COORDINATION OF LYMPHOCYTIC ENZYME SYSTEMS AND RESISTANCE OF MICE TO STAPHYLOCOCCAL TOXIN

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UDC 612.112.94.015.1.014.46: 576.851.252.097.29

Activity of acid phosphatase and of several dehydrogenases was demonstrated cytochemically in the blood lymphocytes of noninbred albino mice. The animals were then given an intraperitoneal injection of 1 LD_{50} staphylococcal toxin, as a result of which 42 of the 80 mice died during the first two days. A statistically significant difference was found between the degree of coordination of the lymphocytic enzyme systems in the surviving and dying animals: correlation of the enzyme levels in the surviving animals was higher than in those which died. The results are discussed from the standpoint of the a priori prognosis of the toxicosis and the coordination levels of the enzyme systems.

KEY WORDS: lymphocyte; cytochemistry; staphylococcal toxicosis.

The search for signs on the basis of which the subsequent course and outcome of a pathological process can be predicted before it has begun is essential on both theoretical and practical grounds.

In this investigation the presence of correlation between the enzyme status of the blood lymphocytes and the outcome of staphylococcal toxicosis was studied.

EXPERIMENTAL METHOD

Blood was taken from the tails of 80 noninbred mice of both sexes weighing 19-20 g, and films were made for cytochemical analysis of the lymphocytes. The animals were then given an intraperitoneal injection of 0.4 ml staphylococcal toxin diluted 1:7.5 with physiological saline. Within a few hours the animals started to die from toxicosis. Death of the animals was observed over a period of two days. Altogether 38 animals survived and 42 died.

Activity of acid phosphatase (AP) (EC 3.1.3.2), succinate dehydrogenase (SD) (EC 1.3.99.1), α-glycerophos-

TABLE 1. Cytochemical Indices of Enzyme Activity of Blood Lymphocytes from Mice Dying and Surviving after Receiving Injection of 1 LD_{50} Staphylococcal Toxin (M ± m)

Animals	No. of animals	SD	α-GPD	α- GPD - NAD	LD	AP
Surviving	38	16,75±0,35	13,06±0,34	14,67±0,35	19 46±0.61	98,7±4,0
Dying	42	15,17±0,42*	12,48±0,30	13,43±0,40*	19,83±0,31	89,9±4,1

*Differences between groups significant by Student's criterion ($P < 0.01$).

Laboratory of Microbiology and Laboratory of Cytochemistry, Institute of Pediatrics, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR N. N. Zhukov-Verezhnikov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 79, No. 6, pp. 74-76, June, 1975. Original article submitted March 29, 1974.

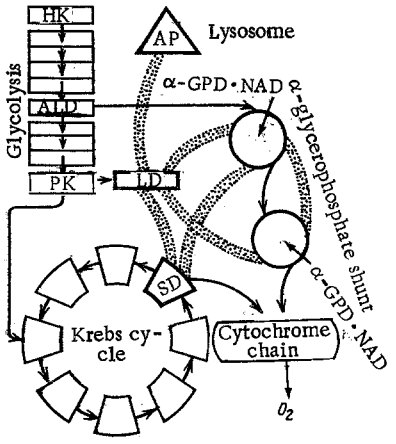

Fig. 1

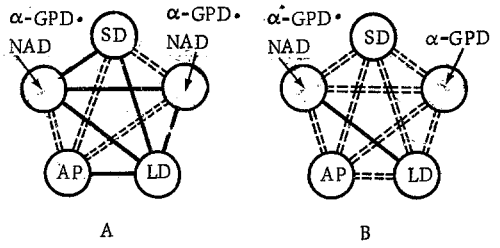

Fig. 2

Fig. 1. Scheme of correlation between metabolic pathways in the lymphocytes. Geometric shapes denote enzymes. Thick lines drawn around enzymes investigated. Arrows point to pathways of conversion of metabolites. Bands of dots show statistically significant correlation ($P < 0.05$) between enzyme activities. HK) Hexokinase; ALD) aldolase; PK) pyruvate kinase; LD) lactate dehydrogenase; AP) acid phosphatase; α-GPD) α-glycerophosphate dehydrogenase; α-GPD·NAD NAD-dependent α-glycerophosphate dehydrogenase; SD) succinate dehydrogenase.

Fig. 2. Correlations between enzyme activities of lymphocytes in surviving (A) and dying (B) animals. Continuous lines denote statistically significant correlations ($P < 0.05$); broken lines denote correlations not statistically significant ($P > 0.05$). Critical values of correlation coefficient for surviving animals $r = 0.332$; for dying animals $r = 0.310$. Line gap represents feedback. Remainder of legend as in Fig. 1.

phate dehydrogenase (α-GPD) (EC 1.1.2.1), NAD-dependent α-glycerophosphate dehydrogenase (α-GPD·NAD) (EC 1.1.1.8), and lactate dehydrogenase (LD) (EC 1.1.1.27) was demonstrated in the blood films. Acid phosphatase activity was determined by the method of Goldberg and Barka [8], and the activity of the dehydrogenases by the method published previously [4]. The enzyme status of the blood cell population was assessed by Kaplow's index for acid phosphatase [9] and by the arithmetical mean number of formazan granules for demonstration of the dehydrogenases. The mean values for the surviving and dying animals were compared by Student's criterion.

As indices of enzyme activity in each of the groups, coefficients of correlation were calculated. The existence of correlation was also verified by graphic analysis. To characterize the coordination of individual enzymes and the enzyme system as a whole, the mean coefficient of correlation was calculated (the "group strength" to use Terent'ev's expression [7], with the aid of the auxiliary function $Z = (1/2) \ln (1+r)/(1-r)$. The difference between the coefficients of correlation was weighted by means of a cumulative sigma.

EXPERIMENTAL RESULTS

The mean indices for the surviving and dying animals are given in Table 1.

As Table 1 shows, differences between the indices of the two groups were small in absolute terms, but for some enzymes they were statistically significant.

More demonstrative results were obtained by correlation analysis. Statistically significant correlation was discovered between the activity of enzymes belonging to the various metabolic pathways (Fig. 1).

It follows from the correlation pattern that with an increase (or decrease) in LD activity changes were recorded in the activity of all other enzymes, but with a change in AP activity changes could be expected predominantly in LD activity. On the whole, the significance of the correlation patterns is clearly shown by analysis of the metabolic pathways, but some relationships were more complex in character. Correlations of SD with LD and α-GPD·NAD were remarkable in this respect: considerable spatial and metabolic separation is a feature of these enzymes, more general regulatory factors begin to operate, and hormonal and neurohormonal regulation also are observed.

All the correlations with high statistical reliability listed above applied chiefly to the surviving animals (Fig. 2).

The correlation diagrams are contrasting: Of 10 possible correlations in the surviving animals 6 were statistically significant, whereas in the dying animals only 1 statistically significant correlation was actually found. This difference in the degree of coordination of the enzyme systems was confirmed by biometric analysis. For instance, the strength of the correlation group ($\bar{r}$) was 0.348 for the surviving animals and 0.145 for the dying animals and the difference between them was not statistically significant ($P < 0.01$). In other words, the enzyme systems of the lymphocytes in animals exposed to the action of the toxin were more regulated than in the dying animals.

The absolute value of the coefficients of correlation was low even in the group of surviving animals. This points to considerable freedom of protein catalysts with respect to one another, as also follows from their association with different metabolic pathways, the action of hormones, and so on. At the same time, a low but definite degree of coordination between enzyme systems was found to be an important factor in the system of defense of the organism against harmful action.

Theoretical analysis shows that correlation between enzyme activity cannot be extremely high or extremely low for a very long time [5]. In the first case the functional flexibility of the cell would be lost – the opposite process to what Setrov [6] calls the labilization of functions, characteristic of the most perfect biological systems. In the second case, as the results of the present investigation show, too low coordination is accompanied by the threat of death in an unfavorable situation. To sum up, signs of potential failure of antitoxic defense exist, and an important place among them is occupied by the level of coordination between lymphocytic enzyme systems.

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