MECHANISM OF THE PROTECTIVE ACTION OF ADAPATAION TO HYPOXIA ON THE DEVELOPMENT OF ALLERGIC ARTHRITIS

F. Z. Meerson, B. A. Frolov,
S. N. Afonina, A. I. Smolyagin,
and V. K. Filippov

UDC 616.72-002-056.43-092:612.
273.2.014.49

KEY WORDS: adjuvant arthritis; hypoxia; adaptation.

The protective action of adaptation of interrupted hypoxia against the development of adjuvant arthritis was demonstrated previously in rats and it was suggested that this action may be based on inhibition of T cell mechanisms of immunity [5]. At the same time, we know that although the formation of adjuvant arthritis is associated with predominant activation of cellular immunity [7], humoral antibodies or immune complexes do play a definite role in its development. Evidence in support of this view is given by the ability to reproduce adjuvant arthritis after elimination of T lymphocytes [8, 9] and potentiation of the immune response in animals with adjuvant arthritis to corpuscular and soluble antigens [3]. Accordingly, when the protective action of adaptation to interrupted hypoxia against the development of adjuvant arthritis is analyzed, it is important to study mediators that play the leading role in reactions involving the participation of humoral immune mechanisms.

In the investigation described below the effect of adaptation to interrupted hypoxia on the development of adjuvant arthritis was studied and compared with the level of biogenic amines (histamine and serotonin) and sensitivity of sensitized animals to serotonin.

EXPERIMENTAL METHOD

Experiments were carried out on 120 Wistar rats weighing 120-150 g. Adaptation to hypoxia was produced by keeping the animals daily in pressure chamber at an "altitude" of 5000 m for 1.5 months. Animals of the control group were kept in the same animal house under ordinary conditions. At the end of the specified time animals of the experimental and control groups received an injection of 0.2 ml of Freund's complete adjuvant into the hind footpads. The rats of the experimental group were then exposed to hypoxia again according to the adaptation program. The intensity of arthritis was assessed on the 7th, 14th, and 21st days of development of the inflammatory reaction according to the degree of edema of the fore- and hind limbs, reflecting an increase in volume of the affected joints. At the same times the blood levels of histamine [6] and serotonin [4] of the experimental and control animals were determined spectrofluorometrically.

Meanwhile, in a special series of experiments on 92 August rats, the effect of adaptation to hypoxia on sensitivity of sensitized and unsensitized animals to serotonin was studied. For this purpose the rats were sensitized with hen's egg albumin in Freund's incomplete adjuvant [2] and their sensitivity to intravenous injection of serotonin creating-sulfate was determined 21 days later. The dose of the preparation was 110 mg/kg, and in preliminary experiments it caused death of about 50% of the animals.

EXPERIMENTAL RESULTS

Data on the effect of adaptation to hypoxia on local and general parameters of the inflammatory reaction in Wistar rats at different times of development of adjuvant arthritis are given in Table 1. Adaptation to high-altitude hypoxia led to weakening of inflammatory changes

Problem Laboratory for the Study of Mechanisms of Natural Immunity, Orenburg Medical Institute. Laboratory of Pathophysiology of the Heart, Institute of General Pathology and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR P. D. Gorizontov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 100, No. 10, pp. 403-405, October, 1985. Original article submitted April 23, 1984.

TABLE 1. Effect of Adaptation of Hypoxia on Local and General Parameters on Inflammatory Reaction in Wistar Rats at Various Times of Development of Adjuvant Arthritis

Parameter	Group of animals	Original value	Adjuvant arthritis		
			7th day	14th day	21st day
Circumference of forelimb, cm	U	1,7±0,03 (80)	1,67±0,02 (40)	2,01±0,04 (20)	2,14±0,04 (20)
	A	1,7±0,03 (80)	1,67±0,02 (40)	2,02±0,02 (20)	1,9±0,02*(14)
Circumference of hind limb, cm	U	2,31±0,02 (80)	3,46±0,06 (40)	3,61±0,08 (20)	3,0±0,11 (20)
	A	2,31±0,02 (80)	3,13±0,06*(40)	3,01±0,11*(20)	3,1±0,07 (14)
Histamine, μg/ml	U	0,12±0,02 (8)	0,47±0,08 (9)	0,15±0,01 (13)	0,13±0,01 (7)
	A	0,04±0,02*(9)	0,12±0,013* (6)	0,07±0,015*(5)	0,07±0,017*(7)
Serotonin, %	U	26,4±3,4 (7)	55,9±7,8 (6)	148,1±9,2 (6)	95,1±13,4 (7)
	A	10,7±1,2*(7)	65,2±3,4 (10)	42,5±8,3*(8)	20,0±2,9*(6)

Legend. Number of animals given in parentheses. U) Unadapted, A) adapted rats. Asterisk indicates significant difference from values for unadapted animals.

TABLE 2. Effect of Adaptation and Hypoxia on Sensitivity of Sensitized and Unsensitized August Rats to Serotonin

Group of animals	Experimental conditions	Number of animals	Number which died	Number which survived	χ^2	% of animals which died
Unadapted	Sensitization	17	14	3	7,29	82,41±9,31
	—	31	13	18		40,0±9,8
Adapted	Sensitization	18	11	7	0,95	61,1±11,5
	—	26	12	14		42,9±10,8

in the experimental animals compared with the controls in joints of the hind limbs, into which Freund's complete adjuvant had been injected. These differences became visible on the 7th and 14th days. By the 21st day of the investigation the circumferences of the joints of the hind limbs of the experimental and control animals were virtually indistinguishable from one another. As regards the spreading of adjuvant arthritis to the forelimbs, this was more marked in the unadapted animals on the 21st day (Table 1).

Analysis of the blood histamine and serotonin concentrations revealed two important facts. The first is that adaptation to hypoxia led to a significant fall in the blood biogenic amine levels. For instance, the original histamine concentration in the unadapted animals was three times higher than in the adapted animals, and the serotonin level was 2.5 times higher. The second important fact is that during the development of the allergic process the biogenic amine levels in the adapted animals were considerably lower (for histamine on the 7th, 14th and 21st day, for serotonin on the 14th and 21st days of observation) than in unadapted rats. The intensity of the allergic inflammatory process was thus found to be inversely proportional to the blood levels of biogenic amines in the adapted and unadapted rats.

Bearing in mind the fact that the effectiveness of the role of biogenic amines in the realization of the pathochemical and pathophysiological stages of development of allergic reactions depends directly on sensitivity of the organism to them [1], the effect of adaptation to hypoxia on sensitivity of the sensitized and unsensitized animals to serotonin was studied (Table 2). Adaptation to hypoxia had no marked effect on the sensitivity of the unsensitized rats to injection of exogenous serotonin. At the same time, it significantly raised the threshold of resistance to the biogenic amine against the background of sensitization compared with the corresponding parameter in unadapted rats.

The protective action of adaptation to interrupted hypoxia against the development of allergic arthritis is thus effected not only through the immune system of the body, but also through its action on the level of biogenic amines (serotonin and histamine) and the sensitivity of the organism to them after sensitization.

LITERATURE CITED

1. A. D. Ado, General Allergology [in Russian], Moscow (1978).
2. V. M. Goritskii, S. S. Vavrinyuk, Yu. K. Bashmakov, et al., in: Problems in Experimental and Clinical Pathology [in Russian], Vol. 4, L'vov (1980), p. 51.
3. T. V. Davydova, Vestn. Akad. Med. Nauk SSSR, No. 6, 32 (1981).

4. B. N. Manukhin, L. V. Berdisheva, and E. V. Volina, Vopr. Med. Khim., No. 3, 317 (1975).
5. F. Z. Meerson, V. A. Evseev, T. V. Davydova, et al., Bull. Éksp. Biol. Med., No. 1, 12 (1980).
6. L. Ya. Proshina, Lab. Delo, No. 2, 90 (1981).
7. V. I. Pytskii, Yu. L. Gulyi, A. V. Leont'ev, et al., Patol. Fiziol., No. 1, 33 (1981).
8. G. Bombara et al., Quad. Sclavo Diagn. Clin. Lab., 9, 636 (1973).
9. J. Hollingworth et al., Proc. Soc. Exp. Biol. (N. Y.), 152, 183 (1976).

PROGNOSTIC VALUE OF DETERMINATION OF LYMPHOCYTE SUCCINATE DEHYDROGENASE ACTIVITY AND THERAPEUTIC EFFICACY OF SODIUM SUCCINATE DURING RESUSCITATION OF RATS

N. A. Baranets, V. T. Dolgikh, and R. P. Nartsissov

UDC 616-036.882-085.31:547.461.4.133-037-07:616.155.32.008.931:577.152.1

KEY WORDS: resuscitation; succinate dehydrogenase; rat lymphocytes; sodium succinate.

The dehydrogenase activity of lymphocytes is known to reflect the enzyme activity and metabolic changes in the internal organs [1, 2, 5, 8]. Clincial and experimental studies in the last few years have shown that low lymphocyte succinate dehydrogenase (SDH) activity is an unfavorable prognostic sign in a number of somatic and infectious diseases [3, 4]. However, the way in which SDH activity of the lymphocytes changes during clincial death and in the postresuscitation period, and whether changes in SDH activity of the lymphocytes are of prognostic value, and finally, whether by using sodium succinate to optimize energy metabolism in terminal states, it is possible to increase the survival rate of animals subjected to clincial death, have not been studied.

EXPERIMENTAL METHOD

Experiments were carried out on anesthetized noninbred male rats weighing 180-210 g kept in the animal house on an ordinary diet. The animals were divided into two groups: one group consisted of animals subjected to clinical death from acute blood loss (58 rats), the other group of animals treated 30 min before clincial death by intraperitoneal injection of sodium succinate in a dose of 20 mg/kg. Clincial death lasting 4 min was induced by acute bleeding from the carotid artery, and compression of the incubation tube for 7 min, and these procedures were followed by resuscitation by the method in [7]. The effect of preliminary injection of sodium succinate was assessed by the time of appearance of cardiac contractions and the corneal reflex, and the duration of survival of the resuscitated rats. In addition, SDH activity of the lymphocytes was estimated by the method in [6] in each experimental animal five times (before blood loss and asphyxia, at the end of clincial death, and 5, 15, and 90 min after resuscitation).

EXPERIMENTAL RESULTS

A fall of SDH activity in the lymphocytes was observed during clincial death, and the worse the outcome of resuscitation, the greater the degree of inhibition of this enzyme. During the first few minutes after resuscitation SDH activity in the lymphocytes increased and exceeded its original level. The group of animals dying in the early postresuscitation period was an exception (Table 1).

Omsk Medical Institute. Research Institute of Pediatrics, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR V. A. Negovskii.) Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny, Vol. 100, No. 10, pp. 405-407, October, 1985. Original article submitted July 17, 1984.

