

EFFECT OF STREPTOMYCIN ON RESISTANCE OF ALBINO MICE TO OXYGEN LACK

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We have been unable to find sufficiently conclusive data on the literature for the explanation of the rapid disappearance of toxic symptoms following administration of streptomycin to tuberculous patients. The effect cannot be explained on the basis of classical views on the bacteriostatic action of streptomycin on M. tuberculosis, as it is well known that the antibiotic acts only relatively slowly on these germs. A number of authors, mostly clinicians, consider that streptomycin, in addition to its antibiotic action, also exerts a certain action on the organism of the patient, and that this action is not only a toxic one, but also a beneficial one, contributing to the therapeutic action of this antibiotic.

This view is supported by the experimental results presented in this paper. We studied the effect of streptomycin on the resistance of the organism to lack of oxygen, which is incontestably a factor in the causation of a number of clinical manifestations of flare-up of tuberculosis.

EXPERIMENTAL METHODS

The experiments were performed on 212 albino mice, which were placed in a hermetically sealed chamber, in which they rapidly died of oxygen lack. The experimental method was worked out by V. A. Konstantinov [1], in V. S. Galkin's laboratory. Two mice of equal weight were taken for each experiment. One of the mice was given 5000 units of streptomycin intramuscularly, and after 40-50 minutes each mouse was placed into a wide-mouthed flask (capacity 145-146 ml), which was stoppered with a rubber stopper, and sealed with molten paraffin wax. The survival time of the mice was then noted.

In some of the experiments both mice were placed in a single flask of 340 ml capacity, which was sealed similarly, and the survival times were noted as before.

EXPERIMENTAL RESULTS

In the first series of experiments survival times were registered for mice placed in separate flasks. The results were found to depend on the weights of the animals.

In this group the weights varied from 17 to 19 g, and the mean survival time of the control group was 16 minutes 49 seconds. The test animals, receiving streptomycin, survived on the average 8 minutes 48 seconds longer than the test group, i. e., their survival time was 52.8% longer.

The mice of the second group weighed 20-29 g, and their mean survival time was 12 minutes 42 seconds in the control group, and 5 minutes 4 seconds longer in the test group, i. e., 39.8% greater.

For both groups together the mean survival time of the test group exceeded that of the control group by 46.3%. It may hence be concluded that streptomycin very considerably prolongs life under conditions of oxygen lack.

The result may be due either to depression of respiration by streptomycin, thus leading to a reduced oxygen uptake, or it may be that streptomycin raises resistance of the organism to oxygen lack, changing the threshold of sensitivity to hypoxemia.

A second series of experiments was carried out in order to elucidate these possibilities. In these the mice were placed together in a single flask.

In these experiments survival time was also found to be correlated with body weight.

In the first group the weights were from 17 to 19.5 g, and the mean survival time was 21 minutes 5 seconds for the control group and 13 minutes 16 seconds longer for the test group, i. e., 62.9% greater.

In the second group the animals weighed 23 g on the average. The mean survival times were 17 minutes 34 seconds for the control group (much shorter than for the first group), and 5 minutes 5 seconds longer in the streptomycin group, an excess of 28.7%.

Thus in this series too the survival time of the heavier test animals exceeded that of the controls by a smaller amount than for the lighter animals.

For both groups of animals of the second series the survival times of the test animals was 45.8% greater than for the control groups.

It follows from our experiments that mice receiving streptomycin are able to survive longer in an oxygen-deficient atmosphere than are the control mice. This is evidence that streptomycin raises resistance of the organism to oxygen lack. Since, however, the test animals of the second group of the second series survived the control animals by a shorter time than in the corresponding group of the first series of experiments, we have to consider a dual mechanism whereby streptomycin raises resistance of the organism to oxygen lack: (i) by lowering consumption of oxygen as a result of depression of respiration, and (ii) by raising resistance of the organism to oxygen lack.

Control experiments were also done on the effect of injecting distilled water, in the same volumes as the streptomycin injections. The survival time of the control group was 14 minutes 36 seconds, and of the test group 13 minutes 45 seconds, i. e., 51 seconds shorter. It follows that the differences in survival time found regularly for mice receiving streptomycin could not have been due to the effect of introducing the given volume of liquid.

It follows conclusively from the above experimental results that streptomycin has a very definite effect on the organism. It must be supposed that its property of raising resistance of the organism to oxygen lack is of significance in the mechanism of its therapeutic action in the treatment of tuberculosis.

LITERATURE CITED

- [1] V. A. Konstantinov, Mechanism of Pathological Reactions (Leningrad, 1949) Nos. 11-15, pp. 1-6.