EFFECT OF SMALL DOSES OF CAFFEINE ON THE DEVELOPMENT OF
EXPERIMENTAL TUBERCULOSIS IN WHITE MICE

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As shown in our previous investigation [1], excessive excitation of the central nervous system unfavorably
affects the development of experimental tuberculosis. In the present work we studied the effect of moderate
excitation of the central nervous system on the development of the indicated pathological process.

Such a condition can be produced with the help of caffeine injections. Prolonged administration of small
doses of caffeine, V. K. Fedorov points out, leads to increased excitability of the cerebral cortex and, through
induction, to an increase in internal inhibition and an increase in the mobility of the nerve processes [V. K. Fedorov, 2].

We studied the effect of small doses of caffeine on the course of experimental tuberculosis in 207 white mice
weighing from 17 to 20 g. Caffeine (0.05 mg for each mouse) was administered to part of them (89); subcutaneously
daily for 7 days prior to infection; caffeine was not administered to 86 mice, which composed the control group.
After 7 days, the experimental and control mice were infected intravenously with a culture of tuberculosis bacteria
(strain 109 of the bovine type) in a dose of 0.015 mg in 0.25 ml of physiological solution. Daily caffeine injections
of the experimental mice were continued until the 41st day from the time of infection. Then caffeine administration
was discontinued for 33 mice of the experimental group, since in the above-mentioned work of V. K. Fedorov it was
established that the effect of small doses of caffeine, administered for 40-45 days, remains during the subsequent
20 days.

Out of 34 which went into the second control group, 4 were killed before the beginning of the experiment as
a control over the original state of the internal organs. The effect of prolonged use of caffeine on the internal
organs was studied on the remaining 28 uninfected mice. Experimental and control mice were killed during the
course of the experiment, on the 6th, 18th, 24th, 30th, 41st, 50th and 60th day after infection, with 12-15 animals
in each group. The mice were weighed before autopsy. The lungs (together with the heart) and the spleen were
weighed and the coefficient of the weight of the organs was determined. At autopsy, the pathological anatomical
changes were found, evident as the appearance of greyish-yellow nodes in the lungs and as an increase in the size
of the spleen. Visible changes were not observed in the other internal organs.

Microscopic appraisal of the tuberculous changes in the lungs was made on the basis of a count of the
number and of a determination of the size of the tubercles.
EXPERIMENTAL RESULTS

Beginning on the 18th day after infection (macroscopically determinable changes were not evident at earlier periods) a difference was found in the number of tubercles formed in the lungs of animals in the control group. (Table 1). Thus, on the 24th day after infection, a considerable number of tubercles was found in 10 out of 13 control animals. At the same time, only in two cases out of 13 was a great number of tubercles found among the experimental animals. On the 24th, 41st and 60th day after infection, tubercles in greater numbers and of a greater size were found in the lungs of the majority of mice of the control group, while at the same times after infection, tuberculous changes in the lungs of the experimental mice were found in the form of single tubercles, and only in a few mice was a large number of tubercles found (*Table 1*).

During the period from the 41st to the 60th day of illness, when the caffeine infections were stopped, a large number of tubercles was discovered in the lungs of part of the experimental mice: in 5 case out of 15 by the 50th day, in 4 animals out of 18 on the 60th day after infection. At those same times, pathological anatomical changes in the lungs of the control animals were incomparably more evident.

| Time of observation (in days) | Control | | | | | Experiment | | | |
| - | number of mice | - | + | ++ | +++ | number of mice | - | + | ++ | +++ |
| 6 | 1 | 1 | - | - | - | 11 | 11 | - | - | - |
| 18 | 10 | 5 | 3 | 2 | - | 12 | 10 | 2 | - | - |
| 24 | 13 | 1 | 2 | 4 | 6 | 13 | 3 | 8 | 2 | - |
| 30 | 10 | 1 | 5 | 3 | 1 | 10 | 2 | 1 | 4 | 3 |
| 41 | 11 | - | 1 | 1 | 9 | 10 | - | 6 | 4 | - |
| 50 | 14 | 6 | 5 | 1 | 2 | 15 | 3 | 6 | 1 | 5 |
| 60 | 17 | 3 | 2 | 3 | 9 | 18 | 1 | 13 | - | 4 |

Symbols: - absence of tubercles, + single tubercles, ++ small number of tubercles, +++ large number of tubercles.

The results of the experiment on all autopsy days were as follows: a large number of tubercles were found in the lungs of 27 out of the control group of 86 mice, single tubercles were found in 18 cases. Single tubercles were observed in the lungs of 36 mice out of 89 experimental animals. A large number of tubercles was observed in only 12 observations (Fig. 1).

![Fig. 1. Number of tubercles in the lungs of mice of the control (a) and experimental (b) groups.](image-url)