other cell types remain unaffected.[1] Apparently, the presence of complement is necessary for the occurrence of this form of prompt cytolysis. Experiments to further elucidate the role that this type of cytolysis plays in the pathogenesis of delayed-type hypersensitivity are in progress.

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An Electrophoretic Study of the Serum Proteins in Scleroderma.

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Scleroderma (literally: "hardening of the skin") occurs in two forms: diffuse and localized. The diffuse form is a progressive systemic disease of the connective tissue throughout the body.[1,2] The localized form on the other hand appears clinically to be limited to the skin and is a much milder disease. In spite of numerous investigations, the pathogenesis of scleroderma remains obscure. Observations on the serum proteins have been limited to an occasional routine determination showing a decrease in the albumin/globulin ratio with little change in the value for total proteins.[3] It seemed possible that a more detailed analysis by the Tiselius method of electrophoresis might yield additional information of value.

Methods and Materials. Serum was obtained in the fasting state from 12 normal subjects, 5 patients with diffuse scleroderma, and one patient with localized scleroderma. Four ml of serum were dialyzed against 2 liters of barbiturate buffer (ionic strength 0.1, pH 8.6) for 48 hours at 4° C, then diluted 1:3 with buffer. Electrophoresis was carried out in the Tiselius apparatus using a double section cell and an optical system of the type described by Philpot.[4] It proceeded for 80 minutes at a potential gradient of 8 volts per cm and a temperature of 1°C. Patterns were photographed directly, enlarged 5×, and the areas measured with a planimeter. Components were delineated by vertical lines drawn from the minima of the curves to the baseline. Ascending and descending pattern areas were averaged for each component except β-globulin; here only the ascending pattern area was used. Total and nonprotein nitrogen were determined by the micro-Kjeldahl method.

Results. In diffuse scleroderma, as shown in Table I, the albumin fraction of the serum proteins decreases and the γ-globulin fraction increases, but no significant change occurs in the total protein value. The alterations in the albumin and γ-globulin fractions are statistically significant. No new components in the electrophoretic pattern and no gross alterations in mobilities are evident. While little weight can be given to data from one case of localized scleroderma, it is interesting to note that the changes are qualitatively and quantitatively similar to those occurring in the diffuse scleroderma group. This is somewhat surprising in view of the apparent absence of systemic involvement in the localized form of the disease.

Discussion. The changes described are in no way diagnostic since similar changes occur in many chronic infections, in disseminated lupus erythematodes, in liver disease, and in other conditions.[5] They may, however, give

1 Matsui, S., *Press. med.*, 1924, **2**, 142.

2 Lindsay, J. R., Templeton, F. E., and Rothman, S., *J. A. M. A.*, 1943, **123**, 745.

3 Banks, B. M., *New Eng. J. Med.*, 1941, **225**, 433.

4 Philpot, J. St. L., *Nature*, 1938, **141**, 283.

5 Stern, K. G., and Reiner, M., *Yale J. Biol. and Med.*, 1946, **19**, 67.

TABLE I.
Electrophoretic Analysis of Serum Proteins in Scleroderma.

Patient No.	% of total protein					Concentration, g %					
		Globulins					Globulins				
	Alb.	α_1	α_2	β	γ	Alb.	α_1	α_2	β	γ	Total protein
					Diffuse Scleroderma.						
1	44.5	4.6	10.3	17.2	23.4	3.30	0.34	0.76	1.27	1.73	7.41
2	57.9	4.6	9.1	14.3	14.1	3.66	0.29	0.58	0.90	0.89	6.32
3	47.1	6.0	9.1	12.6	25.3	3.52	0.45	0.68	0.94	1.89	7.47
4	44.5	4.6	10.3	17.2	23.4	3.19	0.33	0.74	1.23	1.68	7.17
5	44.4	7.9	7.9	17.6	22.0	2.36	0.42	0.42	0.94	1.17	5.31
Mean	47.7	5.5	9.3	15.8	21.6	3.21	0.37	0.64	1.06	1.47	6.74
σ	5.82	1.45	1.00	2.22	4.38	0.508	0.067	0.140	0.178	0.422	0.921
					Localized Scleroderma.						
6	46.9	5.4	8.0	12.0	27.6	3.64	0.42	0.62	0.93	2.14	7.77
					Normal (12 subjects).						
Mean	58.4	4.7	9.2	15.2	12.8	4.00	0.32	0.63	1.05	0.89	6.90
σ	2.81	0.67	1.00	1.95	2.45	0.276	0.039	0.091	0.162	0.207	0.483

σ = Standard deviation.

TABLE II.
Clinical Data on the Patients.

Patient No.	Age	Sex	Duration of disease, yrs	Tissues involved in addition to skin	Course
1	25	F	3		Stationary
2	36	F	2	Joints	"
3	54	M	7	Esophagus, lungs, joints, pleura, pericardium, connective tissue (generalized)	Expired (autopsy)
4	58	M	2½	Joints	Expired
5	62	M	2	Esophagus, lungs, joints, renal and myocardial vessels*	" (autopsy)
6	13	F	6		Progressive

* Patient 5 also showed hypertension. Scleroderma was the only disease noted in any of the other patients.

some clue as to the pathogenesis of scleroderma. The rise in the γ-globulin fraction, which contains most of the known antibodies, suggests an immunological response, such as that which occurs during immunization,[6] or in the course of infectious diseases. Decrease in the albumin fraction, which occurs early in scleroderma, is also a characteristic of the electrophoretic pattern in malnutrition, liver disease and kidney disease.[5] Liver involvement is seldom found at autopsy in scleroderma, but kidney changes do occur, and a poor state of nutrition commonly accompanies the disease.

[6] Van der Scheer, J., Bohnel, E., Clark, F. H., and Wyckoff, R. W. G., *J. Immunol.*, 1942, **44**, 165.