THE HEXOSAMINE CONTENT OF THE SERUM GLOBULINS IN NORMAL AND PATHOLOGICAL SERA[1]

By ALFRED JAY BOLLET[2] with the technical assistance of JURIJ ROZHIN and WILLIAM SIMPSON

(From the Department of Medicine of Wayne State University, College of Medicine, and Detroit Receiving Hospital, Detroit, Mich.)

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Considerable interest has been focused upon the glycoproteins present in serum. The hexoses and hexosamines associated with serum proteins have been found to be elevated non-specifically in a variety of pathologic processes (1–9). The seromucoid, a protein fraction particularly rich in carbohydrate, studied extensively by Winzler (2), also is increased in similar disease states (2, 10–15). The amount of carbohydrate in the alpha globulin fraction has been found to be elevated in tuberculosis (16), gout (4), rheumatoid arthritis and rheumatic fever (17), whereas the carbohydrate in the gamma globulin fraction has been reported to be increased in lupus erythematosus (5, 17).

The present study was undertaken to characterize further the alterations which occur in one of the carbohydrate components, hexosamine, in electrophoretically separated serum protein fractions and in seromucoid in a variety of disease processes, with particular emphasis on the rheumatic diseases, and following the administration of anti-inflammatory hormones.

METHODS

Blood samples were obtained in the fasting state from healthy blood donors and patients with a variety of rheumatic diseases, pneumonia, cirrhosis and hepatitis. The serum was separated within a short time after clotting, and kept frozen until used.

Hexosamine determinations were done by the method of Boas (18), which involves isolation on Dowex-50 columns after preliminary hydrolysis, followed by determination of the hexosamine by a modification of the Elson-Morgan method. Electrophoresis was done in veronal buffer pH 8.6, ionic strength .05, on Whatman No. 3 paper suspended horizontally in a vapor chamber. Runs were performed at approximately 15 m A and 200 V, for 15 hours. The protein content of each fraction was determined by heat fixation, staining with bromphenol blue, cutting into components and eluting the dye in .01 N NaOH. The percentage of the total dye in each component was multiplied by the total protein, determined by the biuret method using Armour's bovine albumin as standard. No correction was made for differences in dye binding by the different protein fractions. Determination of the hexosamine content of the electrophoretically separated protein fractions was done following separation of 0.1-ml. samples of serum. After fixing and staining, the paper was cut into appropriate strips and each component was hydrolyzed and determined individually. This is similar to the method used by Boas, Bollet, and Bunim (4). Appropriate control studies showed that no detectable loss of hexosamine occurred during any of these steps, and added standard solutions of hexosamine were quantitatively recovered. Duplicate electrophoretic runs and determinations of each component were done for both protein and hexosamine. The reproducibility for both protein and hexosamine content of each fraction on replicate electrophoretic separations was found to about ± 5 per cent.

The perchloric acid-soluble, phosphotungstic acid-precipitable fraction (seromucoid) was isolated by a modification of the method of Greenspan, Lehman, Graff, and Schoenbach (15). The phosphotungstic acid precipitate obtained from the perchloric acid filtrate was divided into two fractions. One was analyzed for protein content by the biuret method using a casein standard, and the other analyzed for hexosamine after hydrolysis in 1 N HCl for 15 hours.

RESULTS

Total serum hexosamine

Normal individuals were found to have serum hexosamine levels averaging 79.0 mg. per cent. Elevations of the total serum hexosamine were found in the diseases listed (Table I).

The ratio of total serum hexosamine to total serum protein (× 100) was found to average 1.02 in the normal individuals. In all of the diseases studied, the ratio of total hexosamine to total protein increased, the maximum being an average of 2.06 in the patients with rheumatic fever (Table

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[2] Markle Scholar in Medical Science.

I). This change occurred regardless of the direction of change of the total protein.

Hexosamine content of electrophoretically separated globulins

In order to define more precisely the observed changes in total serum hexosamine, analyses were made of each of the globulin fractions obtained after electrophoretic separation of the serum specimens on filter paper. In this part of the study, analyses were done on pools of sera, each containing equal amounts of sera from three patients with the same disease. Since each determination represents the average of duplicate electrophoretic runs on each pool, it is felt that the mean levels found have validity, but no attempt has been made to establish the range of variation for each globulin fraction in each disease. The amount of hexosamine in the electrophoretically separated serum albumin was found to be too small for accurate determination in the situations studied, and the details are therefore not included in this report.

In three pools of normal sera, the mean hexosamine content of the alpha-1 globulin averaged 17.5 mg. per cent, of the alpha-2 globulin, 25.0 mg. per cent, of the beta globulin, 17.4 mg. per cent, and of the gamma globulin, 24.7 mg. per cent. The amount of protein in each of these fractions was also determined. The ratio of hexosamine to protein (× 100) in the alpha-1 globulin averaged 4.3. In the alpha-2 globulin, the hexosamine to protein ratio averaged 4.1, in the beta globulin 2.9, and in the gamma globulin 1.8 (Table II).

In four pools of sera from patients with active rheumatoid arthritis, the amount of hexosamine in each globulin fraction was found to be increased, although the increment in the beta fraction was minimal. Comparison of the hexosamine levels to the protein content of each fraction showed that the hexosamine to protein ratio in alpha-1 globulin was considerably greater than in the normal pools, reaching 7.4, whereas in the other fractions changes in the hexosamine to protein ratios were of questionable significance.

Two pools of sera from patients with rheumatic

TABLE I

Total serum hexosamine concentration, total serum protein concentration, and ratio of hexosamine to protein in health and disease

Diagnosis	No. of cases		Total hexosamine *mg. %*	Total protein *gm. %*	$\frac{\text{Hexosamine}}{\text{Protein}} \times 100$
Normal	25	Range	65.8–107	6.34–8.45	0.95–1.08
		Mean	79.0	7.34*	1.02*
		S.E.M.	±1.84	±0.55	±0.14
Rheumatoid Arthritis	14	Range	81.6–147	5.09–9.20	1.21–2.26
		Mean	117	7.28	1.63
		S.E.M.	±3.93	±.28	±.077
			(p = >.001)		(p = >.001)
Rheumatic Fever	8	Range	97–193	5.28–9.41	1.48–2.99
		Mean	153	7.59	2.06
		S.E.M.	±10.8	±.49	±.184
			(p = >.001)		(p = >.001)
Systemic Lupus Erythematosus	4	Range	114–150	6.20–8.64	1.40–2.14
		Mean	126	7.47	1.71
Gout	3	Range	88.5–130	6.07–6.92	1.28–2.14
		Mean	104	6.52	1.62
Pneumonia	7	Range	105–179	6.28–7.84	1.43–2.42
		Mean	127	7.22	1.76
		S.E.M.	±9.79	±.21	±.124
			(p = >.001)		(p = .001)
Cirrhosis of Liver	4	Range	105–136	5.98–8.08	1.61–2.15
		Mean	125	6.69	1.89
Hepatitis	3	Range	86.9–111	7.88–8.30	1.05–141
		Mean	102	8.09	1.26

* Based on 11 cases.

TABLE II

Hexosamine and protein content of electrophoretically separated serum protein fractions. Each pool contained equal amounts of serum from three patients

Diagnosis	Hexosamine (*mg.* %)				Protein (*gm.* %)					$\frac{\text{Hexosamine}}{\text{Protein}} \times 100$			
	alpha-1	alpha-2	beta	gamma	alb.	alpha-1	alpha-2	beta	gamma	alpha-1	alpha-2	beta	gamma
Normal I	17.8	20.7	15.4	22.8	4.15	0.41	0.52	0.61	1.46	4.3	4.0	2.5	1.6
Normal II	16.5	23.6	16.8	25.4	4.10	0.40	0.67	0.64	1.44	4.1	3.5	2.6	1.8
Normal III	18.3	30.7	20.5	26.0	4.19	0.40	0.66	0.58	1.40	4.4	4.7	3.5	1.9
(Mean)	(17.5)	(25.0)	(17.4)	(24.7)	(4.15)	(0.40)	(0.62)	(0.61)	(1.43)	(4.3)	(4.1)	(2.9)	(1.8)
Rheumatoid Arthritis I	32.4	49.8	20.5	28.8	3.15	0.42	1.02	0.57	1.85	7.7	4.9	3.6	1.6
Rheumatoid Arthritis II	32.8	51.4	24.7	33.1	2.99	0.44	0.99	0.65	1.98	7.5	5.2	3.8	1.7
Rheumatoid Arthritis III	28.3	35.0	23.8	31.0	3.25	0.47	0.83	0.67	1.49	6.0	4.2	3.6	2.1
Rheumatoid Arthritis IV	20.6	29.5	18.1	40.4	2.45	0.36	0.50	0.58	2.03	8.5	5.9	3.1	2.0
(Mean)	(28.5)	(41.4)	(21.8)	(33.3)	(2.96)	(0.42)	(0.84)	(0.62)	(1.84)	(7.4)	(5.1)	(3.5)	(1.9)
Rheumatic Fever I	36.2	48.1	24.1	34.0	3.32	0.54	1.08	0.83	2.18	6.7	4.5	2.9	1.6
Rheumatic Fever II	30.5	39.6	21.7	30.3	3.22	0.43	0.88	0.82	1.84	7.1	4.5	2.6	1.6
(Mean)	(33.4)	(43.9)	(22.9)	(32.2)	(3.27)	(0.49)	(0.98)	(0.83)	(2.01)	(6.9)	(4.5)	(2.8)	(1.6)
Systemic L. E. I	24.0	37.7	24.9	49.9	2.97	0.42	0.73	0.75	2.85	5.7	5.2	3.3	1.8
Systemic L. E. II	36.8	40.0	15.4	26.2	1.68	0.56	0.79	0.53	1.61	6.6	5.1	2.9	1.6
(Mean)	(30.4)	(38.9)	(20.2)	(38.1)	(2.38)	(0.49)	(0.76)	(0.64)	(2.23)	(6.2)	(5.2)	(3.1)	(1.7)
Pneumonia I	27.9	44.8	20.4	35.0	3.34	0.44	1.04	0.68	2.08	6.3	4.3	3.0	1.7
Pneumonia II	44.3	45.7	25.4	38.0	2.06	0.40	0.62	0.59	2.63	11.0	7.4	4.2	1.4
(Mean)	(36.1)	(45.3)	(22.9)	(36.5)	(2.70)	(0.42)	(0.83)	(0.64)	(2.36)	(8.7)	(5.9)	(3.6)	(1.6)
Cirrhosis I	21.4	29.7	18.4	46.9	2.35	0.53	0.81	0.71	2.61	4.0	3.7	2.6	1.8
Cirrhosis II	16.8	24.0	16.6	56.0	2.20	0.34	0.62	0.55	2.58	4.9	3.9	3.0	2.1
(Mean)	(19.1)	(26.9)	(17.5)	(51.5)	(2.28)	(0.44)	(0.72)	(0.63)	(2.60)	(4.5)	(3.8)	(2.8)	(2.0)

fever showed significant elevations in the hexosamine content of the alpha-1, alpha-2 and gamma fractions, with slight increase in the beta globulin hexosamine. The hexosamine to protein ratios again showed a considerable increase in the alpha-1 globulin, but little change in the other fractions. Similar findings were noted in two pools of sera from patients with active systemic lupus erythematosus. The total gamma globulin was considerably increased in one of these pools, and a correspondingly increased gamma globulin-hexosamine was found, with no change in the hexosamine to protein ratio.

Pools of sera from patients with acute bacterial pneumonia showed changes very similar to those found in rheumatoid arthritis and rheumatic fever. In one of these pools there were marked increases in hexosamine content of the alpha-2 and beta globulins, without corresponding increases in protein in those fractions. This was the only pool which showed apparently significant increases in the ratio of hexosamine to protein in those fractions.

Sera from patients with decompensated Laënnec's cirrhosis were also studied, in view of the suggested relation between liver function and serum glycoprotein components (8, 14). The only significant deviation from the normal findings in these sera consisted of an elevation of gamma globulin with a corresponding elevation of gamma globulin-hexosamine, with no change in the ratio of hexosamine to protein (Table II).

Effect of anti-inflammatory hormones on hexosamine content of alpha globulins

A group of patients with rheumatic fever, gout and rheumatoid arthritis were studied before and during therapy with various anti-inflammatory hormones (Table III). The hexosamine content of the alpha-1 globulin fell during treatment in all instances. The protein content of the alpha-1 globulin fell when it was considerably elevated before treatment, but rose during therapy in one patient with rheumatic fever, and in the pool of three cases of rheumatoid arthritis. The ratio of hexosamine to protein in the alpha-1 globulin fell in all.

The hexosamine content of the alpha-2 globu-

lin fell with therapy in the patients with rheumatic fever, but did not change significantly in the other instances. A diminution in the protein content of the alpha-2 globulin also occurred in the patients with rheumatic fever; the ratio of hexosamine to protein in the alpha-2 globulin did not change significantly in any instance.

The perchloric acid soluble fraction (seromucoid)

Studies of this fraction were done on sera from individual patients and also on the pools of sera used for the electrophoretic separations.

Twenty-five normal sera showed a mean hexosamine content of the seromucoid of 5.69 mg. per cent; the biuret reaction revealed a protein content averaging 79.5 mg. per cent. The ratio of hexosamine to protein (× 100) in this fraction averaged 7.3 with these methods. Of the total hexosamine found in these sera, 5.8 per cent was found in the seromucoid.

Sera from patients with rheumatoid arthritis showed elevations in the protein content of the seromucoid averaging 121 mg. per cent; the hexosamine in this fraction was also elevated, averaging 11.6 mg. per cent. The ratio of hexosamine to protein in this fraction averaged 11.5. This ratio of hexosamine to protein varied from the normal range up to 16.9, and clinically there seemed to be a rough correlation between this ratio and the severity of the joint inflammation. Of the total hexosamine content of these sera, 9.7 per cent was found in this fraction (Table IV).

In active rheumatic fever, systemic lupus erythematosus and acute gouty arthritis similar changes were found, with increases in the ratio of hexosamine to protein (Table IV). As the disease process subsided, the protein and hexosamine content of the seromucoid fraction both fell toward the values found in normal subjects. The ratio of hexosamine to protein also decreased. The greatest increases in the amount of each constituent of the seromucoid were observed in some cases of acute rheumatic fever.

Eight patients with bacterial pneumonia also were studied, and similar increases in hexosamine and protein were found, with a rise in the hexosamine to protein ratio.

Eight patients with decompensated Laënnec's cirrhosis and three with acute viral hepatitis also were studied. The protein content of the seromucoid was found to be lower than normal, but in some instances there was considerable overlap into the normal range (Table IV). The hexosamine content of this fraction was not significantly reduced, resulting in a rise in the hexosamine to protein ratio.

Effect of anti-inflammatory hormones on the seromucoid fraction

Sixteen patients were studied before and after therapy with corticotropin (ACTH), cortisone or related steroids. The findings in the seromucoid fraction given in Table V are the mean values for the patients in each group before and after therapy.

TABLE III

Effect of therapy with anti-inflammatory hormones on hexosamine and protein content of alpha globulins

Disease	Status	Hexosamine mg. %		Protein gm. %		Hexosamine / Protein	
		alpha-1	alpha-2	alpha-1	alpha-2	alpha-1	alpha-2
Rheumatic Fever	Before Rx	35.3	56.5	0.41	1.19	8.6	4.8
	Hydrocortisone Rx	28.5	38.3	0.47	0.75	6.1	5.1
Rheumatic Fever	Before Rx	68.9	86.8	0.82	1.49	8.4	5.8
	Hydrocortisone Rx (2 weeks)	27.1	44.9	0.43	0.80	6.3	5.6
	Hydrocortisone Rx (5 weeks)	20.7	33.0	0.41	0.61	5.1	5.4
Gout	Before Rx	35.5	51.8	0.56	1.20	6.3	4.3
	ACTH Rx	25.0	50.0	0.54	1.16	4.6	4.3
Rheumatoid Arthritis (Pool)	Before Rx	28.3	35.0	0.47	0.83	6.0	4.2
	Prednisone Rx	25.3	36.5	0.51	0.95	4.9	3.8
Mean change with Rx		−17.1	−17.9	−0.08	−0.31	−2.7	−0.1

TABLE IV

Hexosamine and protein content of seromucoid fraction in normal and pathological sera

Diagnosis	No. of obs.		Hexosamine mg. %	Protein mg. %	$\frac{\text{Hexosamine}}{\text{Protein}} \times 100$	$\frac{\text{Seromucoid hexosamine}}{\text{Total hexosamine}} \times 100$
Normal	25	Range	3.76–8.45	47.5–107	5.55–9.02	5.39–7.96
		Mean	5.69	79.5	7.20	6.97
		S.E.M.	±0.26	±3.3	±.26	±.91
Rheumatoid Arthritis	16	Range	5.54–19.9	44.3–264	8.13–16.9	6.00–17.3
		Mean	11.6	121	11.5	9.7
		S.E.M.	±1.6	±15.2	±.76	±.80
			(p = >.001)	(p = .01)	(p = >.001)	(p = .05)
Rheumatic Fever	8	Range	10.5–25.6	134–313	7.4–12.1	8.1–14.2
		Mean	17.9	190	9.5	11.6
		S.E.M.	±2.13	±23.5	±.49	±.77
			(p = >.001)	(p = >.001)	(p = >.001)	(p = .02)
Pneumonia	8	Range	8.22–19.6	50.0–205	7.8–13.0	6.4–10.9
		Mean	9.14	116	9.0	8.2
		S.E.M.	±1.68	±16.9	±.61	±1.0
			(p = .05)	(p = .05)	(p = .01)	(p = .4)
Systemic Lupus Erythematosus	5	Range	6.24–12.5	65.3–167	9.3–16.6	5.2–10.7
		Mean	11.0	95.8	12.0	7.8
Gout	3	Range	7.26–17.1	50.4–128	10.2–14.4	7.7–13.2
		Mean	10.6	83.6	12.7	9.8
Cirrhosis	8	Range	2.31–12.6	33.8–89.3	7.5–16.4	4.3–9.3
		Mean	5.57	59.7	9.8	5.2
		S.E.M.	±1.27	±8.18	±1.2	±1.4
			(p = .4)	(p = .02)	(p = .05)	(p = .3)
Hepatitis	3	Range	4.02–6.02	43.1–69.0	8.5–10.9	4.4–7.0
		Mean	4.90	53.2	9.4	5.3

In five patients with rheumatoid arthritis, the total serum hexosamine and the hexosamine in the seromucoid fraction both decreased with hormone therapy. At the same time an increase occurred in the biuret reacting protein in the seromucoid. In seven patients with acute rheumatic fever, similar decreases in total serum hexosamine and seromucoid hexosamine occurred, but in these patients the protein content of the seromucoid, which was markedly elevated before therapy, fell with treatment. The fall in protein was proportionately less than the fall in hexosamine, however, and the hexosamine to protein ratio in this fraction fell toward normal. In a group of four patients with unrelated disease (acute gouty arthritis, acquired hemolytic anemia, systemic lupus erythematosus, and idiopathic myocarditis) the changes were similar to those found in the rheumatoid arthritis patients. In all instances, the ratio of hexosamine to protein in the seromucoid fraction was decreased after therapy.

TABLE V

Effect of therapy with anti-inflammatory hormones on hexosamine and protein in seromucoid fraction.
(Figures given are mean values)

	Hexosamine mg. %	Protein mg. %	$\frac{\text{Hexosamine}}{\text{Protein}} \times 100$
Rheumatoid Arthritis (5 cases)			
Before therapy	13.4	103.	13.0
On therapy	11.9	130.	9.2
Rheumatic Fever (7 cases)			
Before therapy	17.3	183.	9.5
On therapy	9.9	126.	7.8
Non-rheumatic diseases (4 cases)			
Before therapy	12.1	106.	11.4
On therapy	8.8	112.	7.9

DISCUSSION

The range for normal total serum hexosamine found in this study is very similar to that reported by West and Clarke (1). The non-specific in-

crease found in a variety of diseases also duplicates the reports of others (1–4, 6). Our data indicate that the rise in total serum hexosamine in various diseases is accompanied by an increase in the ratio of hexosamine to total serum protein. An increase in the ratio of total protein-bound hexose to total serum protein has been described in a variety of diseases (7, 19), and an increase in the ratio of total hexosamine to total serum protein has been reported in rheumatic fever (6).

The largest increases in carbohydrate content of the serum proteins in most disease states have been found in the alpha globulins (4, 16, 17). Our data confirm these observations. In addition, it was found that an increase in the ratio of hexosamine to protein occurred in the alpha-1 globulin, in non-specific fashion. The ratio of hexosamine to protein in the other fractions, as determined by these methods, did not change significantly despite rather large increases in the amount of alpha-2 globulin in most of the diseases studied, and in the gamma globulins in some clinical states.

With suppression of the inflammatory process by means of hormone therapy, the amount of hexosamine in the alpha-1 globulin decreased, and the ratio of hexosamine to protein also fell. Changes in the amount of hexosamine in the alpha-2 globulin during therapy were accompanied by changes of similar magnitude in the protein content of that fraction, so that no significant alteration in the ratio of hexosamine to protein occurred. The change in the ratio of hexosamine to protein in the alpha-1 globulin in the diseases studied could be due to an increase of one of the components which migrates with the alpha-1 fraction which is considerably richer in hexosamine than the bulk of the protein in that fraction.

The electrophoretic method used in this study achieved good separation of the albumin and alpha-1 globulins, and the serum albumin was found to contain very small amounts of hexosamine. This has been noted in purified specimens for both hexose and hexosamine (5, 20). In the diseases studied, increases in the ratio of total serum hexosamine to total serum protein were noted (Table I), but electrophoretic studies showed significant increases in the ratio of hexosamine to protein in only one fraction. The observed changes in the alpha-1 globulin could not account for the increase in ratio of total serum hexosamine to total protein. The data for the electrophoretically separated serum pools revealed a fall in albumin in each case (Table II), which was quantitatively great enough to account for the bulk of the increase in ratio of total hexosamine to total protein, since the albumin contained so little of the total hexosamine.

Studies of the seromucoid have revealed similar changes in protein content in various diseases, but no change in the ratio of hexose to tyrosine in this fraction was found in several diseases (11, 12), although an increase in hexose/tyrosine was reported in rheumatoid arthritis, gout (7), and experimental scurvy (21). Our findings revealed a non-specific increase in the ratio of hexosamine to protein in the seromucoid fraction in disease. Much of the protein in the seromucoid migrates, at pH 8.6, as an alpha-1 globulin (2, 22). It is therefore of interest that the alpha-1 globulin alone among the electrophoretic serum protein fractions studied revealed an increase in the hexosamine to protein ratio with disease. When comparisons were made on individual sera or pools of sera it was apparent that the entire change in hexosamine content of the alpha-1 globulin could not be accounted for by the change in seromucoid hexosamine. It was not possible, with these methods, to determine if the entire change in hexosamine to protein ratio in the alpha-1 globulin could be accounted for by the change in hexosamine to protein ratio in the seromucoid.

Corticotropin has been found to produce an increase in the seromucoid in normal individuals (23). In patients with rheumatic fever, corticotropin lowered the initially elevated seromucoid level, but not entirely to normal, reaching a plateau and remaining somewhat elevated after other "acute phase reactants" were normal. When the corticotropin was discontinued, the seromucoid level fell the rest of the way to normal (24). Our findings in regard to the protein content of the seromucoid are similar. Those patients who had small elevations of the seromucoid protein level before therapy had an increase in the protein content of this fraction during therapy with anti-inflammatory hormones. In patients with rheumatic fever, who had markedly elevated levels before therapy, we also noted that hormones resulted in a fall of the protein content of the seromucoid toward, but not to, normal. It seemed that the direction of change with therapy depended on

the initial level, but the final level achieved was similar in all instances. In addition, the hexosamine content of the seromucoid fraction, was found to decrease during hormone administration in all instances. Thus the hexosamine decreased while the protein content of the seromucoid increased in those instances in which the protein rose with therapy. The ratio of hexosamine to protein fell toward normal in all.

These data seem to indicate that there are physiological differences among the components of the seromucoid fraction also. One or more components particularly rich in hexosamine may be increased by disease, while others containing proportionately less hexosamine may remain unchanged or undergo less of an increase. The hexosamine to protein ratio thereby increases during activity of the disease process. Suppressive hormone therapy apparently lowers the hexosamine to protein ratio by lowering the hexosamine-rich material selectively or predominantly. Since the protein level rises with hormone therapy if it is low initially, one component of this fraction, at least, must be increased by these agents. Presumably the latter component is not as rich in hexosamine as that lowered by therapy, since the total hexosamine and hexosamine to protein ratio decreases with hormone therapy.

The available information in the literature and that obtained by the methods used in this study seem to indicate differences in the significance of the various carbohydrate-containing fractions in the serum. It seems likely that further study of the physiology of individual components will be of interest.

SUMMARY

1. The total serum hexosamine rises in several diseases, leading to an increase in the ratio of total serum hexosamine to total serum protein.

2. Electrophoretic separation of serum proteins at pH 8.6 showed, in most of the diseases studied, a rise in the hexosamine associated with the alpha-1 globulin which was greater than the accompanying rise in protein content of the alpha-1 globulin, resulting in an increase in the ratio of hexosamine to protein. In the alpha-2, beta and gamma globulin fractions, parallel changes in hexosamine and protein occurred, with no significant changes in ratio.

3. The perchloric acid-soluble fraction, or seromucoid, also increases non-specifically with disease, but the hexosamine content was found to increase more than the protein, raising the ratio of hexosamine to protein in this fraction.

4. Suppression of inflammation with hormone therapy was found to decrease the hexosamine content of the alpha-1 globulin and seromucoid and lower the ratio of hexosamine to protein in those fractions.

5. These observations are interpreted as indicating that in the seromucoid and the alpha-1 globulins there seems to be an increase in at least one component which is richer in hexosamine than the rest of the fraction in a variety of illnesses, and that there is a fall in a hexosamine-rich component with anti-inflammatory hormone therapy.

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