

THE SERUM PROTEINS IN INFECTIOUS MONONUCLEOSIS. ELECTROPHORETIC STUDIES

By KENNETH STERLING¹

(From the Department of Medicine, the University of Chicago)

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Previous investigations have shown the very frequent occurrence in infectious mononucleosis of abnormal findings on liver function tests (1-7), and of hepatic involvement on histologic examination of both autopsy (8-11) and biopsy material (1, 12-14) in cases with and without jaundice.

Alterations observed in the composition of the serum proteins (2, 4, 6, 15, 16a) appear to be compatible with the occurrence of positive cephalin-cholesterol flocculation and thymol turbidity

tests, notwithstanding the various interpretations advanced to explain the mechanisms of these tests (16-22).

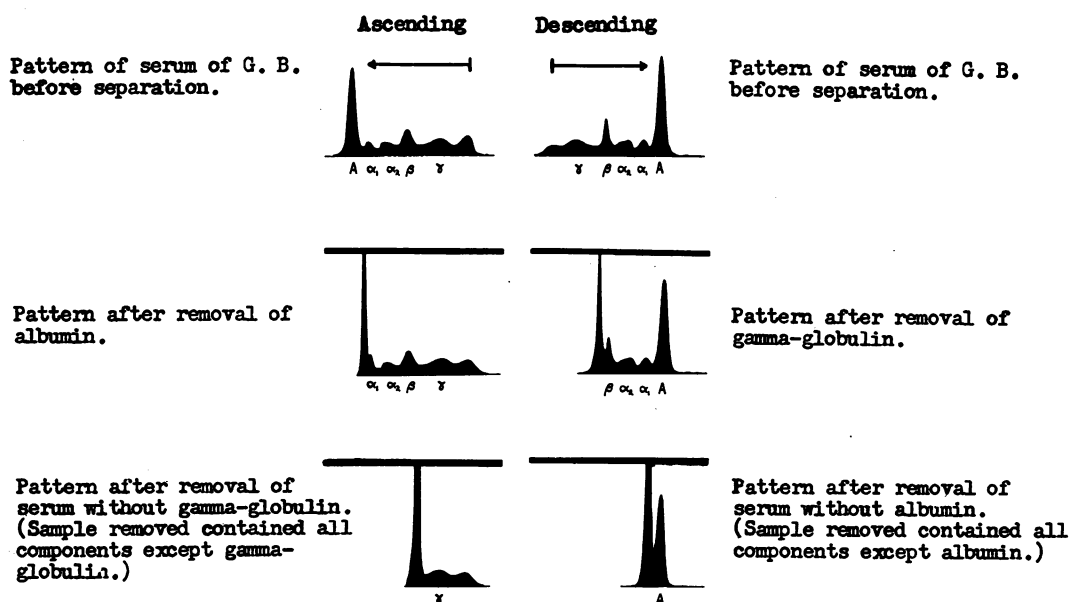
The present work was undertaken to study in detail the serum proteins in infectious mononucleosis by the electrophoretic method and to examine separated protein fractions for the presence of heterophile antibodies.

METHODS

The electrophoretic runs were performed with the standard apparatus and technique described by Longsworth (23) using sodium diethylbarbiturate (veronal)

¹ Present address: Department of Medicine, Harvard Medical School, Boston, Mass.

SEPARATION OF SERUM PROTEIN FRACTIONS



The four samples obtained from each serum were: (1) separated albumin, (2) serum without albumin, (3) serum without gamma-globulin, (4) separated gamma-globulin.

FIG. 1

The albumin peaks are indicated by "A"; the alpha-1-, alpha-2-, beta- and gamma-globulins are designated by their respective Greek letter prefixes. The unlabelled peaks next to the gamma-globulins are not protein components but are stationary anomalous boundaries due to gradients of buffer salt. Each steep peak reaching top of photograph is due to the sharp gradient between buffer and protein solution occurring at the level of the capillary tip after withdrawal of a sample.

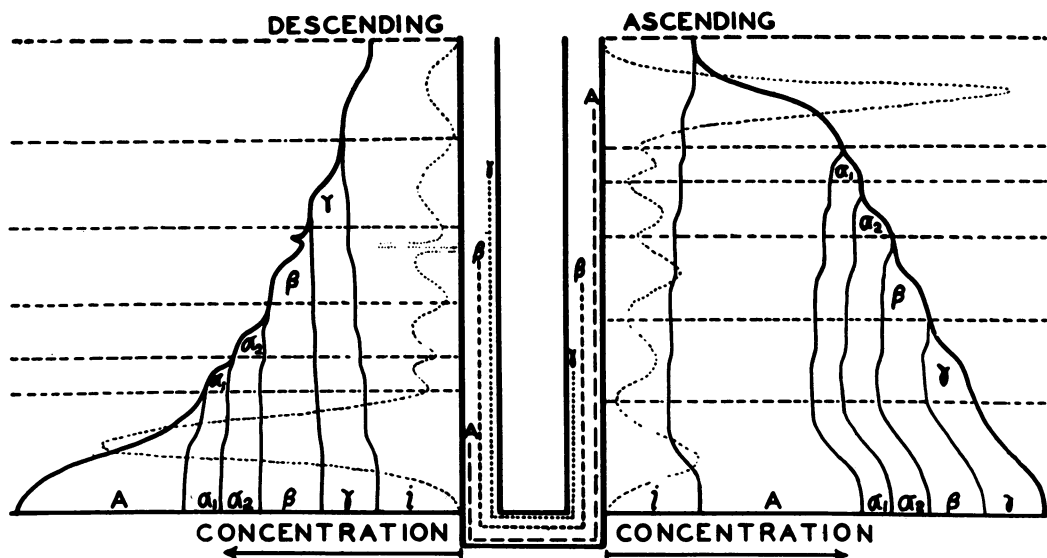


FIG. 1a. CONCENTRATION DIAGRAM OF SERUM COMPONENTS IN CELL AFTER ELECTROPHORESIS *

Buffer salt concentration is designated by "i," albumin by "A," and the alpha-1-, alpha-2-, beta-, and gamma-globulins by their respective Greek letter prefixes.

The solid line curves indicate the concentrations of components. The dotted lines are outlines of electrophoretic patterns as photographed, and show refractive index gradients caused by the components. Since the dotted lines represent the slopes (first derivatives) of the solid line curves, the areas under the peaks of the electrophoretic patterns give the relative concentrations of protein constituents.

buffer of pH 8.6 and ionic strength 0.1. After dialysis against the buffer the serum was diluted with buffer solution to four times its original volume prior to dialysis.

Electrophoresis was carried out at approximately 1.5°C. for 120 minutes at a potential gradient of 7.7 volts per centimeter. Photographs were taken by the schlieren scanning method.

In the estimation of the fractions as per cent of the serum proteins both ascending and descending patterns were used, the areas being divided by ordinates from the nadirs between peaks to the base line. The quantities of the fractions as grams per cent represent the products (24) of the percentages and the total proteins from the conventional Kjeldahl method, neglecting recent theoretically valid refinements (25, 26).

The separation of fractions was carried out by means of a capillary pipette lowered into the electrophoresis cell by rack and pinion. In this manner four fractions were obtained. From the ascending limb the *separated albumin* layer above the other components was aspirated. The pipette tip was then lowered further into the cell to a point just above the start of the ascending gamma-globulin peak and a sample was drawn off containing all components except gamma-globulin (*serum without gamma-globulin*). From the upper part of the descend-

ing limb *separated gamma-globulin* was obtained. Lowering the pipette tip to a point just above the start of the descending albumin peak yielded a sample with all components except albumin (*serum without albumin*). All these collections were performed with careful visualization of the peaks and pipette tip by the cylindrical lens method and schlieren band method when needed. After the removal of each sample a photograph was taken to show the remaining undisturbed pattern as a check on the level of the pipette tip during collection and as an indication of the accuracy of the separation. (See Figures 1 and 1a.)

In a few instances the attempt was made to verify further the accuracy of separation by reanalyzing fractions electrophoretically in the micro-cell. (See Figure 2.)

Heterophile antibody titration (27) was done on the four fractions obtained from each serum, and also on the dialyzed buffer diluted serum (not subjected to electrophoresis) which served as a control. The titres are reported as "final serum dilutions" considering the samples of fractions or controls as representing the "undiluted serum"; actually the controls were 1:4 dilutions, and the fractions were still further diluted to an indeterminate extent because of unavoidable dilution with buffer in the separation of fractions.

Absorption of heterophile antibodies was carried out by repeated incubation of inactivated serum with packed sheep red cells.

* Diagram from Moore, D. H., and Abramson, H. A.: Electrophoresis, to appear in Medical Physics (ed., O. Glasser), Chicago, The Year Book Publishers, Inc., 1949 (vol. 2).

CASE MATERIAL

As normal controls the fasting sera of ten volunteer medical students and physicians were examined.² All were normal with respect to total proteins, albumin and globulin, alkaline phosphatase, bromsulfalein retention, hippuric acid excretion, prothrombin time, cephalin-cholesterol flocculation and thymol turbidity tests.

Seven hospitalized cases of infectious mononucleosis where the diagnosis was considered certain were selected for study. All exhibited definite enlargement of lymph nodes as well as other suggestive clinical manifestations. At some time during the hospital course each patient showed lymphocytosis as high as 50% or greater, including cells considered characteristic of the disease. Heterophile antibody titres of 1:512 or higher were present in all cases.

Two patients (T. S. and L. M.) had moderate jaundice, and one (R. S.) had slight jaundice, subsiding at the time his serum was studied. The serum bilirubin was normal in the other four cases.

To compare the findings with those in infections of approximately similar severity but without known hepatic disorder, two hospitalized cases of upper respiratory tract infection were chosen at random: one beta-hemolytic

² These sera form part of a larger study of liver disease being done in collaboration with Drs. William E. Ricketts, Joseph B. Kirsner, and Walter L. Palmer.

streptococcal pharyngitis and one "acute upper respiratory tract infection, type unspecified," both with negative heterophile antibody determinations and thymol turbidity tests.

For comparison with known hepatic disease the following three cases² were studied:

- C. G., subsiding infectious hepatitis followed with serial punch biopsies of the liver;
- E. H., fatal hepatitis of probable virus etiology with progressive downhill course characterized by jaundice, edema, ascites, and hemorrhagic phenomena, and showing at autopsy massive hepatic necrosis with regeneration of pseudolobules;
- M. S., Laennec's cirrhosis with jaundice, ascites, and edema, the diagnosis being confirmed by liver punch biopsy.

RESULTS

Normal Sera

The electrophoretic and chemical data on the serum proteins of the ten normal volunteers with negative liver function tests are listed in Table I. The findings are comparable with those of other workers.

Infectious Mononucleosis Sera

The electrophoretic and chemical data on the serum proteins of the infectious mononucleosis patients with results of simultaneous liver function tests are listed in Table II.

In both the per cent compositions and the absolute amounts there were diminutions of the albumin fractions and elevations of the gamma-globulin fractions as compared with the normal sera. These deviations appear to be significant in all but the non-jaundiced patient D. C. who was also the only case with negative cephalin-cholesterol flocculation and thymol turbidity tests, and in whom the only normal alkaline phosphatase occurred among the six determinations done. The studies on this patient were done on the 24th day of illness when he had become afebrile three days before discharge.

Less pronounced and less frequently observed alterations were the elevations of the alpha-1-globulin and beta-globulin fractions.

The jaundiced cases, T. S. and L. M., exhibited somewhat more pronounced changes in serum protein composition than most of the non-jaundiced cases, but the non-jaundiced patient G. B. showed the most abnormal patterns of all, as well as the highest thymol turbidity. It will be noted from Table II that the two jaundiced cases were studied a second time, ten days later, when the

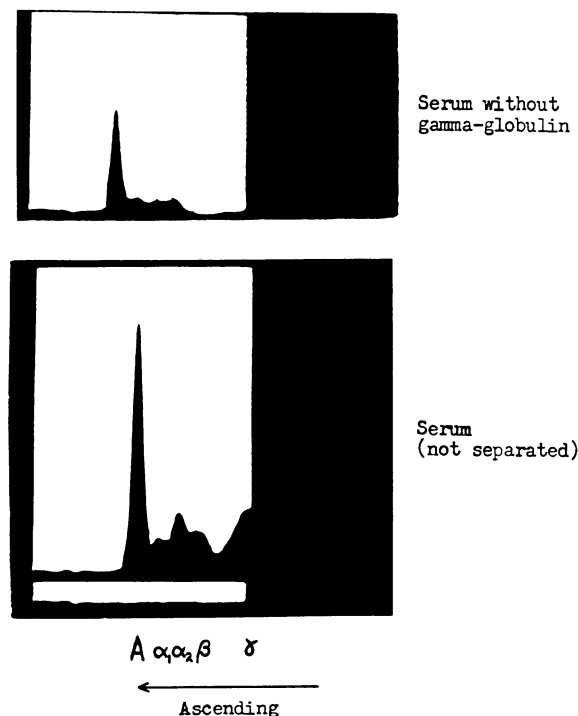
MICRO-CELL ELECTROPHORESIS

FIG. 2

TABLE I

NORMAL SERA

	Electrophoretic data											Howe sodium sulfate			
	per cent					grams per cent					A/G	grams per cent			
	Alb	α_1	α_2	β	γ	Alb	α_1	α_2	β	γ		Alb	Glob	Tot	
1.	63.3	2.5	8.8	12.0	13.5	4.52	0.18	0.63	0.86	0.96	1.73	2.43	5.06	2.08	7.14
2.	61.1	3.3	9.1	12.7	13.9	4.70	0.25	0.71	0.98	1.07	1.57	2.38	5.43	2.28	7.71
3.	60.0	4.7	10.6	14.3	10.4	3.93	0.31	0.70	0.94	0.68	1.50	2.32	4.58	1.98	6.56
4.	60.6	3.6	8.5	13.2	14.1	4.07	0.24	0.57	0.89	0.95	1.54	2.95	5.02	1.70	6.72
5.	61.3	4.6	9.5	13.4	11.2	4.18	0.31	0.65	0.91	0.77	1.58	2.67	4.96	1.86	6.82
6.	55.0	4.6	12.9	13.2	14.3	3.80	0.32	0.89	0.91	0.99	1.22	1.93	4.55	2.36	6.91
7.	56.8	5.3	11.3	13.7	12.9	4.02	0.38	0.80	0.97	0.91	1.32	1.77	4.52	2.56	7.08
8.	64.8	4.5	9.2	9.9	11.6	4.53	0.32	0.64	0.69	0.81	1.84	2.41	4.94	2.05	6.99
9.	58.6	3.6	9.6	12.1	16.1	4.06	0.25	0.66	0.84	1.11	1.42	1.97	4.59	2.33	6.92
10.	61.9	3.0	7.3	13.2	14.6	4.48	0.22	0.53	0.95	1.06	1.63	2.55	5.20	2.04	7.24
AVERAGE	60.3	4.0	9.7	12.8	13.2	4.23	0.28	0.68	0.89	0.93	1.52	2.31	4.89	2.12	7.01
Standard Deviation	2.8	0.8	1.5	1.2	1.7	0.29	0.06	0.10	0.08	0.13	0.18	0.34	0.30	0.24	0.30

jaundice and other clinical symptoms were subsiding, but the abnormalities of the serum proteins and liver function tests were still present.

Upper Respiratory Tract Infections

There were no significant deviations from normal in the per cent compositions of the serum proteins in the two hospitalized cases of upper respiratory tract infection.

The albumin depression and gamma-globulin elevation were least pronounced in C. G., the case of subsiding infectious hepatitis, where the abnormalities were somewhat less marked than in most of the infectious mononucleosis cases. These deviations from normal were more pronounced in E. H., the case of fatal hepatitis, and were most striking in M. S., the case of Laennec's cirrhosis, where the gamma-globulin actually exceeded the albumin.

	Albumin	α_1 -glob.	α_2 -glob.	β -glob.	γ -glob.	A/G ratio
Beta-hemolytic streptococcal pharyngitis	58.0%	5.2%	10.6%	11.6%	14.6%	1.38
Upper resp. tr. infect., type unspecified	62.9%	4.3%	8.7%	11.5%	12.6%	1.70

Known Hepatic Disease

The findings in the three cases of histologically proven liver disease are shown in Figure 3, together with data from normal and infectious mononucleosis sera.

Heterophile Antibody Titres of Separated Fractions

After electrophoresis each infectious mononucleosis serum was separated into the following four fractions:

1. *Separated albumin*
2. *Serum without albumin*
3. *Serum without gamma-globulin*
4. *Separated gamma-globulin.*

The dialyzed buffer diluted serum (not subjected to electrophoresis) served as a control.

The results of the heterophile antibody titrations are listed in Table III. The figures express "final serum dilutions," considering the samples of fractions or controls as representing the "undiluted serum"; actually the controls were 1:4 dilutions and the fractions were still further diluted to an indeterminate extent.

As shown in Table III, heterophile antibodies were demonstrated in the *separated gamma-globulin* in every case, and were never present in the *separated albumin*. Heterophile antibodies were absent from the *serum without gamma-globulin* in seven of the ten experiments recorded, but present in three.

The low titres in the *separated gamma-globulin* samples in comparison with the controls were presumed due to the unavoidable dilution in the process of fractionation. To test the supposition that these samples contained minute amounts of protein, micro-Kjeldahl determinations were done on three samples of *separated gamma-globulin* with the following findings (after subtraction of buffer nitrogen):

T. S., 12th day—30.8 mg. nitrogen per 100 cc.
D. C., 24th day—22.4 mg. nitrogen per 100 cc.
M. W., 11th day—18.2 mg. nitrogen per 100 cc.

Assuming a nitrogen factor of 6.25, these samples contained approximately one-tenth to one-seventh the gamma-globulin concentration of their respective undiluted whole sera.

Attention was directed toward the occurrence of heterophile antibodies in a few of the samples of *serum without gamma-globulin*. It was suspected that the separations might not be accurate, but

TABLE II

Day of illness indicated below initials of each patient. Values for each serum protein fraction expressed as grams per cent, and per cent of total proteins. Alkaline phosphatase activities in Bodansky units.

INFECTIOUS MONONUCLEOSIS SERA

<div style="display: inline-block; transform: rotate(-45deg);"> Ascending Descending </div>		Electrophoretic data						Howe sodium sulfate				bilirub		ceph	thym	alk. phos.
		Alb	α_1	α_2	β	γ	A/G	A/G	Alb	Glob	Tot	dir	tot			
	T.S. 12th day	3.44 46.8%	0.49 6.7%	0.75 10.2%	0.91 12.3%	1.76 23.9%	0.88	1.32	4.18	3.17	7.35	1.3	2.4	4+	10.7	12.8
	T.S. 22nd day	3.26 45.7%	0.44 6.1%	0.51 7.2%	1.23 17.2%	1.70 23.8%	0.84	1.44	4.21	2.93	7.14	0.5	0.9	3+	11.3	8.2
	L.M. 13th day	3.24 50.6%	0.25 3.9%	0.58 9.0%	1.16 18.1%	1.19 18.5%	1.02	1.66	4.01	2.41	6.42	1.8	2.9	4+	11.8	21.8
	L.M. 23rd day	3.84 56.7%	0.34 5.0%	0.45 6.6%	1.06 15.7%	1.09 16.0%	1.31	1.92	4.46	2.32	6.78	0.7	1.3	3+	9.8	13.5
	R.S. 17th day	3.51 50.7%	0.18 2.6%	0.83 12.0%	1.02 14.7%	1.39 20.0%	1.03	1.42	4.07	2.86	6.93	0.9	1.3	4+	13.0	9.4
	D.C. 24th day	3.90 54.4%	0.52 7.2%	0.88 12.2%	0.86 12.0%	1.02 14.3%	1.19	2.03	4.81	2.37	7.18	0.3	0.5	2+	3.9	4.2
	D.D. 17th day	3.88 53.1%	0.34 4.6%	0.81 11.1%	1.15 15.8%	1.12 15.4%	1.13	2.17	5.00	2.30	7.30	0.1	0.5	4+	9.1	
	G.B. 16th day	2.91 42.2%	0.52 7.6%	0.73 10.5%	1.22 17.7%	1.52 22.0%	0.73	1.30	3.90	3.00	6.90	0.2	0.3	4+	13.4	
	M.W. 11th day	3.32 48.9%	0.51 7.5%	0.85 12.5%	0.98 14.4%	1.14 16.7%	0.96	1.62	4.20	2.60	6.80	0.2	0.5	3+	8.2	
	AVERAGE	3.48 49.9%	0.40 5.7%	0.71 10.1%	1.07 15.3%	1.33 19.0%	1.00	1.62	4.31	2.66	6.98					

this appeared quite unlikely on study of the photographs taken after the steps of the separation procedure in the manner of Figure 1.

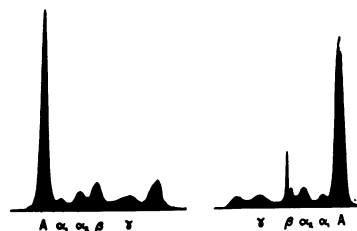
Although L. M. on the 13th day of illness

showed heterophile antibodies in the *serum without gamma-globulin*, there were none in the analogous sample on the 23rd day, as shown in Table III. Lacking more serum from the 13th day

NORMAL SERUM

Patterns of normal serum #5; figures are averages of ten normal sera.

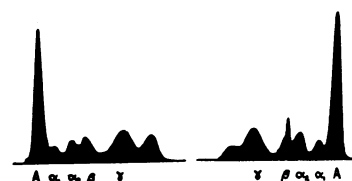
	Alb	α_1	α_2	β	γ	A/G
per cent	60.3	4.0	9.7	12.8	13.2	1.52
grams per cent	4.23	0.28	0.68	0.89	0.93	
Howe sod. sulfate	4.89	Glob-2.12		Tot-7.01		2.31



INFECTIOUS MONONUCLEOSIS

Patterns of T.S., 12th day of illness; figures are averages of data from the cases studied.

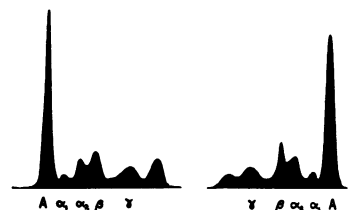
	Alb	α_1	α_2	β	γ	A/G
per cent	49.9	5.7	10.1	15.3	19.0	1.00
grams per cent	3.48	0.40	0.71	1.07	1.33	
Howe sod. sulfate	4.31	Glob-2.66		Tot-6.98		1.62



INFECTIOUS HEPATITIS, MILD

Patterns and figures of C.G. with subsiding hepatitis, verified by serial punch biopsies of the liver.

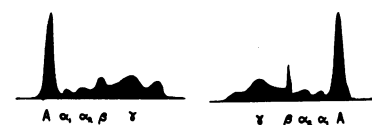
	Alb	α_1	α_2	β	γ	A/G
per cent	50.2	4.6	12.9	16.5	15.8	1.01
grams per cent	3.54	0.32	0.91	1.16	1.11	
Howe sod. sulfate	4.50	Glob-2.54		Tot-7.04		1.77



FATAL HEPATITIS

Patterns and figures of E.H. with rapid course of fatal hepatitis, confirmed at autopsy. Virus etiology probable.

	Alb	α_1	α_2	β	γ	A/G
per cent	43.5	4.4	6.8	14.0	31.3	0.77
grams per cent	2.08	0.21	0.32	0.67	1.49	
Howe sod. sulfate	2.33	Glob-2.44		Tot-4.77		0.96



LAENNEC'S CIRRHOSIS

Patterns and figures of M.S. with decompensated cirrhosis; jaundice, ascites, and edema; liver punch biopsy done.

	Alb	α_1	α_2	β	γ	A/G
per cent	31.0	5.0	8.0	17.0	39.0	0.45
grams per cent	2.01	0.32	0.52	1.10	2.53	
Howe sod. sulfate	2.56	Glob-3.92		Tot-6.48		0.65

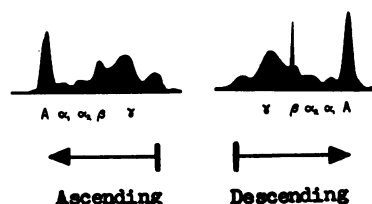


FIG. 3

The albumin peaks are indicated by "A"; the alpha-1-, alpha-2-, beta-, and gamma-globulins are designated by their respective Greek letter prefixes. The unlabelled peaks are not protein components but are stationary anomalous boundaries due to gradients of buffer salt.

TABLE III

As explained in the text, the titres below cannot be regarded as precise quantitative expressions because of unavoidable (and variable) dilution in the process of fractionation.

HETEROPHILE ANTIBODY TITRES OF SEPARATED FRACTIONS

	Buffer diluted serum (CONTROL)	Separated albumin	Serum without albumin	Serum without gamma globulin	Separated gamma globulin
T.S. 12th day	1:256	neg.	1:256	neg.	1:128
T.S. 22nd day	1:256	neg.	1:64	neg.	1:16
L.M. 13th day	1:512	neg.	—	1:16	1:32
L.M. 12th day	1:512	neg.	1:128	1:8	1:32
L.M. 23rd day	1:256	neg.	1:128	neg.	1:16
R.S. 17th day	1:256	neg.	1:128	neg.	1:16
D.C. 24th day	1:64	neg.	1:16	neg.	1:8
D.D. 17th day	1:512	neg.	1:256	neg.	1:8
G.B. 16th day	1:128	neg.	1:64	neg.	1:16
M.W. 11th day	1:128	neg.	1:32	1:8	1:8

to repeat the original experiment, serum from the 12th day was used instead, with similar findings. This duplication of results also argues against technical error in the separation.

As a further check, micro-cell electrophoretic runs (see Figure 2) were performed on the three samples in question. Because part of each sample (already dilute) had been used for heterophile antibody titration, it was necessary to add buffer to obtain the 2 cc. required for a micro-cell run. Consequently, the peaks were quite low and the patterns could be interpreted as no more than suggestive evidence of the absence of gamma-globulin.

Absorption of Heterophile Antibodies

By absorption with sheep red cells the heterophile antibody titre of the serum of G. B. (19th day of illness) was reduced from 1:2048 to 1:32.

The electrophoretic patterns before and after antibody absorption were practically identical.

DISCUSSION

The serum protein compositions of the infectious mononucleosis patients showed definite diminutions of the albumin fractions and elevations of the gamma-globulin fractions as compared with normal sera. Less pronounced and less frequently observed deviations from normal were the elevations of the alpha-1-globulin and beta-globulin fractions.

The cases studied were limited to hospitalized patients in whom the diagnosis could be made with certainty; it cannot be asserted that an unselected series would necessarily have shown as pronounced changes.

Numerous investigators have observed generally

	Albumin	α_1 -glob.	α_2 -glob.	β -glob.	γ -glob.	A/G ratio
Before absorption (titre 1:2048)	43.4%	8.0%	17.4%	10.7%	20.5%	0.77
After absorption (titre 1:32)	43.2%	7.7%	18.3%	10.5%	20.3%	0.76

similar if more conspicuous abnormalities in hepatitis and cirrhosis (16, 18, 28-33). As suggested by Figure 3 these changes in infectious mononucleosis may bear some relationship to the type if not the degree of hepatic dysfunction.

The cephalin-cholesterol flocculation and thymol turbidity tests may merely reflect directly the abnormalities of the serum proteins (16-22). The concomitance, however, of occasional hyperbilirubinemia, frequent elevation of alkaline phosphatase activity (2, 5, 6), and histopathologic evidence of liver involvement (1, 8-14) makes plausible the association of disturbed hepatic function and the alterations of the serum proteins. Such a conception is not in any sense incompatible with the probable extra-hepatic *origin* of serum globulins.

That the widespread pathologic involvement of the lymph nodes and the foci of mononuclear cell infiltration in various organs may be directly responsible for changes in the serum proteins is an attractive hypothesis. This idea has been advocated on the basis of electrophoretic findings in infectious mononucleosis and the blood dyscrasias, the latter group exhibiting rather varied alterations (15).

The possibility that the changes in the serum proteins in infectious mononucleosis may be related to the infectious process *per se* deserves consideration in the light of somewhat similar abnormalities described in infectious diseases such as syphilis, tuberculosis, typhus, malaria, lymphogranuloma venereum, leprosy, kala-azar, and others (34). It must, however, be noted that most of the above conditions are characterized by chronic proliferative granulomata or by widespread cellular destruction, hence are not too closely analogous to infectious mononucleosis. On the other hand, in lobar pneumonia there are conspicuous elevations of the alpha-2-globulins usually without significant changes in the gamma-globulins (34, 35).

In an effort to compare the findings in infectious mononucleosis with those in infections of approximately similar severity but without known hepatic disorder, the sera of two hospitalized cases of upper respiratory tract infection were analyzed electrophoretically with the finding of normal patterns. It would appear that the extent to which the serum protein changes are attributable to

the non-specific effects of the infectious process is debatable.

That the gamma-globulin increase could be due to the heterophile antibodies is excluded by the experiment showing no change in electrophoretic pattern after antibody absorption. In other human diseases absorption of clinically important specific antibodies has produced no change in electrophoretic pattern, the antibodies being present in too small quantities to cause visible alterations in schlieren patterns even though easily detectable by serological methods (34, 36). Immuno-chemical studies corroborate the minute concentrations of antibodies in human serum (37).

The data on the distribution of heterophile antibodies in relation to the serum protein fractions are interpreted as indicating that they are predominantly in the gamma-globulin fraction, not always being exclusively confined to this fraction.

The occurrence of various antibodies in the gamma-globulin fractions of animals has been demonstrated repeatedly (37, 38) since the original work of Tiselius and Kabat (39) showing pneumococcal antibodies in the gamma-globulins of rabbit and monkey sera. It must, however, be recalled that Tiselius and Kabat found in the horse that pneumococcal antibodies migrated between the beta- and gamma-globulins forming a separate peak. Since then equine antibodies to diphtheria toxin, tetanus toxin, and others have been found outside the gamma-globulin fraction (37, 38). Virus-neutralizing antibodies to Venezuelan and Western equine encephalomyelitis have been demonstrated in both the beta- and gamma-globulins of rabbit sera (40).

The extensive work of Enders (41) on the products of human plasma fractionation revealed that Fraction II, composed of almost pure gamma-globulin, contained in high concentration antibodies reacting with diphtheria toxin, streptococcal erythrogenic toxin, influenza A virus, mumps virus, and the H-antigen of *E. typhosa*. On the other hand, isoagglutinins and antibody reacting with the O-antigen of *E. typhosa* were recovered from Fraction III-1, containing mostly beta-globulin and less gamma-globulin. Furthermore, smaller amounts of the antibodies concentrated in Fraction II were found in other fractions free of gamma-globulin. Subsequently, division of human gamma-globulin into sub-fractions with differ-

ing antibody contents has been reported (42).

Electrophoretic separation of sera from allergic patients has suggested that ragweed and rabbit antibodies (or reagins) are confined to the gamma-globulin fraction (43).

In a study employing electrophoretic, ultracentrifugal, and immuno-chemical methods the Wassermann antibody (or reagin) has been clearly shown to have a mobility intermediate between beta- and gamma-globulins and overlapping both (44).

It is hoped that the present findings on heterophile antibodies in infectious mononucleosis will be supplemented by further physico-chemical studies.

SUMMARY

1. Electrophoretic analyses of the serum proteins of seven cases of infectious mononucleosis revealed deviations from the normal composition in both jaundiced and non-jaundiced patients.

2. The principal abnormalities observed were diminutions of the albumin fractions and elevations of the gamma-globulin fractions.

3. Less pronounced and less frequently observed alterations were elevations of the alpha-1-globulin and beta-globulin fractions.

4. Liver function tests showed abnormalities in six of the seven cases.

5. The alterations of the serum proteins were considered as possibly related to hepatic dysfunction, among other hypotheses entertained.

6. Separation experiments indicated the heterophile antibodies were contained predominantly in the gamma-globulin fractions of the sera, not always being exclusively confined to this fraction.

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