BIOCHEMISTRY AND BIOPHYSICS

A COMPARATIVE STUDY OF THE PROTEIN FRACTIONS OF THE PLASMA AFTER A SINGLE EXPOSURE TO HIGH-ENERGY PROTONS AND TO X-RAYS

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(Received November 10, 1958. Presented by Active Member AMN SSSR V. N. Orekhov)

In order to make a comparative study of the biological action of different forms of penetrating radiation, an investigation of the protein fractions of the plasma was carried out in rabbits exposed to the action of high-energy protons and in animals irradiated with x-rays.

Radiation sickness due to x-rays is accompanied by a very definite dysproteinemia, the characteristics of which was described in papers by several authors [1, 3, 4]. Information on the effect of protons of this order of energy is not be found in the literature.

EXPERIMENTAL METHOD

The study of the composition of the fractionated plasma proteins was carried out by the method of electrophoresis in a Tiselius-Svenson apparatus. Animals were exposed to the action of high-energy protons. The mean energy of the protons in the emitted beam was 480 Mev.

A layer of tissue of thickness 80 g/ cm^2 (80 cm) weakens the energy of 480 Mev protons to roughly 200 Mev. The value of the relative ionization in the tissue for this energy range of protons (200-480 Mev) remains practically constant (on the average 15 ion pairs/ micron of tissue), which is approximately the same as the relative ionization during exposure to x-rays with an energy of 200 kev.

The maximum ionization density (Bragg's curve) for primary protons with an energy of 480 Mev is situated at a distance of 110-120 cm [2]. Secondary processes, however (elastic and inelastic interaction of protons with nuclei of tissue elements) may bring about the appearance of particles with a higher relative ionization and, consequently, more effective in their biological action.

Animals in a securely fixed position were placed at a point in the first link of the proton tract at a distance of 5 and 45 cm from the outlet orifice, with the head directed toward the source of radiation. So that they could be compared with the action of x-rays, the doses of protons were expressed in physical roentgen equivalents. The measured dose rate on the body surface of one of the rabbits was 8.55 physical roentgen equivalents per minute.

In order to study the biological action of the high-energy protons, 17 rabbits were used, which received different doses of irradiation. The total dose of irradiation of the individual rabbits varied from 88 to 1220 physical roentgen equivalents. Blood was taken from the various rabbits for investigation, 1, 3, 9, 11, 19, 25, 31 and 50 days after a single exposure to different doses of protons. To compare the biological action of x-rays and protons, experiments were performed on 6 rabbits after exposure to equivalent doses of x-rays. The condictions of irradiation were as follows: voltage 180 kv, current 15 ma, filter 0.5 mm Cu + 1.0 mm Al, focal distance 60 cm, dose rate 18-25 r/ min.

Changes in the Protein Fractions of the Plasma of Rabbits Exposed to the Action of High-Energy (480 Mev) Protons and X-Rays.

Animal No.	Dose, rep	Time after exposure, in days	Protein fractions, in per cent				Fibrinogen
			albumins	globulins			
				α	β	γ	
	Normal (mean of 21 rabbits)		58,1±3,6	9,3±0,9	14,3±1,4	8,9±3,2	9,4±1,4
	Protons						
169	1 220	10	23,4	21,3	23,6	9,2	22,5
5	1 000	1	47,7	12,6	14,7	10,2	14,8
347	650	11	34,4	13,6	18,6	15,9	17,4
147	550	9	29,7	23,7	19,3	5,5	21,7
322	500	11	39,4	12,8	24,8	11,7	11,2
131	500	50	69,8	7,2	9,9	6,2	6,8
161	325	3	55,4	14,5	14,7	4,9	10,4
302	325	11	37,9	18,2	20,7	12,5	10,7
4	325	19	39,8	12,3	14,9	17,1	15,9
483	325	25	47,6	10,3	18,1	15,8	8,2
696	325	31	45,5	16,3	14,6	10,3	13,3
648	325	50	51,4	9,3	14,2	14,6	10,5
2	250	25	58,1	10,3	12,5	9,1	10,0
91	240	24	53,7	13,6	14,7	10,3	7,7
212	156	30	51,3	11,9	13,2	10,5	14,1
204	88	24	55,2	10,4	12,0	13,9	8,5
	x - Rays						
171	1 000	10	30,9	20,9	22,3	7,4	18,4
6	1 000	1	52,1	12,0	10,0	10,0	15,8
22	1 000	1	52,3	12,1	12,7	9,8	13,1
6	650	11	57,3	10,6	14,9	8,8	8,4
1	500	11	58,5	13,0	13,0	12,4	8,1
43	325	3	47,4	14,5	13,6	13,6	10,9
42	325	3	54,7	15,3	13,1	6,3	10,5
42	325	11	60,6	7,8	12,8	11,1	7,8
43	335	11	59,0	9,8	11,4	12,0	7,7
43	325	19	44,4	12,5	16,3	13,7	13,0
42	325	19	60,2	9,8	12,6	8,4	9,0
42	325	40	51,4	13,0	14,1	11,4	10,2

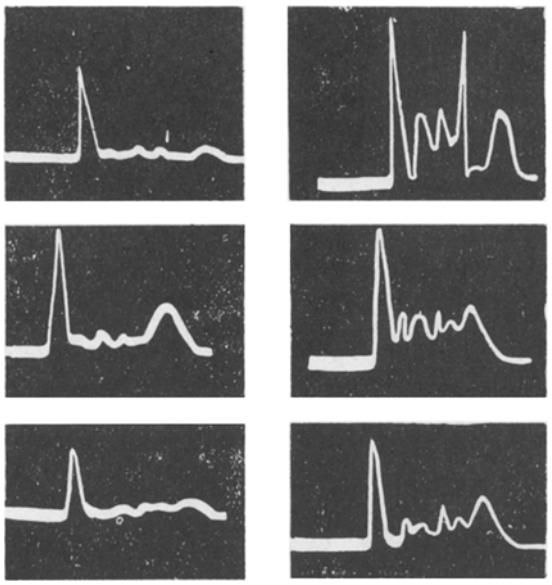
EXPERIMENTAL RESULTS

The results of the analyses for the two groups of animals are given in the table.

The results obtained show that as the disease developed, the relative proportion of albumins fell, the α- and β-globulin fractions and the plasma fibrinogen rose, while the changes in the γ-globulin fraction were not characteristic. The most considerable changes were found in animals irradiated with massive doses of protons.

In rabbit No. 169, for instance, on the 10th day after exposure to a dose of 1200 physical roentgen equivalents, a well-marked dysproteinemia was evidently found in the agonal period of the disease. An appreciable fall in the albumin fraction was detected in the first few days after exposure to protons in a dose of 1000 physical roentgen equivalents (see table).

Sublethal doses of protons (650, 550 and 500 physical roentgen equivalents) also caused well-marked variations in the composition of the plasma protein fractions. Analyses carried out on the 9th and 11th days after exposure to protons in the doses mentioned showed significant dysproteinemia (see figure, a and b).



Electrophoregrams of the plasma protein fractions of rabbits. a) Normal; b) 9 days after exposure to protons in a dose of 550 physical roentgen equivalents; c) 11 days after irradiation with x-rays in a dose of 325 physical roentgen equivalents; d) 11 days after exposure to protons in a dose of 325 physical roentgen equivalents; e) 19 days after irradiation with x-rays in a dose of 325 physical roentgen equivalents; f) 19 days after exposure to protons in a dose of 325 physical roentgen equivalents.

Comparison of the changes in the fractional composition of the plasma proteins, caused by x-rays and high-energy proteins in sublethal doses, at similar times after exposure, revealed a particularly great difference in the biological effect of these two types of radiation. Whereas on the 9th and 11th days after irradiation with protons, the rabbits showed considerable dysproteinemia, electrophoretic analysis of the plasma proteins at approximately the same time after x-rays irradiation did not show this feature.

With smaller doses (325 physical roentgen equivalents) no essential differences could be found in the actions of protons and x-rays in the first period of the disease (the first 24 hours). On the 11th and 19 th days, however, the difference was now apparent (see figure, c, d, e, f).

Electrophoretic analysis at a later period of the disease (on the 25th-31st day) showed some degree of normalization of the plasma protein relationships. On the 50th day full restoration to normal was observed, apart from a slight increase in the γ-globulin fraction (14.6 instead of a normal 8.9%).

Investigation of the protein fractions in rabbits exposed to the action of small doses of protons (from 88 to 250 physical roentgen equivalents) was carried out at a later period after exposure. In all the rabbits of this group that were examined the proportions of the plasma protein fractions remained within normal limits.

It must, therefore, be emphasized that dysproteinemia in animals exposed to the action of protons was more severe than in rabbtis irradiated with x-rays. Animals exposed to protons of such high energy values did, in fact, die after exposure to comparatively small doses (325-600 r), after showing signs of radiation sickness at relatively early stages.

If our findings are considered from the point of view of primary radiochemical processes, it may be postulated that the elastic and inelastic interaction of protons with the nuclei of the tissue elements (mainly carbon, nitrogen and oxygen) plays an essential role in the general effect of exposure of animals to radiation.

SUMMARY

By electrophoretic method with Tiselius apparatus the authors conducted a comparative study of the blood plasma protein fractions in rabbits following single irradiation with high energy protons and equivalent x-ray doses.

It was acertained that following irradiation with the protons, the fractional quantitative composition of blood plasma is altered in the same way as after x-ray irradiation: the albumin fraction level progressively decreases, while the α- and β-globulin fractions and fibrinogen contents rise. The changes consequent upon proton action, however, are more intense, this, evidently, resulting from the formation in the tissues of secondary ionized particles, more effective biologically than the protons.

LITERATURE CITED

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