EXCRETION OF ADRENALIN, NORADRENALIN, AND VANILLYL-MANDELIC ACID IN THE URINE OF RATS WITH EXPERIMENTAL PNEUMOCOCCAL INFECTION

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UDC 616.981.252-092.9-07: 616.834.452-074

During development of pneumococcal infection in rats, changes are observed in the intensity of catecholamine metabolism. At the beginning of the disease in rats excretion of catecholamines in the urine is increased, reaching a maximum on the 2nd day, and this is accompanied by more marked catecholamine inactivation, expressed by an increase in the excretion of vanillyl-mandelic acid. At the height of the infection, the level of catecholamines in the body rises, their excretion in the urine is increased, and excretion of the end-product of their metabolism, vanillyl-mandelic acid, is reduced.

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Conversions of catecholamines in the body take place mainly through oxidative deamination and O-methylation, with the participation of monoamine oxidase and catechol-O-methyltransferase. The object of this investigation was to study the activity of these enzymes in pneumococcal infection by determining the urinary excretion of catecholamines and of the end-product of their metabolism, vanillyl-mandelic acid.

EXPERIMENTAL METHOD

Experiments were carried out on 70 male albino rats weighing 180-250 g. Type 1 pneumococci were injected intradermally into the right flank of the experimental animals in a dose of 0.1 ml of an 18-h culture diluted 1 : 10. Intact rats served as controls. The animals were kept on a normal diet of food and water in special cells enabling the urine to be collected separately from the feces. The 24-h sample of urine was collected from the experimental and control rats before the experiment began (normal) and then every 3 h after infection with pneumococci. Catecholamines in the urine were determined by the quantitative fluorometric method of V. O. Osinskaya and by Men'shikov's modification [2] of the method of Euler and Lishajko. Fluorescence of the catecholamines was recorded with a modified ÉF-3 fluorometer. L-adrenalin hydrotartrate and L-noradrenalin hydrotartrate (Khar'kov Institute of Experimental Endocrinology) were used as standards.

Vanillyl-mandelic acid in the urine was determined by the methods of Klein and co-workers and Studnitz and co-workers, as modified by Men'shikov and Bol'shakova [3], using electrophoresis on paper. The standard was dl-3- methoxy-4-hydroxy mandelic acid (Cox, England).

The quantity of catecholamines and vanillyl-mandelic acid excreted in 24 h with the urine was calculated per kg body weight. The percentage yield of the vanillyl-mandelic acid standard added to the samples of urine averaged 74.1. The mean discrepancy between the results of parallel tests in these experiments was ±3.61%.

Statistical analysis of the results was carried out by the constant method of Montsevichyute-Éringene [5] and the results of the analysis were plotted as curves. Differences were regarded as significant when $P \leq 5\%$.

EXPERIMENTAL RESULTS

Changes in the intensity of catecholamine metabolism discovered in rats with pneumococcal infection were closely connected with the degree of development of the disease. At the beginning of the disease (1st

Division of Infectious Pathology and Experimental Therapy of Infectious Diseases, N. F. Gamaleya Institute of Epidemiology and Microbiology, Academy of Medical Sciences of the USSR, Moscow (Presented by Academician V. D. Timakov, Academy of Medical Sciences of the USSR.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 68, No. 7, pp. 31-34, July, 1969. Original article submitted May 8, 1968.

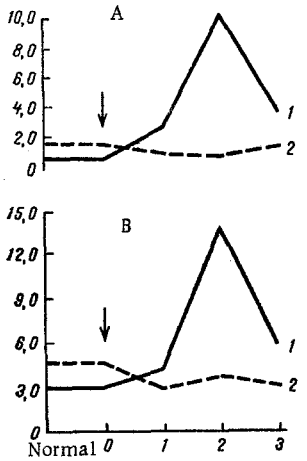

Fig. 1

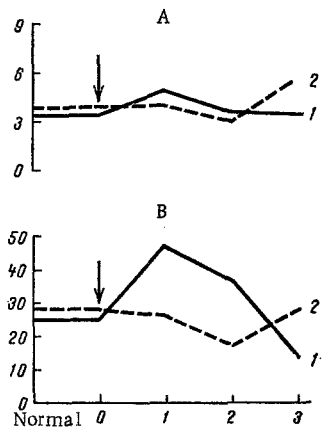

Fig. 2

Fig. 1. Excretion of adrenalin (A) and noradrenalin (B) with the urine of rats with experimental pneumococcal infection. 1) Rats infected with pneumococci; 2) control rats; arrow indicates time of injection of pneumococci. Abscissa, time (in days); ordinate, content of adrenalin or noradrenalin (in μg/day/kg).

Fig. 2. Excretion of vanillyl-mandelic acid with urine of rats with experimental pneumococcal infection. 1) Rats infected with pneumococci; 2) control rats; arrow denotes time of injection of pneumococci. Abscissa, time (in days); ordinate, volume of urine (A: in ml/day) and content of vanillyl-mandelic acid (B: in μg/day/kg).

day after injection of pneumococci) changes in the catecholamine content were found in several organs: a decrease in the adrenalin content in the heart and the noradrenalin content in the heart, liver, and kidneys, with a simultaneous increase in the content of adrenalin in the kidneys and noradrenalin in the blood. These changes in the catecholamine levels were accompanied by their more intensive inactivation, reflected in increased excretion of adrenalin (by 2.5 times; $P < 0.1\%$) in the urine and an increase in the excretion of vanillyl-mandelic acid (by twice; $P = 2\%$) (Figs. 1 and 2).

With progressive development of the pneumococcal infection (2nd day) the catecholamine content in the heart, liver, and spleen was lowered but the excretion of adrenalin (by 11.5 times; $P < 0.1\%$) and of noradrenalin (by 3.7 times; $P < 0.1\%$) in the urine was sharply increased. The degree of inactivation of catecholamines was reduced and the excretion of vanillyl-mandelic acid was close to normal.

Toward the time of death of the animals from pneumococcal infection (3rd day), adrenalin accumulated in the blood, liver, spleen, and hypothalamus, and excretion of catecholamines in the urine was increased (by 1.5-2.5 times; $P = 1.3$ and 0.4%), while excretion of vanillyl-mandelic acid, the product of their metabolism, was decreased (by half; $P = 5\%$).

In the course of the pneumoccal infection, the quantitative ratio between noradrenalin and adrenalin (NA/A) in the urine was disturbed. NA/A in the urine of intact rats averaged 3.8 ± 0.6. After infection of the animals the value of NA/A fell on account of a greater increase in the adrenalin concentration in the urine: NA/A on the first day of the disease was 1.6 ± 0.2, on the 2nd day 1.2 ± 0.08, and on the 3rd day 1.5 ± 0.2. The decrease in NA/A in the urine of rats infected with pneumococci was statistically significant ($P = 0.6$, 0.1, and 0.5%) at all times of the disease.

The diuresis of rats infected with pneumococci was not significantly different from the diuresis of healthy rats.

Hence, during the development of pneumococcal infection in rats, a significant and lasting increase in the excretion of catecholamines in the urine is observed, reaching a maximum on the 2nd day of the disease.

At the height of the disease, accumulation of catecholamines in the body and an increase in their excretion in the urine are accompanied by a lowering of the intensity of their inactivation, as shown by a decrease in the excretion of vanillyl-mandelic acid. The increase in the catecholamine level in the animals under the influence of bacterial endotoxins can evidently be attributed to the depression of activity of enzyme systems catalyzing their inactivation in the body and an increase in the activity of enzyme systems participating in catecholamine biosynthesis. Indirect confirmation of this view was obtained by a number of investigators [1, 4, 7] in 1966-67 during the study of other infectious diseases.

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