PARTIAL OXYGEN PRESSURE IN THE TISSUES DURING ADAPTIVE CHANGES IN XANTHINE OXIDASE ACTIVITY

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UDC 612.26.015.11

Polarographic studies show increased oxygen utilization by the liver of albino mice associated with an increase in xanthine oxidase activity in the organ induced by repeated intraperitoneal injection of xanthine. Under these same conditions an increase in pO_2 is observed in muscle tissue. The significance of the results is discussed in connection with adaptation to repeated exposure to chemical substances and to the pattern of their administration.

By studying patterns of CCl_4 exposure Sarkisov et al. [5-7] showed that more frequent administration of this compound can result in a lower mortality among the animals, accompanied by the intensification of reparative regeneration, of intracellular compensatory processes, and of DNA synthesis. These results were confirmed in experiments with furfural [10, 14], benzene, and aminobenztrifluoride [12]. The relationship discovered is evidently of general biological character: depending on its chemical structure and metabolic pathways every chemical substance has its own rhythm of action in which intracellular regeneration and DNA and protein synthesis are intensified. There is a corresponding increase in the activity of the adaptive enzymes controlling the detoxication of particular poisons so that the mortality among the animals is reduced. Experiments with furfural in fact have shown that if the poison is administered more often, with a consequent reduction in mortality, increased activity of xanthine oxidase, an enzyme responsible for the conversion of aldehydes, including furfural, is observed [10]. Meanwhile an increase in the activity of the adaptive enzymes and in the rate of protein synthesis must evidently be accompanied by increased production of high-energy compounds and an increased supply of oxygen to the tissues. The preliminary observations made during an adaptive increase in xanthine oxidase activity produced by exposure to furfural indicate an increase in the partial pressure of oxygen (pO_2) in albino mice under these conditions [11].

This paper describes a special study of changes in pO_2 in the tissues and the rate of oxygen utilization by the tissues during an adaptive increase in xanthine oxidase activity.

EXPERIMENTAL METHOD

Male albino mice weighing 18-20 g were used. Xanthine was injected intraperitoneally once daily for 14 days in a dose of 120 mg/kg into the group of experimental animals. The control animals received distilled water. Xanthine oxidase (xanthine: oxygen – oxidoreductase, E.C. 1.2.3.2) activity in the liver of the experimental and control animals was determined 14 days later colorimetrically by the method of Litwack [18]. Meanwhile the rate of oxygen utilization by the liver tissue was determined polarographically and pO_2 was investigated in the gastrocnemius muscle of the animals. Intravital investigation of pO_2 in the tissues was carried out on unanesthetized animals by the PA-3 polarograph modified so as to record the diffuse current in I – t coordinates. The pO_2 detector was a spherical gold electrode [3] and a calomel electrode was used for reference. The indicator electrodes were calibrated before and after the experiment [1, 2]. The rate of oxygen consumption in the liver was determined by recording the rate of decrease

(Presented by Academician of the Academy of Medical Sciences of the USSR, A. P. Avtsyn.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 77, No. 5, pp. 34-36, May, 1974. Original article submitted May 7, 1973.

TABLE 1. Changes in Parameters of the Oxygen Balance during an Adaptive Increase in Xanthine Oxidase Activity (M ± m)

	Xanthine oxidase activity (in mmoles xanthine/g liver)	P	Constant of rate of O_2 utilization by liver tissue	P*	pO_2 in muscle (in mm Hg)	P	Overall oxygen consumption (in mm^3/100 g weight)	Red cell count (in millions/mm^3 blood)	P
Control	11.1 ± 1.35	0.05	0.14 ± 0.015	< 0.05	19.77 ± 1.07	≤0.002	10.83 ± 0.23	6.64 ± 0.24	≤0.01
Expt.	14.8 ± 0.8		0.18 ± 0.01		24.54 ± 1.02		10.21 ± 0.3	7.66 ± 0.2	

*P determined by Watt's criterion.

of pO_2 in the organ. The constant of this process was determined [13]. The red cell count in the peripheral blood was obtained in a Goryaev's chamber. The oxygen consumption also was studied by Miropol'skii's method [4]. Statistical analysis of the results was carried out by Student's method and also by a nonparametric method using Watt's criterion [8].

EXPERIMENTAL RESULTS AND DISCUSSION

The results are given in Table 1. Daily injection of xanthine into albino mice for 14 days led to an adaptive increase in xanthine oxidase activity in agreement with data in the literature [16, 17]. The adaptive increase in xanthine oxidase activity was accompanied by increased oxygen consumption by the liver tissue, an increase in pO_2 in the muscles, and some increase in the red cell count of the blood. The overall oxygen consumption was unchanged.

The results suggest that during repeated exposure to chemical substances in optimal rhythms, accompanied by activation of adaptive enzymes and intensification of DNA and protein synthesis, bioenergetic processes are profoundly reorganized. The oxygen utilization by organs responsible for biological transformation of the poison is increased at the expense of oxygen consumption in tissues not containing systems metabolizing the compound. In the present case the adaptive increase in xanthine oxidase activity in the liver was accompanied by an increase in the oxygen consumption of that organ. Meanwhile in the muscles, which do not contain this enzyme, an increase in pO_2 was observed, evidence of reduced oxygen consumption of this tissue. This hypothesis is confirmed by the fact that, despite the increase in the red cell count in the peripheral blood, the overall oxygen consumption was unchanged. The increase in resistance to poisons when administered in certain rhythms is connected with changes in the activity of the enzyme systems responsible for metabolizing these substances and, in turn, this is accompanied by the reorganization of some of the biochemical and physiological systems of the organism. This hypothesis is confirmed by data in the literature. For instance, repeated administration of phenobarbital, increasing the activity of the microsomal enzymes of the liver, was accompanied by increased production of ATP in the liver [14, 15, 19]. Increased ATP formation is evidence of changes in oxygen metabolism, intensification of oxidative phosphorylation, and an increased oxygen consumption by the tissue concerned, in agreement with the results of the experiments described in this paper.

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