INCREASED RESISTANCE OF ANIMALS TO X-RAY IRRADIATION FOLLOWING A PERIOD OF ACCLIMATIZATION TO HYPOXIA IN THE PRESENCE OF A NORMAL BAROMETRIC PRESSURE

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A number of investigators have noted the positive effect of acclimatization upon the subsequent exposure to roentgen irradiation [1-3]. The acclimatization is conducted in a pressure chamber so that the barometric pressure can be lowered to pressures corresponding to heights of 7000-8000 meters.

The aim of the present study was to investigate whether the resistance to generalized irradiation would be increased by another form of acclimatization, namely, when the animals were placed in a pressure chamber having a lowered oxygen content but a normal barometric pressure.

Simultaneously, we investigated the changes in the activity of the blood catalase and the catalase present in animal organs with the different acclimatization procedures. The study of catalase activity presented a theoretical interest in association with the radiochemical hypothesis as to the method of action by the ionizing radiation [7, 8]. It is known that catalase prevents an excess accumulation of hydrogen peroxide within the tissues of the organism, this apparently being the basis of its protective function. On the other hand, there have been many studies [5, 6] which showed a marked decrease in catalase activity in the blood and organs under the influence of roentgen irradiation.

EXPERIMENTAL METHODS

The studies were conducted on male white mice weighing from 18 to 20 grams. In the first series of experiments acclimatization to hypoxia was attained by daily stepped "climbs" within the pressure chamber according to the following procedure. At first, the pressure was lowered to that existing at a height of 5000 meters. At this height the animals were held for 30 minutes. Then the mice were "raised" to "heights" of 7000 meters for 5 minutes, further elevation to "heights" of 10,000 meters was attained and the mice kept there until the animals lay down on their sides or until one of them had convulsions.

In the second series the animals were acclimated to hypoxia by being kept in a pressure chamber where the barometric pressure was normal but the partial oxygen pressure was lowered. The gas mixture was prepared by diluting the air with nitrogen. Oxygen concentration was determined in the Orsat apparatus. The procedural sequence was as in the first series, i.e., the partial oxygen pressures were 82, 65 and 45 mm of mercury pressure corresponding to heights of 5000, 7000 and 10,000 meters.

In the third experimental series the animals were acclimated to decreases in barometric pressure while the partial pressure of the oxygen remained at normal levels. To accomplish this, the partial pressure of oxygen within the pressure chamber was raised to 506 mm mercury at the beginning of the experiment. Then the barometric pressure within the pressure chamber was lowered to that existing at a height of 10,000 meters, but the partial pressure of the oxygen was the same as in sea level atmosphere. The animals were kept in this condition for 35 minutes.

In all the series the training was continued daily for 30 days. One day after the last training session the animals were generally irradiated with roentgen rays by means of apparatus RUM-3. In each instance 16 mice

were irradiated: 8 controls and 8 experimental. The irradiation was done at 195 kv, current of 15 ma, filter of 0.5 mm of Cu and 1 mm of Al at a distance of 50 cm the strength of the dose being 20.3 r/ minute.

As controls for the first two series we employed unacclimated mice of the same weight, age and sex as the experimental animals. As controls for the third series (in which lowering of the barometric pressures was preceded by placing the animals in an atmosphere with a raised partial pressure of oxygen) we employed mice acclimated to hypoxia in a pressure chamber according to the schedule indicated for the first series. Before beginning their acclimatization, these mice were placed daily for 3-4 minutes in an atmosphere having a partial pressure of the oxygen of 506 mm mercury. Such a control was needed as the mice of the third series were, at the beginning of each training period, placed for 3-4 minutes in an atmosphere having an increased content of oxygen.

The irradiated mice were studied for 30 days. The animals were regularly weighed, examined as to their general condition and a record made as to when they succumbed. The catalase activity of the unirradiated mice of the three series was determined 24 hours after cessation of the acclimatization sessions. Unacclimated mice were used as controls. The blood catalase was determined by the manometric method of A. N. Bakh and S. R. Zubkova [4]. The catalase activity within organs such as the liver, kidneys, spleen and the lungs was determined by the same method but with the modification by G. V. Voskoboinikov [5].

EXPERIMENTAL RESULTS

Our experiments seem to indicate that acclimatization to hypoxia at normal barometric pressures increases the resistance of the animals to subsquent irradiation at least as much as, and possibly somewhat more than acclimatization to hypoxia induced by general lowering of the barometric pressure (Table 1).

TABLE 1

Influence of Various Methods of Acclimatization to Hypoxia Upon the Survival of White Mice After Irradiation With 600 r.

Series	Method of acclimatization	Total number of animals	Number of animals		Statistical treatment according to Student and Fisher*		
			succumbing	surviving 30 days after the irradiation	Difference between the number of control animals dying and the number of the experimental animals succumbing	t	P(in %)
First	Acclimatization to hypoxia by lowering of barometric pressure	40	25	15	+ 15± 3.1	±4.84	< 0.27
	Control (unacclimated animals)	40	40	0			
Second	Acclimated to hypoxia without lowering of the barometric pressure	40	21	19	+ 19± 3.16	±6.02	< 0.27
	Control (unacclimated animals)	40	40	0			
Third	Acclimated to lowered barometric pressure without hypoxia	16	16	0	-6± 1.94	± 3.1	< 0.27
	Acclimated to hypoxia by lowering of the barometric pressure and a preliminary stay in an oxygen-enriched atmosphere	16	10	6			

* See A. A. Sapegin. Statistical Variations , Moscow, 1935.

TABLE 2

Influence of Acclimatization Upon Hypoxia and Decreased Barometric Pressure in Relation to the Catalase Activity Within the Blood and Internal Organs of White Mice

Organs investigated	Controls (unacclimated mice)	Acclimated to hypoxia by lowering barometric pressure				Acclimated to hypoxia without lowering barometric pressure				Acclimated to decreased barometric pressure without hypoxia			
		exptl.	Statistical treatment (Student and Fisher)			exptl.	Statistical treatment (Student and Fisher)			exptl.	Statistical treatment (Student and Fisher)		
			difference between control and exptl.	t	P (%)		difference between control and exptl.	t	P (%)		difference between control and exptl.	t	P (%)
Catalase index of blood	0.31	0.45	0.14±0.023	6.00	<0.27	0.44	0.13±0.024	5.37	0.27	0,26	—0.05±0.094	0.534	>50
Catalase numbers:													
Liver	16.50	19.80	3.30±0.61	5.40	<0.27	20.50	4.00±1.380	2.90	1.00	16,20	—0.30±0.57	0.520	>50
Kidneys.	7.55	9.80	2.25±0.81	2.70	1.00	10.90	3.35±0.820	4.10	<0.27	8,80	1.25±0.78	1.600	10
Spleen	0.61	0.82	0.21±0.06	3.40	<0.27	0.85	0.24±0.070	3.43	<0.27	0,54	—0.07±0.09	0.600	>50
Lungs	1.73	2.72	0.99±0.28	3.50	<0.27	2.60	0.87±0.310	2:76	1.50	1,64	—0.07±0.183	0.380	>50

Note: The catalase number of an organ is the difference between the quantity of permanganate used in titrating 1 mg of the weight of the raw experimental tissue and the control and it is statistically valid (each average taken from 10 mice).

The animals conditioned to a lowered barometric pressure without hypoxia (third series) had the same resistance to irradiation as did the controls.

Study of catalase activity within the blood and organs of the acclimated animals indicated that acclimatization to hypoxia with a simultaneous lowering of the barometric pressure (first series) as well as acclimatization with the aid of a gas mixture (second series) increases the activity of the catalase both within the blood and the organs being examined (Table 2).

In animals conditioned only to a drop in the barometric pressure (third series), catalase activity both in the blood and the organs remained unaltered in the absence of hypoxia.

Our data agree with the findings of K. Mezey and H. Staffe [9] who observed an increase of 60% in the catalase activity of mountain dwellers acclimated to hypoxia.

Our results seem to allow the following conclusions:

In the mechanism of the increased resistance to irradiation, acclimatization to lowered barometric pressure has as its chief factor hypoxia. Animals can develop increased resistance to irradiation by hypoxia in the presence of normal barometric pressure. Conditioning to lowered barometric pressure without hypoxia does not increase radioresistance of mice. The definite rise in catalase activity within the blood and organs of organisms subjected to acclimatization with hypoxia proves that catalase plays a definite role in increasing radioresistance in acclimated mice.

SUMMARY

It was established as a result of experiment that the endurance of white mice to irradiation by x-rays is increased under the effect of acclimatization to hypoxia without decrease of barometric pressure. The activity of catalase in the blood and organs of acclimatized animals is increased.

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* In Russian.