

# CHANGES IN BLOOD SERUM PROTEIN FRACTIONS AS INDICATORS OF THE COURSE OF INFLAMMATORY PROCESSES

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The nature of the changes in protein fractions of blood serum as indicators of the course of inflammatory processes has not as yet been adequately studied.

Since there are references in the literature to the influence of inflammatory processes on the interrelations of serum protein fractions as revealed by electrophoretic separation [2, 3, 5, 6] this method was adopted for the present study of the proteinograms of those patients in whom a brief exudative inflammatory reaction could be expected to arise in connection with therapeutic measures. With this aim in view a survey was made of patients with pulmonary tuberculosis; these were subdivided into the following two groups, depending on the therapy received:

1. Patients who had been subjected to surgical intervention accompanied by inflammatory reaction of traumatic origin.

2. Patients treated with tuberculin which can cause focal reaction.

## EXPERIMENTAL METHODS

The total amount of protein was determined by an immersion refractometer; the ratio of protein fractions by paper electrophoresis. Separation of the serum was carried out in the A. E. Gurvich [1] electrophoretic chamber over a period of 16 hours, on paper soaked in Veronal-Medinal buffer (pH 8.6, ionic strength 0.1) at constant current of 250 v and 0.1 mA per 1 cm of paper width. The paper strips were stained with bromophenol blue. Measurements of the electrophoregram were made in the specially constructed apparatus for direct photometry [4].

TABLE 1.

Percentage Content of Protein Fractions in the Blood  
Serum of Healthy Subjects

Globulins				Albumins
$\gamma$	$\beta$	$\alpha_2$	$\alpha_1$	
16.5 $\pm 2.1$	13.0 $\pm 1.8$	8.5 $\pm 1.0$	4.3 $\pm 0.9$	57.7 $\pm 2.5$

Studies on the blood serum protein fractions in the patients were preceded by similar studies on 20 healthy subjects. The following data were obtained as the result of these studies; calculations were performed by the variation method (Table 1).

These data served as a certain standard with which the changes in protein composition of blood serum in the patients could be compared.

## EXPERIMENTAL RESULTS

The first group of patients was made up of 21 persons aged 16 to 40 years. They were subdivided according to the form of illness as follows: infiltrative pulmonary tuberculosis — 5 patients, focal — 3, chronic hematogenic-disseminated — 2 and chronic fibrous-cavernous — 11. Four patients had been subjected to thoracocauterization, 13 to extrapleural pneumolysis, one to conservative resection of the pulmonary lesion and three to lobectomy.

Blood for investigation was taken 3 times: prior to operation, on the 4th postoperative day and after disappearance of postoperative inflammatory changes. Development of unfavorable postoperative complications occurred in 2 patients. In one of them the last proteinogram determination was carried out shortly before death.

Table 2 reflects the dynamics of the protein composition of blood serum in all the patients under observation.

Data from 4 and 5 graphs enabled us to summarize the obtained material as follows (Table 3).

As Tables 2 and 3 show, in 17 patients there was a decrease in the amount of total protein as compared to preoperative values; in 3 patients it remained unchanged and in one there was an increase. In 16 of the 21 patients studied diminution of  $\gamma$ -globulin content occurred and only in five this fraction showed a slight rise. Concurrently with this there was an increase of total  $\alpha$ -globulin in all patients, of  $\alpha_2$ -globulin in 20 and  $\alpha_1$ -globulin in 16. Concentration of albumin was decreased in all 21 patients. Changes in the  $\beta$ -globulin content varied: increases and decreases of this fraction were noted in an equal number of cases.

Thus the changes in protein values of blood serum in patients with pulmonary tuberculosis following operative intervention were characterized by a certain decrease in the concentration of total protein and of its  $\gamma$ -globulin and albumin fractions and an increase in  $\alpha$ -globulins at the expense of  $\alpha_2$ -globulin first of all.

Examination of the differences in the changes of the protein composition of serum associated with different operations revealed the following:

a) the least marked changes were seen after cauterization of pleural adhesions complicated by transient mild pneumopleurisy, and after segmental resection and lobectomy without postoperative complications. The average increase in the  $\alpha_2$ -globulin level in this group of patients was 2.2% and the average reduction of albumins — 3.5%;

b) the most pronounced changes in the protein composition of the blood were seen in operated patients whose postoperative period following lobectomy was stormy and characterized by deterioration of the general condition, progressive course of the pulmonary process, development of empyema.

Clinical deterioration was accompanied by hypoproteinemia and a sharp fall in the albumin and  $\gamma$ -globulin levels with concurrent considerable increase in  $\alpha$ -globulin content and moderate increase of  $\beta$ -globulin. The average increase in  $\alpha_2$ -globulin in this group of patients was 6.6% and the average decrease in albumins — 9.4%.

c) the changes in the protein composition of the blood following extrapleural pneumolysis were of the same character but not so pronounced, occupying an intermediate position between the two degrees mentioned above. The average increase in  $\alpha_2$ -globulin in this group was 4.2%, and the average reduction in albumins — 4.5%. Changes in protein fractions were accompanied by formation of exudate in the extrapleural cavity, serous-hemorrhagic at first, then serous. These inflammatory changes resolved favorably.

The data obtained showed that various operative procedures on the thorax caused changes in the protein composition of the blood whose degree depended on the presence and extent of postoperative exudative inflammation of the tissues. The persistence of such changes with respect to the individual serum fractions as well as subsequent dynamics of these changes usually reflected the intensity and duration of the inflammatory reaction in the postoperative period. As the postoperative inflammatory manifestations settled down the changes in the protein composition of the blood associated with them also disappeared: the amount of  $\alpha$ -globulins decreased while that of albumins and  $\gamma$ -globulin increased.

TABLE 2

Dynamics of the Protein Composition of Blood Serum in Patients Treated Surgically (the total serum protein content is expressed in grams-per cent, protein fraction content — in percentage of total protein)

## I. Operation — Cauterization of Pleural Adhesions

Exper. No.	No. of case history	Name	Prior to operative intervention						After operative intervention											
			Globulins			Albu- mins	Total pro- tein	During development of pneumopleurisy					After complete resol. of pleural exudate							
			γ	β	α <sub>1</sub>			γ	β	α <sub>1</sub>			Total pro- tein	Globulins			Albu- mins	Total protein		
					γ					β	α <sub>1</sub>	α <sub>2</sub>		α <sub>3</sub>	γ	β			α <sub>1</sub>	α <sub>2</sub>
1	1	3	4						5					6						
1	520	Kt-ba, E.M.	19.2	20.1	11.3	7.1	42.3	7.87	20.2	19.5	14.2	6.0	40.1	7.63	20.0	18.5	9.3	4.2	48.0	7.63
2	28	Od-va, V.L.	32.2	9.5	5.6	3.0	49.7	6.88	30.3	8.2	10.0	3.3	48.2	6.77	21.8	13.0	9.8	4.1	51.3	6.96
3	484	St-aya, E.M.	21.1	13.9	12.9	4.9	44.2	6.77	22.9	10.4	13.3	9.5	43.9	7.20	25.6	6.4	11.6	8.4	48.0	7.46
4	416	Ga-ev, G.D.	19.5	12.5	9.6	5.4	52.6	7.73	20.0	14.5	13.2	7.4	44.9	7.46	25.0	9.9	10.6	4.3	50.2	7.87

## II. Operation — Extrapleural Pneumolysis

Prior to operative intervention			After operative intervention										After complete exudate resolution							
			During exudate formation																	
1	457	An-va, R.N.	29.4	12.4	7.3	4.2	46.4	7.87	24.1	10.0	14.1	6.5	45.3	6.98	26.8	13.8	4.7	4.1	50.6	7.20
2	548	St-va, A.M.	20.1	13.8	10.5	10.3	45.3	8.1	18.1	15.5	16.9	6.3	43.2	7.98	26.7	13.2	9.5	8.6	48.0	7.98
3	469	Ma-ev, B.V.	15.9	15.3	10.9	5.8	52.1	7.44	17.4	11.7	15.6	6.5	48.8	7.55	17.7	15.7	9.0	5.0	52.6	7.32
4	439	Ze-an, M.S.	17.1	16.0	9.5	3.6	53.8	6.92	17.7	13.7	13.2	4.8	50.5	6.79	18.9	10.9	11.3	4.6	51.3	6.94
5	9	Mo-va, P.V.	23.2	19.3	5.0	4.0	48.5	7.42	12.6	13.4	10.4	11.5	43.1	6.85	18.7	15.9	9.6	8.6	49.2	7.45
6	539	Al-ev, M.M.	19.3	15.4	16.6	12.3	36.4	6.38	18.1	17.4	19.3	12.0	33.2	6.12	18.5	15.2	14.7	6.4	45.2	7.02
7	355	Ku-ish, M.S.	25.5	7.0	16.2	3.4	47.9	7.61	20.6	11.0	16.0	7.5	44.9	6.88	21.1	18.6	7.0	5.9	47.4	7.46
8	32	Ok-ev, A.I.	22.7	9.5	11.7	3.2	52.9	7.53	21.8	10.9	14.3	4.4	48.6	7.57	24.7	12.9	9.9	4.5	48.0	7.44
9	24	Se-ev, N.Ya.	25.7	11.9	6.3	3.2	52.9	7.85	24.3	5.9	16.1	3.7	50.0	7.42	20.5	11.9	10.6	5.7	51.3	8.06
10	23	Pa-in, N.S.	19.6	13.0	15.1	5.1	47.2	6.88	26.3	14.5	17.0	5.0	37.2	6.88	20.0	10.5	13.0	6.7	43.8	7.20
11	419	Fo-ev, N.F.	22.4	14.6	8.4	7.0	47.6	8.13	17.5	14.9	15.9	9.1	42.6	7.55	29.1	15.2	7.5	4.9	43.8	7.61
12	474	Li, Ch. S.	22.8	11.7	11.1	6.1	48.3	7.42	21.5	16.4	13.6	6.5	42.0	6.98	18.8	17.8	9.3	6.3	47.8	7.42
13	386	Zhi-na, M.I.	19.6	11.4	14.6	5.8	48.6	6.83	22.4	12.4	15.8	8.9	40.5	6.55	21.9	13.0	10.7	5.3	49.1	6.94

## III. Operations Involving Resection of Pulmonary Tissues

		Prior to operative intervention										After operative intervention										No signs resol. congestive pleural exudate or partial resolution	
												During development of empyema											
1	452	Bu-ov, M.M.	26.9	13.1	13.2	6.2	40.6	7.44	22.3	15.0	20.5	10.8	31.4	6.34	20.2	17.1	23.4	11.7	27.6	6.12			
2	348	Zi-B, A.P.	25.6	12.2	11.0	4.7	46.5	7.59	17.9	15.3	16.9	12.8	37.1	6.49	19.9	11.5	14.0	6.2	48.4	7.89			
		Prior to operative intervention										In the absence of pleural reaction										During further smooth postoperative course	
3	450	Sa-in, D.I.	25.9	8.5	12.9	5.8	46.9	7.96	23.5	18.1	13.8	5.1	39.2	6.53	20.5	17.4	10.5	7.2	44.4	6.94			
4	463	Ba-va, O.G.	24.4	11.8	13.1	2.9	47.8	7.63	22.8	11.0	14.5	5.7	46.0	7.22	23.4	12.7	10.8	1.7	51.4	8.06			

TABLE 3

Nature of the Changes in Blood Serum Proteins Seen in Patients with Pulmonary Tuberculosis Following Operative Intervention

Nature of changes in proteins after operative intervention	Total protein	Fractions of globulins					Albumins
		$\gamma$	$\beta$	$\alpha_1$	$\alpha_2$	Total $\alpha$	
Number of patients							
Increase in protein indicators	1	5	10	20	16	21	—
Unchanged protein indicators	3	—	—	—	—	—	—
Decrease in protein indicators	17	16	11	1	4	—	21

The second group consisted of 10 patients aged 16 to 45 years. Five of these suffered from infiltrative, four from focal and one from chronic hematogenic-disseminated pulmonary tuberculosis. All 10 patients were being treated with tuberculin against the background of preceding and continuing streptomycin and PASA therapy. The addition of subcutaneous injections of tuberculin was determined by the wish to facilitate the penetration of the antibacterial preparations mentioned into the foci of tuberculous inflammation and to stimulate healing processes.

The blood proteins were determined 3 times in this group: on admission to the clinic, immediately before beginning tuberculin therapy following preliminary treatment with antibacterial preparations, and on completion of treatment. In those cases in which clinico-radiologic data following one of the tuberculin injections showed development of focal reaction additional determinations were carried out.

In two of the 10 patients the supplementary tuberculin therapy did not produce any appreciable improvement in the course of the disease. Correspondingly, the content of  $\alpha$ -globulins remained high, that of albumins low and of  $\gamma$ -globulin almost unchanged in these patients.

TABLE 4

Dynamic Changes in the Protein Composition of Blood Serum  
Patient R-g (Case History No. 460)

Proteinogram	Globulins					Albumins	Total protein
	$\gamma$	$\beta$	$\alpha_2$	$\alpha_1$	Total $\alpha$		
I	23.4	10.0	15.3	3.5	18.8	47.8	6.64
II	19.5	12.9	14.1	4.2	18.3	49.3	7.20
III	15.6	14.3	16.3	5.4	21.7	48.4	7.20
IV	20.9	11.6	9.2	7.0	16.2	51.3	6.98

Patient I-na (Case History No. 559)

I	13.8	10.6	14.8	3.8	18.6	57.0	6.98
II	15.1	10.5	8.1	6.7	14.8	59.6	6.77
III	16.0	15.2	11.1	5.7	16.8	52.0	7.20
IV	16.9	15.8	9.6	3.7	13.3	54.0	6.80

In 6 patients the combination of tuberculin therapy with antibacterial preparations exerted a positive effect on the course of the tuberculous process. It assisted the resolution of infiltrative and focal lesions and in some patients the closure of necrotic cavitation in the pulmonary tissue. Definite changes in the protein composition of blood serum accompanied this; normalization of  $\alpha$ -globulins content, increase in the concentration of albumins and increase in the  $\gamma$ -globulin content.

In 2 patients very marked changes in the ratio of the protein fractions were noted during treatment. They were associated with focal reaction caused by tuberculin. The latter took the form of perifocal infiltration around the main focal lesion. At this time there was an increase in the total  $\alpha$ -globulins content, mainly the  $\alpha_2$ -globulin. The  $\gamma$ -globulin decreased in one patient and remained almost unchanged in the other. After a brief interruption the tuberculin injections were resumed. The patients' general condition and the local process showed considerable improvement; concurrently there was lowering of total  $\alpha$ -globulins and increase in blood serum albumins. The dynamic changes in the protein composition of blood serum in these two patients are presented in Table 4. Proteinogram I reflects the state of serum proteins on admission of these patients, II — before adding tuberculin therapy to treatment with antibacterial preparations, III — during development of focal reaction, produced by subcutaneous injection of tuberculin, and IV — just before discharge from the clinic, with favorable outcome. The total serum protein content is expressed in grams-per cent, while protein fractions — in percentage of total protein.

Changes in  $\beta$ -globulin did not show clear consistency in all the 10 patients; fluctuations in total protein did not leave the limits of normal.

Thus, inflammatory changes of an exudative nature in the lungs, pleura and extrapleural cavity proceed against the background of appreciable disturbances of the blood serum protein composition; the latter are characterized by increased content of  $\alpha$ -globulins (mainly  $\alpha_2$ -globulin) and decreased level of albumins.

Changes in the protein composition of blood serum, determined by electrophoretic fractionation, can serve, together with other methods of investigation, as one of the indicators of the phase of inflammatory processes.

#### SUMMARY

Paper electrophoresis was used in the determination of serum proteins in patients with various forms of tuberculosis. The dynamics of the exudative inflammation of the lungs, pleura and extrapleural cavity was characterized by a rise on  $\alpha$ -globulins, mostly  $\alpha_2$ -globulins of the blood serum and a decrease of the albumin level.

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