

## BLOOD COAGULATION INDICES IN RABBITS VACCINATED WITH BCG

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The blood clotting system plays a definite part in the development of immunity to certain infectious diseases, possibly including tuberculosis [1]. This has led to the study of certain indices of the blood clotting system in experimental animals vaccinated with BCG. Only isolated reports on this subject are to be found in the literature. A. M. Khoma-Lemishko [2], for example, discovered that after vaccination of animals with massive doses of BCG the total serum protein concentration rose on account of the globulin fraction, while the prothrombin time remained essentially unchanged.

### EXPERIMENTAL METHOD

Experiments were conducted on 14 male chinchilla rabbits, 6 of which acted as controls and 8 were vaccinated intradermally with dried BCG vaccine in a dose of 10 mg, made up in 0.2 ml physiological saline. The following indices were studied in the experimental and control animals: the clotting time of the blood by the Lee-White method, the recalcification time (by the method of Beregelhof and Rock, modified by Baluda), and the prothrombin time and plasma fibrinogen concentration by the method adopted by the Leningrad Institute of Blood Transfusion.

The selected indices were determined four times before vaccination and on the 3rd, 9th, 15th, 30th, 45th, 60th, 75th, 90th, 105th, and 120th day of the experiment in both immunized and control rabbits. The mean values of each of the blood clotting indices at all times of the investigation were compared with controls. The difference between the two values was regarded as significant if its probability ( $\alpha$ ) exceeded 95%.

### EXPERIMENTAL RESULTS

The clotting time of the blood underwent considerable changes after vaccination. On the 3rd and 15th day of the experiment, for instance, it fell from the control level by 40-55 sec, which was statistically significant ( $\alpha = 96.0$  and 97.7%). Conversely, on the 60th day it had risen by 70 sec, also significantly ( $\alpha = 99.0\%$ ).

As regards the recalcification time, characterizing the first phase of coagulation of the blood, during the period of immunization no significant change took place in its value until the 60th day of the experiment, when it had fallen by 53 sec ( $\alpha = 99.1\%$ ). Hence the clotting time of the blood and the recalcification time had changed in opposite directions on the 60th day after vaccination of the rabbits with BCG: the clotting time had increased and the recalcification time decreased.

Active immunization of the rabbits against tuberculosis also affected their prothrombin activity, characterizing the second phase of blood clotting. By the 3rd and 9th days after vaccination, for instance, the prothrombin time showed a clear tendency to fall ( $\alpha = 92.1$  and 92.1%). On the 15th day of the experiment it had fallen by 4 sec, which is statistically significant ( $\alpha = 98.7\%$ ). Two months after vaccination the prothrombin time had changed in the opposite direction: it had increased by 6 sec ( $\alpha = 96.7\%$ ), but on the 90th day of the experiment this index again showed a significant fall - by 7 sec ( $\alpha = 98.9\%$ ).

Comparison of the mean values of the plasma fibrinogen concentration in the rabbits of the experimental and control ground showed that by the 9th day of the experiment this index had increased in the vaccinated animals by 39 mg% ( $\alpha = 98.7\%$ ). A tendency for the fibrinogen concentration to be raised over the control level was also observed 2 months after vaccination, although the probability that the difference was significant had fallen to 93.8%.

On the 120th day of observation the fibrinogen concentration showed changes in the opposite direction: a significant fall of 124 mg% ( $\alpha = 98.6\%$ ). Consequently, after vaccination, the index characterizing the third phase of the coagulation of the blood also revealed changes.

It is clear from these findings that the changes in the indices of blood clotting in the rabbits immunized with BCG took place within a short time after vaccination. In the initial period of development of immunity to tuberculosis the clotting time and prothrombin time both changed in the same direction (both fell), thus demonstrating an increase in the general ability of the blood to coagulate. During the same period the fibrinogen concentration rose, while there was no significant change in the recalcification time. By the 60th day of observation the changes in the recalcification and prothrombin times were in the same direction (both had fallen), while the fibrinogen concentration maintained its tendency to increase. The clotting time was increased on the 60th day of the experiment.

The impression was created that during the first 2 months after BCG vaccination of rabbits the coagulability of the blood showed a tendency to increase. To some extent the changes in the indices of blood clotting discovered in the later periods of observation were opposite in character. For instance, on the 90th day after vaccination the prothrombin time was raised, while on the 120th day the fibrinogen concentration was lowered, reflecting on the whole a decrease in the general ability of the blood to coagulate.

#### SUMMARY

Determination was made of the blood coagulation time, recalcification time, prothrombin time and fibrinogen content in the plasma of 8 BCG-vaccinated rabbits and 6 control animals. On the 3rd-15th days after vaccination changes occurred in the blood coagulation indices of the immunized animals. During the initial immunization period (up to 6th observation day) there was a reduction of the blood coagulation time and prothrombin time, whereas the initially increased fibrinogen content began to drop, without however reaching the control figures. Consequently, there is a tendency for a rise in the total blood coagulation capacity at the initial period of immunity production. On the 90-120th experimental days the blood coagulation capacity proved to be reduced as indicated by a decreased fibrinogen content and a rise in prothrombin time.

#### LITERATURE CITED

1. A. A. Bagdasarov, I. L. Chertkov, and M. O. Raushenbakh, The Properdin System of the Organism [in Russian], Moscow (1961).
2. A. M. Khoma-Lemishko, Problems in the Prophylaxis and Therapy of Tuberculosis [in Russian], p. 41, L'vov (1958).

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.

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