IMMUNOLOGY

CHANGES IN ANTIGENIC PROPERTIES OF TISSUES OF WHITE RATS IN RADIATION SICKNESS

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Every animal or plant species has its own special type of biosynthesis, which leads to the elaboration of the proteins specific to a given species; this specifity applies in particular to their antigenic properties.

It is known that different kinds of changes in protein metabolism lead to changes in their antigenic properties, and N. N. Zhukov-Verezhnikov [2, 3] has studied the problem of the significance of changes in immunospecificity of cells and tissues. L. A. Zilber and V. D. Timakov [5] have shown that new antigens arise in human tissues in certain chronic diseases. O. E. Vyazov [1], V. A. Karev [7], and others have demonstrated changes in antigenic properties of tissues during ontogenesis. V. A. Parnes [13] has found that specific antigens appear in leukemia. Finally, changes in antigenic properties of tissues have been established during growth of tumors by L. A. Zilber [4], I. N. Maisky [12], P. N. Kosyakov [9], and others.

There are numerous references in the literature [11, 14, 15] to the effect of ionizing radiation on protein metabolism in animals. Although this should be associated with changes in the antigenic properties of tissues, we have not found any published work on this subject.

EXPERIMENTAL METHODS

We applied the method of active anaphylaxis and desensitization introduced by L. A. Zilber [6]. Since the changes in metabolism are the most marked in the nuclear proteins of irradiated animals [10, 17], we made separate studies of the antigens of cell nuclei and cytoplasm.

The antigens studied were taken from the nuclei of cells of the liver and jejunal mucosa of albino rats, as well as from the cytoplasm of liver cells of normal rats and of rats subjected to total irradiation (dose 800 r), and killed 3-5 days later. The cell nuclei and cytoplasm were prepared by Dounce's method [16], and the nuclei were dissolved in 0.005 N NaOH before the experiments. The cytoplasmic material was dissolved in physiological saline. The solutions contained 10 mg of protein per ml; the protein content was derived from the nitrogen content, as determined by a micro-Kjeldahl method.

Guinea pigs were sensitized by subcutaneous injections of the antigens, and development of sensitization was tested 21-30 days later by intravenous injection of the antigen into a fore or hind limb.

Guinea pigs sensitized with antigens from normal rats were desensitized with the corresponding antigens from irradiated rats, and vice versa. Having checked the completeness of desensitization, we gave challenging doses of the antigen used for sensitization. An interval of 1-2 hours was allowed between the two intravenous injections.

The anaphylactic reaction was evaluated according to the following: infrequent scratching of the nose and sneezing ±, repeated scratching of the nose and sneezing +, the same, to a more marked degree, with cough ++, scratching of the nose, sneezing, cough, involuntary evacuation of urine and feces, convulsions +++, death of the animal ++++, absence of reaction −.

Active Anaphylactic Reactions with Cross Desensitization with Antigen Preparations from Tissues of Irradiated (800 r) and Normal Albino Rats

No. of guinea pig	Sensitized with		Desensitized with							Challenging injection		
				1st injection		2nd injection		3rd injection				
	antigen	dose (mg protein)	antigen	dose (mg protein)	reaction	mg protein	reaction	mg protein	reaction	antigen	mg protein	reaction
2	Nuclei of cells from the jejunal mucosa of normal rats	10	Nuclei from the jejunal mucosa of irradiated rats	1,5	++	3	—	4	—	Nuclei of cells from the jejunal mucosa of normal rats	4	+++
3		10		2	+	4	++				4	+
4		10		1,5	++	4	—				3	++
5		10		2	++	3	—				4	+
13	Nuclei from liver cells of normal rats	10	Nuclei from liver cells of irradiated rats	3	+	4	—			Nuclei from liver cells of normal rats	4	+
14		10		3	++	4	—				4	+
15		10		3	+	4	±	4	—		5	—
16		10		3	+	4	±	4	—		5	+
17		10		3	+	4	—				4	+
18		10		3	+	4	—				6	+
19		10		3	+	4	—				4	±
7	Nuclei from the jejunal mucosa of irradiated rats	10	Nuclei of cells from the jejunal mucosa of normal rats	1,5	++	3	—			Nuclei from the jejunal mucosa of irradiated rats	4	—
8		10		1,5	+	2	—				3	—
9		10		2	++	4	—				5	—
10		10		1,5	+	4	+	4	—		5	—
21	Nuclei from liver cells of irradiated rats	10	Nuclei from liver cells of normal rats	1	+	1,5	±	2	—	Nuclei from liver cells of irradiated rats	6	—
22		10		2	+	2,5	—				2,5	—
23		10		2,5	+	3,5	—				5,5	—
24		10		3	++	3,5	—				5,5	—
25		10		1,5	+	2,5	—				4	—
26		10		2,5	+	3,5	—				4	—
27		10		3	++	3,5	—				4	—
30	Cytoplasm from liver cells of normal rats	25	Cytoplasm from liver cells of irradiated rats	2,5	+++	5	—			Cytoplasm from liver cells of normal rats	5	+++
31		25		2,5	++	5	—				7,5	++
32		25		2,5	++	5	—				7,5	+
33		25		2,5	++	5	—				7,5	+++
34		25		1,25	++	5	—				6	+
35		25		1,25	±	2,5	+	7,5	—		7,5	++
36		25		2,5	++	6	—				5	++
37		25		2,5	++	6	—				2,5	++
38		25		2,5	++	6	—				3,5	++
40	Cytoplasm from liver cells of normal rats	25	Cytoplasm from liver cells of normal rats	1,25	++	3,5	—			Cytoplasm from liver cells of irradiated rats	5	+
41		25		1,25	++	3,5	—				5	++
42		25		2,5	++	5	±	5	—		10	±
43		25		2,5	+	3,5	—				3,5	+
44		25		2,5	++	3,5	±	5	—		7,5	±
45		25		1,25	++	5	+	5	—		5	+
46		25		1,5	++	3,5	+	5	—		7,5	++

EXPERIMENTAL RESULTS

The results are presented in the Table.

The results for the guinea pigs used as sensitization controls are not included in the Table; they all gave strong anaphylactic reactions to the challenging doses of antigen, with a fatal issue in some cases. The results for tests of toxicity of the preparations are also not given in the Table; in no case did any visible reaction follow injection of the antigens into unsensitized animals.

The upper part of the Table, down to No. 27, shows changes in antigenic properties of nuclear proteins of liver and jejunal mucosa cells of rats suffering from radiation sickness. It is evident that full desensitization of guinea pigs sensitized to antigens from the nuclei of normal rats is not achieved by injection of the corresponding antigens from irradiated rats; the rats react positively to challenging injections of antigen. Conversely, rats sensitized to nuclear antigens from the same tissues of irradiated rats can be fully desensitized by injections of the corresponding antigens from normal rats, and do not react positively to challenging doses of the sensitizing antigen.

It may hence be concluded that the nuclei of liver and jejunal mucosa cells of irradiated rats contain fewer antigenic complexes than do those of normal rats.

The lower part of the Table, beginning with No. 30, shows changes in the antigenic properties of the cytoplasm of liver cells. It appears that sensitization to cytoplasmic antigens of irradiated rats cannot be fully suppressed by injections of the corresponding preparation from normal rats, and that similarly rats sensitized with cytoplasmic antigen from normal rats are not fully desensitized by corresponding preparations from irradiated animals. It follows that not only is the number of cytoplasmic antigenic complexes of liver cells reduced following irradiation, but also that new ones, not present in normal animals, make their appearance.

We have thus been able, by means of the reactions of anaphylaxis and desensitization, to demonstrate changes in the antigenic properties of cells of animals suffering from radiation sickness.

It is not clear what part, if any, these changes play in the pathogenesis of radiation sickness. It is conceivable that, in view of the enhanced permeability of tissues encountered in radiation sickness [8], antigenically modified proteins may enter the blood stream and produce immunological reactions of the organism, from formation of antibodies to development of sensitization to these antigens. This question is of considerable theoretical and practical importance.

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