THE POSSIBLE ROLE OF RIBONUCLEIC ACID IN THE MECHANISM OF RESISTANCE TO TUBERCULOSIS

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A number of reports have appeared in the last few years in the Soviet and foreign literature which deal with nucleic acid metabolism in tuberculosis. A. Ya. Fridenshtein [1], S. Vasilescu et al. [5], B. Sher et al. [4] employed histochemical analytical methods to show an increase in the content of ribonucleic acids (RNA) in the tissues of guinea pigs affected by tuberculosis and vaccinated with BCG. O. G. Shchepetil'nikova [2] found an acceleration of replacement of nucleic acid phosphorus in the liver of tuberculous guinea pigs.

The experimental animals used in all of the research cited were guinea pigs – animals sensitive to tuberculosis. Definite interest would exist now in a comparison of the nucleic acid metabolism in the tissues of animals which vary with respect to immunity to tuberculosis, in the event of tuberculosis infection or BCG immunization.

METHOD

Experiments were carried out on white mice and guinea pigs. These animals were selected because of the difference in their resistance to tuberculosis.

The animals were immunized by administration of 1 mg of BCG vaccine (subcutaneously in the mice and intracutaneously, in the guinea pigs). The 109 (bovine) strain BK was employed for infection. The mice were infected intravenously with 0.1 mg of the culture, the guinea pigs, subcutaneously, with 0.005 mg BK in the first series of experiments and with 0.015 mg in the second series. In each test series, the mice or the guinea pigs were separated into three groups: infected, immunized and control. The infection and immunization were carried out on the very same day. To measure the RNA content in the liver and lungs the animals were killed 3-5 days after the immunization and infection and then about every ten days for a period of 2-2½ months. Controls were put to death at the same time as the experimental animals. In the first series in all three groups, two animals were examined (parallel tests). In the second series, to lessen the influence of individual fluctuations on the results, each of the two parallel tests used liver or lung sections from three mice or two guinea pigs. The mice in the first series of tests were decapitated. But,in the latter,hemorrhage was induced into the lungs of some of the animals which significantly distorted the results. Therefore, in the second series of tests, ether narcosis was chosen instead of decapitation. The guinea pigs in both series were killed by ether narcosis. The liver and lungs were rapidly removed from the killed animals and sections of the organs were homogenized by grinding in small mortars, in the cold. The separation of nucleic acids was carried out by the method of Schmidt and Thannhauser.[3] The RNA was determined by its phosphorus and recalculated to 1 g. of wet tissue.

RESULTS

Visible lesions in the organs examined were observed in the mice and in the guinea pigs, on about the 20th to 30th day after infection; in the mice, the lungs were affected, in the main (in the course of both series no macroscopically visible changes in the liver could be found); in the guinea pigs the liver was primarily affected, and it wasn't until the 40th day that macroscopic damages were observed in the lungs (scattered, non-fusing tubercles in insignificant amounts) which, even in the later periods, were significantly less sharply expressed than in the lungs of the mice.

The results of the examinations are presented in Figures 1 and 2 (in construction of the diagrams the content of RNA in the immunized and affected animals is referred to as the content of RNA in the control animals, killed at the same time, and is expressed in percents).

In comparing the effect of immunization on the content of RNA in the organs of the guinea pigs (see Fig. 1) and white mice (see Fig. 2) a quantitative difference only was found. In this group and in another group of animals, an increase in the quantity of RNA in the lungs and liver was observed, but in the mice it reached a much higher level (up to 33% in the lungs, up to 32% in the liver) and persisted up to the 50th day after immunization; in the guinea pigs this increase was not as strongly expressed (up to 16% in the lungs, up to 18% in the liver), was less stable and persisted 30-40 days after immunization. Infection had no visible effect at all on the content of RNA in the liver of both groups; the quantity of RNA fluctuated within the normal range, lessening only a little in the mice in the latter period – on the 60th to 75th day.

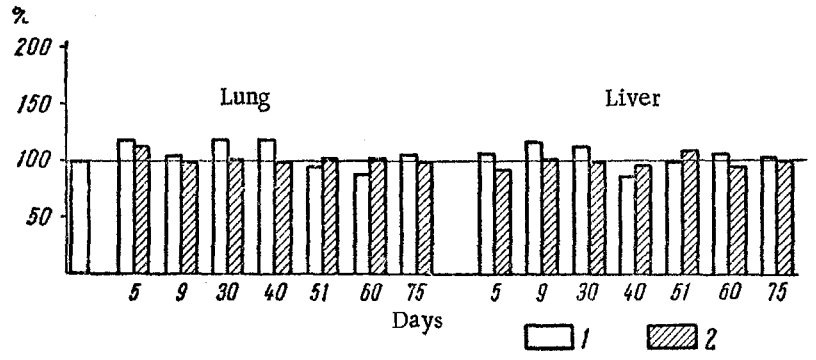

Fig. 1. Content of RNA in the lungs and liver of BCG-immunized and BK-infected guinea pigs, expressed in percents of control. 1) Immunized; 2) infected.

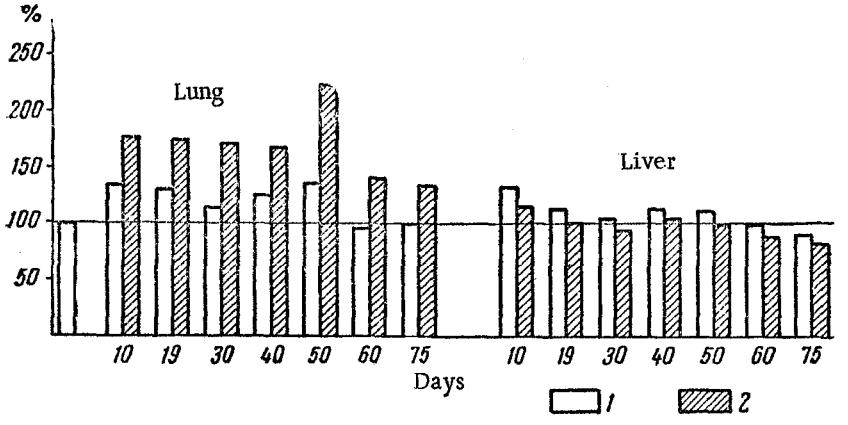

Fig. 2. Content of RNA in the lungs and liver of BCG-immunized and BK-infected mice, expressed in percents of control. 1) Immunized; 2) infected.

A comparison of the content of RNA in the lungs of the tuberculosis-infected white mice and guinea pigs gives quite another picture. In the lungs of the guinea pigs (see Fig. 1) the infection did not cause any deviation of the RNA level from the control, but in the lungs of the mice, a 73% rise in RNA was noted on the 10th day. The rise was stable and only toward the end of the test (after two months) was any tendency noted to a decrease in the content of the RNA.

Thus, in the affected organs of the guinea pigs – animals sensitive to tuberculosis, the quantity of RNA remained unchanged, but in the affected lungs of mice, which are comparatively resistant to tuberculosis, the content of

RNA was significantly increased*. The results obtained lead to the idea that an intensification of the synthesis of RNA (which in all probability, took place in those organs where the amount of RNA increased) is a link in the complex biochemical mechanism of resistance to tuberculosis. Judging from the direction of the shifts in the RNA level which we observed in immunized animals and in animals resistant to tuberculosis, when they are infected, we think that a common mechanism lies at the basis of natural and artificial immunity.

SUMMARY

The ribonucleic acid level in the lungs and liver of albino mice and guinea pigs proved to increase considerably under the effect of immunization with the BCG vaccine. Infection with a virulent tuberculosis strain provoked a considerable rise of the ribonucleic acid concentration in the lungs of albino mice relatively resistant to tuberculosis, whereas the organs of guinea pigs sensitive to tuberculosis exhibited a normal range of variations in the ribonucleic acid level. It is suggested that the rise of the ribonucleic acid level in the organs of the immunized animals and in the lungs of the infected mice is connected with the mechanism of artificial immunity and natural resistance to tuberculosis.

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*The absence of marked changes in the RNA level in the liver of infected mice is explained, apparently, by the fact that this organ was affected to only a slight degree by the tuberculosis.