statement already made regarding the cause of the reduced amount of complement found in the two cases (Cases 22 and 23), which showed a double infection, does not hold in the present instance. It may be noted, however, that the pleurisy and pneumonia differed clinically from a pneumococcal infection, and the condition was considered as probably due to the typhoid infection. The behaviour of the complement at this time was somewhat similar to that observed in the other cases showing a true enteric recrudescence.

GROUP C.—Fatal Cases of Enteric Fever.

Ten cases have been included in this group. In five of them (Cases 31, 32, 33, 39, and 40) several examinations of the serum were made, and in the others (Cases 34, 36, 37, and 38) only single examinations were possible. It was found in all of these cases except one (Case 39), that, even when the complement was present in small amount, the lowest figure was higher than the mean obtained from examinations of normal sera already noted, namely, 4·84 units. In none of them was there any absence of complement. A very notable increase in the amount of complement was found immediately prior to death in four cases (Cases 31, 32, 33, and 34).

In the first three of these, the difference in the amount of complement at this time compared with what it was several days before death was very great. Death cannot be ascribed, therefore, to a lack of complement in these four cases particularly, but rather to a lack of sufficient immune bodies. In other five cases, where only single estimations were made (Cases 35, 36, 37, 38, and 40), the amount of complement, although more or less small in comparison with that in the previous fatal cases, sustains this view to some extent. In a single instance (Case 39), however, the amount of complement was small even at the time of death, and this has been taken to signify a failure in production of both immune body and complement, or the production of only a very weakly acting complement.

NOTE.

A Note on Hæmolysis in the presence of an excessive amount of Fibrin in a Serum which caused complete Coagulation of the whole content of each Tube in the Test Series.

In one fatal case (Case 34), when the serum was being examined, great difficulty was experienced in obtaining it free from fibrin, of which an excessive amount was present. Coagulation of the serum occurred several times after each removal of the coagulum. During an interval between coagulations, when the serum could be drawn into a pipette, it was added to the series of test tubes containing 1 c.c. of the suspension of sensitised ox corpuscles, in quantities varying from 0.02 to 0.28 c.c., as already described in connection with the technique of this work. The amount of serum in each of the twenty-four test tubes was, therefore, very small. Five minutes after the tubes had been placed in the incubator, complete coagulation of their contents occurred. This, however, did not interfere with the progress of hæmolysis. At the end of an hour the hæmolytic power of the serum could be readily observed by the presence of complete hæmolysis. This phenomenon was only present in this instance, although an excessive amount of fibrin was frequently observed, especially in the blood of patients who were very ill.

Summary of the Results obtained in Enteric Fever.

1. Complement is always present during enteric fever, and is, as a rule, more abundant throughout the period of pyrexia than during convalescence.

2. Diminution in the amount of complement in favourable cases seems to coincide with the production of immune body, as shown by the condition of the patient.

3. Complete immunity is not established in all cases at any definite time, after the temperature has settled, and it does not seem to bear any definite relation to the degree of severity of the attack, but it would appear to depend to some extent on the length of the period of illness; immunity being established sooner after a brief than after a prolonged illness.

4. Severity of the attack bears some relation to the amount of complement present during the fever. In patients who are very ill complement as well as immune body may be produced slowly, or only a weak type of complement may be produced. On the other hand, in patients who are moderately ill, a relatively small amount of complement seems to indicate the presence of a considerable amount of immune body, but not sufficient to terminate the attack. In the intermediate type of illness, which is the most common, a large amount of complement is found.

5. The variation in the amount of complement during some prolonged types of primary fever seems to indicate that the terminal portion of the pyrexia may be of the nature of a recrudescence.

6. Complement is increased in amount during relapses, and diminished when recovery is taking place. The diminution appears to

occur sooner after a relapse than after a primary attack. This might mean that immune body is produced earlier than in the original attack. The extent of the variation of the complement does not bear any definite relation to the severity of the relapses which have been observed.

7. Death from enteric fever appears to be due chiefly to absence of immune body. Complement is sometimes very abundant in fatal cases, but at other times only a weak type of complement may be present.

8. All the results show that complement and immune body are not produced in any fixed ratio to one another.

B. ERYSIPELAS.

This disease, characterised by an acute onset, a moderately short period of pyrexia, and a critical termination in most cases, ends in the first or in the early part of the second week, but occasionally may continue a longer period, as, for example, in the migrating type of the disease. There is usually considerable pyrexia and general disturbance in the condition of the patient during the acute stage of the illness. Relapses are common. This brief clinical outline indicates that the immunity processes once begun develop rapidly, and that the immune substances are equally rapidly produced. McCririck (1911¹⁰) has observed, for instance, that the opsonic index in erysipelas, at first relatively low, reaches normal between the fourth and eighth days from the onset of the disease, and that during a relapse the normal index is restored between the second and fourth days. Altogether thirty cases of erysipelas have been investigated, and estimations of the complement were made as frequently as was practicable.

GROUP A.—Uncomplicated Cases, including a Case of Erysipelas Migrans.

This group consists of uncomplicated cases of the disease. In the first twelve cases (1 to 12) the complement diminished in amount at short but varying intervals after the temperature had reached normal, and quantitatively it showed no definite relationship to the type or duration of the attacks. Only small fluctuations were observed during the acute stage and convalescence in eight cases (13 to 20), but it may be noted that all of these were of a mild type of erysipelas, and it seems possible that immune bodies were being produced fairly constantly throughout the attack, causing a balancing of the immunity factors in these cases. In five of these cases (16 to 20) complement showed a tendency to increase in amount as convalescence became established.

CASE 27. *A Case of Erysipelas Migrans.* — In this case the erysipelas began on the face, and at different times affected the body, arms, and one leg. The patient was most acutely ill during the first seven days, and from

that time onwards the inflammatory process became less and less acute. The amount of complement present during the first seven days was relatively small, only varying between 4 and 5 complement units. The patient's general condition at that time indicated a weak degree of reaction. During the less acute stage of the disease, however, when recurrences of a progressively less severe type were appearing on different parts of the body, marked fluctuations in the amount of complement were observed. This behaviour of the complement, along with the clinical evidence, seems to indicate an instability in the balance of the immunity factors at the different stages of the illness. An increase in the amount of complement was also observed during convalescence. The only further examination of the serum which was possible was made on the fifty-fourth day of illness, when the patient was perfectly well and about to be dismissed from hospital. The complement content was then observed to be 4.34 units, or the normal average. During the interval between the two final observations, made on the thirty-second day of illness, and the fifty-fourth respectively, a slight recurrence of the facial erysipelas lasting three days occurred. This is of some interest, as it tends to support the remarks regarding the instability of the balance of the immunity in this case. For the figures relating to this case, see Appendix B, Case 27.

GROUP B.—Cases complicated with Relapse.

No definite conclusions have been drawn from the small number of observations made in cases which relapsed (Cases 21 to 26).

Erysipelas associated with Suppuration.

In this case (Case 26), fourteen observations were made. The patient suffered from erysipelas of the face and scalp arising from a septic scalp wound. There was extensive suppuration of the scalp and forehead, followed by sloughing of the subcutaneous tissue. At no time after the eleventh day was the inflammatory process nearly so acute as during the antecedent period, although suppuration occurred in the scalp necessitating incisions at various times, up to the forty-third day of illness. The patient was still in hospital on the seventy-second day, when the final estimation of the complement was made. The scalp and forehead at that period had not quite healed, but the patient was very well.

The variations in the amount of complement in this case are shown in Appendix B, Case 26. They indicate three phases: the first rise corresponds to the attack of erysipelas, with abscess formation under the scalp; the second to the abscess formation in the forehead, and the reaccumulation of pus under the scalp; and the third to the recurrence of the abscess in the forehead.

These fluctuations of complement are consistent with the interpretation that there was a deficiency of immune substances during most of the time the observations were made, except for a few days after the first collection of pus had been evacuated. The indirect evidence supplied by the amount of complement regarding the presence of immune substances points to a considerable deficiency of the latter during the worst period of the erysipelas, and at such times as reaccumulation of pus was taking place in the scalp and the forehead.

GROUP C.—Fatal Cases of Erysipelas.

Three fatal cases have been investigated. In two (Cases 27 and 29), an increase in the amount of complement was noted at the time of death. In the third (Case 30), a single examination was made when the patient was dying, and although the amount of the complement found was not so high as in the other fatal cases, yet it was a little above the normal average. The fatal issue in these cases cannot, therefore, be ascribed to absence of complement.

Summary of the Results obtained in Erysipelas.

1. In the majority of the cases examined complement was present in greater amount during the acute stage of the illness than during convalescence. The clinical course of these cases supports the view that the diminution coincides with the production of immune substances (Cases 1 to 12).

2. No definite relationship has been found to exist between the severity or the duration of the illness, and the period at which immunity in the primary attack is established, although this seems to occur within a few days after the inflammatory process has subsided, as is also shown by the rapid recovery made by most of the patients.

3. The greatest amount of complement present in any case has no relation to the severity or the duration of the illness.

4. This amount is considerably less than already observed in enteric fever, which observation suggests that the production of immune substances occurs comparatively early in erysipelas.

5. In some mild cases only slight variations in the amount of complement present have been observed (Cases 13 to 20).

6. An increase in the amount of complement has been observed in some instances during convalescence, and is possibly due to an early diminution in the amount of immune substances present. It is well known in this connection that the immunity established by an attack of erysipelas is in many instances of short duration.

7. On account of the comparatively small number of observations which it has been possible to make during relapses, no definite conclusion has been drawn from the results obtained during this phase of the disease.

8. Complement was found to be increased in amount in one case in which prolonged suppuration was associated with erysipelas.

9. Irregularity in the amount of complement present during illness seems to indicate a certain degree of instability in the immunising mechanism, as is shown by the clinical course of a case of erysipelas migrans.

10. The amount of complement present in fatal cases has been found to be above the normal average.

C. DIPHTHERIA.

Unlike the two preceding diseases, diphtheria is not associated with any definite period of fever, nor is the temperature a guide in determining the severity of the illness. The toxæmia, however, is as a rule proportionate to the extent of the local infection, and the virulence of the attack has been estimated by this symptom in the cases of diphtheria examined. These were considered in three groups—(a) Faucial diphtheria; (b) faucial and nasal diphtheria; (c) laryngeal diphtheria; and a summary of the results obtained is given below. Attention is here drawn to the fact that the amount of complement was below the normal average, 4.84 units, in four cases (12, 13, 17, and 18) during the acute stage of the disease, and in ten cases (1 to 7, 14, 17, and 18) during part of convalescence. The significance of this is not clear.

Summary of the Results obtained in Diphtheria.

1. In seven cases of severe faucial, and in three of severe faucial and nasal diphtheria, there was a greater amount of complement present during the acute stage of the illness than during convalescence (Cases 1 to 7).

2. In three cases of faucial diphtheria, one of which was very severely, and the other two moderately ill, complement was greater in amount during convalescence than during the acute stage of the illness (Cases 9, 10, and 11).

3. In two cases of faucial diphtheria, both moderately ill, complement was practically absent during the acute stage in both, and only present in small amount during the convalescence in one of them (Cases 12 and 13).

4. The complement in two severe cases of faucial and nasal diphtheria was small in amount, during the whole illness, and more especially so during the acute stage than at any other time (Cases 17 and 18).

5. In two fatal cases of severe faucial and nasal diphtheria, one of which was of the hæmorrhagic type, the complement content was relatively great two days before death (Cases 19 and 20).

6. In thirteen of the cases of diphtheria investigated, the diminution in the amount of complement occurred during the period at which the throat was healing and the toxæmia disappearing. In four others a varying degree of increase in the amount of complement was observed at this period.

7. The observations made during the occurrence of post-diphtheritic paralysis were insufficient to base any conclusions upon, single examinations being made in three cases only. Complement was present in smaller amount at this period than during the acute stage of the illness in two of the cases, and less than the amount present during convalescence in all (Cases 13, 17, and 18).

8. The amount of complement showed a tendency to lessen in some instances within twenty-four hours after the administration of antitoxin, but this did not always occur. Although the degree of diminution was not definitely related to the amount of antitoxin administered, yet there seemed to be a tendency for the greatest diminution to occur after the injection of a large dose. Observations upon this point were made in Cases 4, 6, 7, 8, 11, 14, 15, 16, 17, and 19.

D. SCARLET FEVER.

The observations on the serum complement in scarlet fever have been carried on in the same way as those already described, with this difference, that in all the cases except four, 0.5 c.c. of sensitised ox corpuscles were used instead of 1 c.c. This measure was adopted because of the difficulty met with in obtaining sufficient blood from the younger patients. In recording the results, however, the reciprocal of twice the amount of serum, which was found to produce complete hæmolysis of 0.5 c.c. of the sensitised ox corpuscles was taken to represent the amount of complement present, and in this way the results have been brought into line with those in the other sections of this paper. Twenty-two cases were investigated, and a summary of the results is given.

Complement in Scarlatinal Nephritis.

In two cases of scarlet fever, which were complicated by nephritis, complement was practically absent in one (Case 19), and very markedly deficient in the other (Case 20). Death occurred in the latter. Complement at the time of death was found present to the extent of 4.00 units. In the former case 0.46 c.c. of serum only produced slight hæmolysis of 0.5 c.c. of the sensitised ox corpuscles.

Somewhat similar results were observed by another observer in other two cases of scarlatinal nephritis, the records of which are as follows:—

CASE A.—In this case at a period when the patient—a child—was very ill, and the urine markedly suppressed, 0.37 c.c. of the serum was required to produce complete hæmolysis of 1 c.c. of sensitised ox corpuscles, which gives the reciprocal 2.70 complement units.

CASE B.—In this case also the illness was very acute. Extensive œdema was present, and the urine contained much blood and albumin. The result of the observation made at this period showed that 0.34 c.c. of the patient's serum produced practically no hæmolysis. No greater amount of serum was used. A second observation was made some time later when the œdema had almost gone, and the albumin and blood were diminished. On this occasion 0.4 c.c. of the patient's serum was found to produce distinct but not nearly complete hæmolysis. The results of these investigations in scarlatinal nephritis agree with those obtained by Longcope (1903¹¹), whose observations in the complement content in certain cases of uræmia following chronic nephritis, were carried out by a bacteriolytic method. No explanation can be given for the

marked reduction of the complement of the serum of these cases of scarlatinal nephritis.

In two cases (Cases 21 and 22) which were of the malignant type only one examination was possible before death occurred. Complement was present to the extent of 16.66 units in the first on the day preceding death, and to the extent of 8.00 units in the second on the day of death. This observation is in accord with the results already referred to in some of the fatal cases of enteric fever, erysipelas, and diphtheria.

Summary of the Results obtained in Scarlet Fever.

1. In six mild cases of scarlet fever no definite type of variation in the amount of complement was observed (Cases 1 to 6, Appendix D).
2. In ten cases of a more severe type of scarlet fever a diminution in the complement content occurred during the period of pyrexia. A subsequent increase during convalescence was observed in four cases, while in two others a somewhat similar, though less well-marked variation, occurred (Cases 7 to 16).
3. In four cases of scarlatinal nephritis complement was almost absent or present in very small amount only (Cases 19, 20, and A and B).
4. In two fatal cases of the malignant type of scarlet fever, a large amount of complement was present at the time of death (Cases 21 and 22).

APPENDIX A.

ENTERIC FEVER.

Numerical Results of the Series of Complement Estimations in some Cases.

S. = Amount of patient's serum required to produce complete hæmolysis of 1 c.c. sensitised ox corpuscles.

Complement = Represented by the reciprocal of the amount of the patient's serum required to produce complete hæmolysis of 1 c.c. sensitised ox corpuscles. The figure 1 has been taken as the complement unit.

Case.	Day of Illness.		S.	Complement.	
1 Age, 23 years . .	{	Pyrexia . .	C.c.		
			11th	0·1	10·00
		Convalescence	15th	0·11	9·09
			32nd	0·13	7·69
			42nd	0·23	4·34
6 Age, 23 years . .	{	Pyrexia . .	63rd	0·28	3·57
			23rd	0·06	16·66
		Convalescence	25th	0·08	12·50
			30th	0·08	12·50
			45th	0·18	5·55
8 Age, 22 years . .	{	Pyrexia . .	69th	0·21	4·76
			25th	0·18	5·55
		Convalescence	26th	0·22	4·54
			30th	0·18	5·55
			36th	0·17	5·88
10 Age, 20 years . .	{	Pyrexia . .	41st	0·15	6·66
			51st	0·18	5·55
		Convalescence	64th	0·25	4·00
			78th	0·24	4·16
			12 Age, 25 years . .	{	Pyrexia . .
25th	0·15	6·66			
Convalescence	28th (secondary part)	0·08			12·50
	36th	0·13			7·69
	47th	0·16			6·25
12 Age, 25 years . .	{	Pyrexia . .	61st	0·21	4·76
			20th	0·08	12·50
		Convalescence	23rd	0·135	7·40
			36th	0·13	7·69
			44th	0·09	11·11
12 Age, 25 years . .	{	Pyrexia . .	52nd	0·14	7·14
			80th	0·17	5·88
		93rd	0·22	4·54	

APPENDIX A—continued.

Case.	Day of Illness.	S.	Complement.
16 Age, 22 years . .	{ Pyrexia . . { 11th 14th 18th 25th 46th 59th 65th Convalescence {	C.c.	
		0.1	10.00
		0.085	12.42
		0.14	7.14
		0.22	4.54
		0.17	5.88
		0.15	6.66
		0.14	7.14
19 Age, 23 years . .	{ Primary fever { 13th 19th Apyretic in- terval { 33rd 38th 48th 55th 66th Relapse . . { 87th 102nd Convalescence {	0.12	8.33
		0.18	5.55
		0.29 +	3.44 -
		0.23	4.34
		0.14	7.14
		0.17	5.88
		0.28 +	3.57 -
		0.28 +	3.57 -
		0.28 +	3.57 -
		0.28 +	3.57 -
21 Age, 20 years . .	{ Pyrexia . . { 20th (secondary part) 22nd 27th Apyretic in- terval { 41st 50th 58th 76th Relapse . . { 86th Convalescence {	0.18	5.55
		0.09	11.11
		0.085	11.76
		0.14	7.14
		0.06	16.66
		0.19	5.26
		0.24	4.16
		0.24	4.16
26 Age, 21 years . .	{ Pyrexia . . { 18th 21st 31st Erysipelas . 42nd Abscesses of neck and thigh { 55th 71st 84th 100th Convalescence 133rd	0.1	10.00
		0.12	8.33
		0.09	11.11
		0.2	5.00
		0.15	6.66
		0.11	9.09
		0.14	7.14
		0.16	6.25
		0.28 +	3.57 -
		28 Age, 36 years . .	{ Pyrexia . . { 11th 16th 21st Thrombosis of saphenous vein { 35th 42nd Convalescence 55th
0.08	12.50		
0.2	5.00		
0.17	5.88		
0.17	5.88		
0.17	5.88		
30 Age, 23 years . .	{ Pyrexia . . 17th Pleurisy and pneumonia { 20th 27th 35th 51st Convalescence 80th	0.145	6.89
		0.05	20.00
		0.085	12.42
		0.08	12.50
		0.19	5.26
		0.27	3.70
31 Age, 27 years . .	{ 34th 37th Death . . 39th	0.125	8.00
		0.055	19.80
		0.04	25.00
32 Age, 27 years . .	{ 6th 11th Death . . 16th	0.2	5.00
		0.21	4.76
		0.06	16.66

APPENDIX A—continued.

Case	Day of Illness.	S.	Complement.
34 Age, 25 years . . {	Death . . 27th . . .	C.c. 0·07	14·28
37 Age, 37 years . . {	3 days before death } 25th . . .	0·17	5·88
40 Age, 24 years . . {	{ 11th . . . Death . . { 14th . . . 17th . . .	0·08 0·04 0·13	12·50 25·00 7·69

APPENDIX B.

ERYSIPELAS.

The Numerical Results of the Series of Complement Estimations in some Cases.

Case.	Day of Illness.	S.	Complement.
1 Age, 48 years . . {	Erysipelas . { 5th . . . 7th . . . 11th . . . Convalescence { 14th . . . 20th . . .	C.c. 0·13 0·12 0·13 0·17 0·18	7·69 8·33 7·69 5·88 5·55
5 Age, 30 years . . {	Erysipelas . { 3rd . . . 5th . . . 9th . . . Convalescence { 19th . . .	0·12 0·17 0·17 0·27	8·33 5·88 5·88 3·70
11 Age, 25 years . . {	Erysipelas of { 5th . . . arm and { 7th . . . body { 11th . . . 14th . . . 25th . . . Convalescence { 55th . . . 3 months later . . .	0·08 0·2 0·15 0·2 0·24 0·26 0·34	12·50 5·00 6·66 5·00 4·16 3·84 2·94
18 Age, 42 years . . {	Erysipelas . { 4th . . . 6th . . . 8th . . . Convalescence { 14th . . .	0·2 0·12 0·19 0·12	4·00 8·33 5·26 8·33
21 Age, 40 years . . {	Erysipelas . { 3rd . . . 6th . . . Convalescence { 11th . . . 22nd . . . Relapse . . { 3rd . . . Convalescence { 14th . . . 25th . . .	0·14 0·12 0·18 0·24 0·21 0·25 0·23	7·14 8·33 5·55 4·16 4·76 4·00 4·34

APPENDIX B—continued.

Case.	Day of Illness.	S.	Complement.	
25 Age, 58 years . .	Pneumonia 6th	C.c. 0·18	5·55	
	Convalescence { 7th	0·17	5·88	
		9th	0·16	6·25
		13th	0·14	7·14
		20th	0·16	6·25
	Relapse 3rd	0·12	8·33	
	Convalescence 10th	0·14	7·14	
	Further re- currence, and death from septicæmia { 6th	0·14	7·14	
	26 Age, 51 years . .	Erysipelas { 6th	0·12	8·33
7th			0·06	16·66
9th			0·14	7·14
Abscess of scalp { 11th		0·21	4·76	
		13th	0·28	3·57
		15th	0·3	3·33
Separation of sloughs from scalp { 17th		0·3	3·33	
		19th	0·16	6·25
		21st	0·11	9·09
		23rd	0·11	9·09
Recurrence of abscess { 29th		0·17	5·88	
		39th	0·09	11·11
		50th	0·12	8·33
Convalescence 72nd		0·22	4·76	
27 Age, 31 years . .		Erysipelas mi- grans, face and body in- volved { 2nd	0·21	4·76
			3rd	0·24
	5th		0·23	4·34
	7th		0·21	4·76
	9th		0·09	11·11
	11th		0·2	5·00
	Convalescence { 12th	0·25	4·00	
		21st	0·1	10·00
		26th	0·2	5·00
	Recurrence			
	Convalescence { 32nd	0·12	8·33	
		54th	0·23	4·34
	This patient had a subsequent mild recurrence			
28 Age, 50 years . .	Death { 3rd	0·14	7·14	
		5th	0·12	8·33
30 Age, 85 years . .	Death 5th	0·18	5·55	

APPENDIX C.

DIPHTHERIA.

The Numerical Results of the Series of Complement Estimations in some Cases.

Case.	Day of Illness.	S.	Complement.
1 Age, 29 years . .	6th (14,000 units antitoxin) .	C.c. 0·1	10·00
	9th	0·2	5·00
	19th	0·18	5·55
	24th	0·27	3·70
	40th	0·31	3·22
3 Age, 9 years . .	2nd (20,000 units antitoxin)
	3rd	0·19	5·26
	4th	0·17	5·88
	7th	0·21	5·00
	9th	0·21	4·76
	16th	0·28	3·57
	27th	0·28	3·57
5 Age, 7 years . .	36th	0·24	4·16
	2nd (6000 units antitoxin)
	3rd	0·06	16·66
	5th	0·17	5·88
	11th (serum rash)	0·21	4·76
12 Age, 10 years . .	19th	0·25	4·00
	4th (8000 units antitoxin)
	5th	0·36 ¹	2·77 -
	7th	0·34 ¹	2·94 -
	12th	0·46 ¹	2·17 -
	15th	0·44 ¹	2·27 -
13 Age, 7 years . .	33rd	0·54 ¹	1·85 -
	5th (8000 units antitoxin)
	6th	0·36 ¹	2·77 -
	9th	0·38 ¹	2·77 -
	11th (serum rash)	0·40 ¹	2·50 -
	13th	0·44 ¹	2·17 -
	16th (palatal paralysis)
14 Age, 13½ years . .	20th	0·43 ¹	2·32 -
	37th	0·26	3·84
	4th (8000 units antitoxin) .	0·1	10·00
	5th	0·145	6·89
	8th	0·2	5·00
	15th (serum rash)	0·28	3·57
15 Age, 33 years . .	17th (serum arthritis)	0·28	3·57
	22nd	0·36	2·77
	38th	0·26	3·84
	4th (20,000 units antitoxin) .	0·06	16·66
	5th " " "	0·13	7·69
	7th	0·14	7·14
19 Age, 3½ years . .	10th	0·09	11·11
	19th (serum rash)	0·16	6·25
	38th	0·15	6·66
	3rd (22,000 units antitoxin) .	0·06	16·66
20 Age, 6 years . .	4th	0·18	7·69
	6th (death)
20 Age, 6 years . .	4th (16,000 units antitoxin) .	0·16	6·25
	6th (death)

¹ Hæmolysis not complete.

- Complement figure lower than this.

APPENDIX D.

SCARLET FEVER

The Numerical Results of the Series of Complement Estimations in some Cases.

Case.	Day of Illness.	S.	Comple- ment. ¹	
		C.c.		
1 Age, 10 years . .	Pyrexia . .	3rd	0·115	4·34
		6th	0·135	3·70
		8th	0·105	4·76
	Convalescence	11th	0·155	3·22
		14th	0·2+	2·50 -
		30th	0·24	2·08
2 Age, 9 years . .	Pyrexia . .	3rd	0·12	4·16
		6th	0·135	3·70
		8th	0·15	3·33
	Convalescence	12th	0·13	3·84
		29th	0·17	2·94
7 Age, 43 years . .	Pyrexia . .	6th	0·08	6·25
		7th	0·095	5·52
		8th	0·095	5·52
		10th	0·09	5·55
	Convalescence	13th	0·12	4·16
		15th	0·12	4·16
		20th	0·16	3·12
		32nd	0·06	8·33
10 Age, 27 years . .	Pyrexia . .	4th	0·055	9·90
		7th	0·145	3·44
		9th	0·05	10·00
		11th	0·11	4·54
	Convalescence	25th (peritonsillar ab- scess)	0·065	8·76
		59th	0·06	8·33
18 Age, 36 years . . Pyrexia.	Parotitis and empyema	4th	Slight hæmolysis with 0·27 c.c.	...
		6th	0·33 "	...
		9th	Complete hæmo- lysis with 0·25 c.c.	2·00
		31st	Incomplete hæmo- lysis with 0·26 c.c.	...
Scarlatinal Nephritis.				
19 Age, 9½ years . .		1st	Very slight hæmo- lysis with 0·27 c.c.	...
		3rd	Very slight hæmo- lysis with 0·46 c.c.	...
20 Age, 4 years . .		30th	Very slight degree of hæmolysis with 0·2 c.c.	Very small amount of complement present.
		32nd (death)	0·125 c.c.	4·00
Malignant Scarlet Fever.				
21 Age, 1½ years . .		6th (death) . .	0·06 "	16·66

¹ As the amount of serum used in scarlet fever was tested against 0·5 c.c. sensitised ox corpuscles, the reciprocal of twice this amount of serum represents the amount of complement necessary to hæmolys 1 c.c. sensitised ox corpuscles. In this way the results have been made uniform with those of the other sections of this paper.

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