EFFECT OF VIRUS INFECTION ON THE ISOENZYME COMPOSITION OF LACTATE DEHYDROGENASE IN MOUSE LIVER

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A032 influenza vaccine caused an increase in the content of the M type of lactate dehydrogenase (LDH) isoenzymes and a decrease in the fraction of the H-type in the liver of infected mice, in harmony with views regarding the depression of respiratory metabolism in the cells in influenzal infection. The greatest changes in the structure of the LDH isoenzyme spectrum coincided in time with the maximal development of the toxic manifestations in the mice. Preliminary injection of interferonogenic Newcastle disease virus into the mice reduced the effect of the influenza virus on the composition of LDH isoenzymes in the liver cells.

Lactate dehydrogenase (LDH; EC 1.1.1.27) isoenzymes of the H type are adapted for aerobic, and those of the M type for anaerobic metabolism in the cell [5, 8, 9]. Correlation has been established between the intensity of respiratory metabolism and the composition of LDH isoenzymes in the cells of various tissues [4, 6, 7]. The isoenzyme composition of LDH thus reflects the specificity of the energy metabolism of the cell.

Experiments in vitro [1] have shown that influenza virus stimulates the respiratory function of cells resistant to it and inhibits respiration in susceptible infected cells. The degree of inhibition of respiration depends on the virulence of the virus. Considering the different roles of the LDH isoenzymes in respiratory metabolism, it would evidently be useful to study the character of action of viruses, differing in their virulence and toxicity, on the LDH isoenzyme spectrum in cells of animal origin.

The object of this investigation was to study the isoenzyme composition of LDH in the liver of mice infected with a highly toxic strain of type A032 influenza virus and also with the Victoria strain of Newcastle disease virus (NDV), which does not cause appreciable toxic manifestations in mice.

EXPERIMENTAL METHOD

Albino mice weighing 16-18 g were used. Influenza or toxemia was produced by intravenous injection of 1 ml (10^8 EID_{50}) of A032 influenza virus. Resistance to the toxic action of the virus was produced in the mice by induction of endogenous interferon by intravenous injection of 0.5 ml allantoic NDV with a titer of 10^8 $TCID_{50}$ 24 h before injection of the influenza virus. Mice receiving the interferonogen (NDV) only also were used in the experiments. The animals were decapitated 6, 24, and 48 h after injection of the viruses.

The liver was rinsed to remove blood and homogenates prepared from it in physiological saline (1:3 w/v) were centrifuged at 800 g for 10 min. The supernatant was treated with an equal volume of a 0.5% solution of Triton-X-100 made up in 0.1 M potassium phosphate buffer, pH 7.4; the suspension was kept at 4°C for 1 h and then centrifuged for 20 min at 12,000 g. The isoenzyme composition of LDH in the super-

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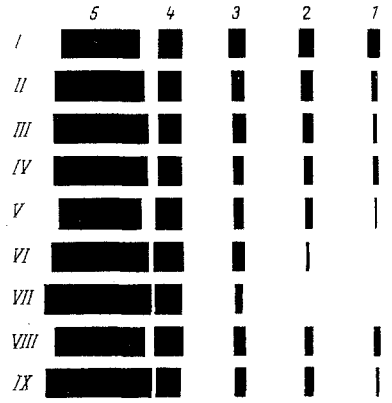

Fig. 1. Composition of LDH isoenzymes in liver of mice infected with influenza and Newcastle disease viruses. 1-5) Relative percentages of five isoenzymes respectively. I) Normal; II-IV) injection of NDV and decapitation 6, 24, and 48 h later, respectively; V-VII) injection of A032 and decapitation 6, 24, and 48 h later, respectively; VIII, IX) injection of NDV + A032 and decapitation 24 and 48 h later.

natant was determined by disc electrophoresis in polyacrylamide gel. The conditions of electrophoresis and the methods used for staining and densitometry and for determination of protein after electrophoresis were described previously [2].

EXPERIMENTAL RESULTS

Five LDH isoenzymes were clearly detected in the liver of the intact mice (Fig. 1). They were present in the following relative percentages: LDH_1 7.5 ± 0.4, LDH_2 10 ± 0.55, LDH_3 10.5 ± 0.6, LDH_4 16 ± 0.9, LDH_5 56 ± 2.7. Injection of NDV into the animals led to a decrease in the content of the H type of isoenzymes (LDH_1, LDH_2) and to an increase in the LDH_4 and LDH_5 fractions. These changes were significant 6 h after injection of NDV. The clearest changes in the spectrum occurred after 24 h and they still persisted after 48 h (Fig. 1). A032 influenza virus had a more marked action, although analogous in character, on the isoenzyme composition of LDH. The content of the LDH_1 fraction in the liver cells was sharply reduced 6 h after infection of the mice with influenza virus. This fraction could no longer be detected after 24 h, while after 48 h the LDH_2 fraction had disappeared and the content of the LDH_3 fraction, containing equal numbers of M and H subunits, was reduced by 2.5 times compared with the control.

Changes in the LDH isoenzyme spectrum in the mouse liver toward an increase in the content of "anaerobic" and a decrease in the content of "aerobic" forms of the enzyme, produced by influenza virus and NDV are thus in harmony with view regarding the inhibition of respiratory metabolism in the liver during virus infection. Differences between the action of the two viruses were purely quantitative: the highly toxic influenza virus caused more severe disturbances of the LDH spectrum. It is important to note that the greatest changes in the isoenzyme composition of LDH, occurring 48 h after injection of A032, coincided in time with the maximal development of the toxic manifestations in the mice during influenzal infection [3]. Changes in the respiratory function of the cells are evidently linked both with reproduction of the virus in sensitive cells and with the toxic action of the virus on the body as a whole.

The diminution of the effect of A032 virus on the LDH isoenzyme spectrum if injected 24 h after NDV (Fig. 1) can be explained by the protective action of NDV against viral toxicosis.

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