

THE EFFECT OF TUBERCULOSIS ANTIGEN ON THE BLOOD OF ANIMALS

COMMUNICATION III

FORMATION OF THE CONDITIONED LEUCOCYTIC REFLEX TO TUBERCULOSIS ANTIGEN ADMINISTRATION

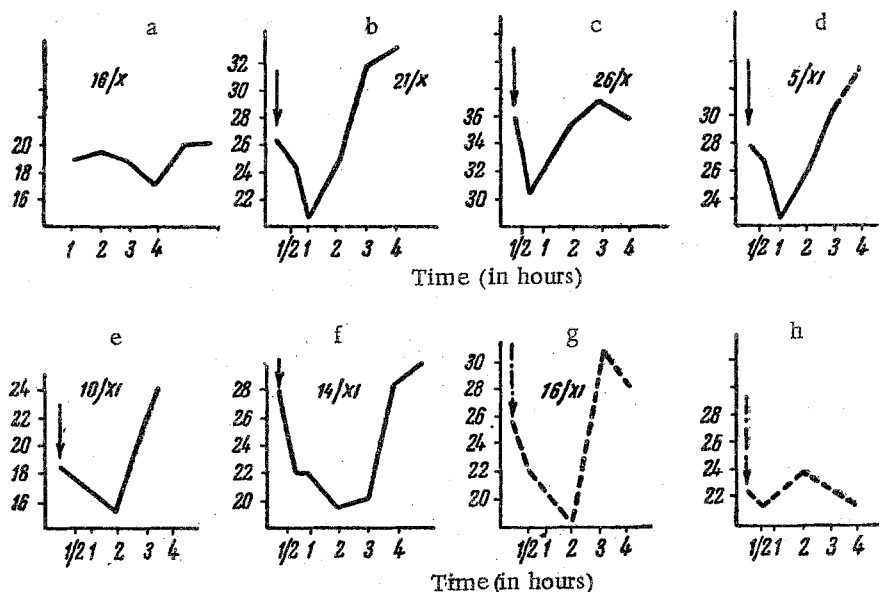
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The basic problem of the research which we carried out was the study of the peculiarities of the neural regulatory system of the blood during tuberculosis.

In the previous investigation of healthy cats [8] it was shown that parenteral administration (into the thigh muscle of a hind limb) of tuberculosis antigen (tuberculin, BCG culture) produced distinct reflex changes in the leucocytic portion of the peripheral blood. To be exact, it was established that tuberculin administered into the thigh muscle of a healthy cat causes a decrease in the number of leucocytes in the peripheral blood.



Development of conditioned tuberculin reflex. Cat No. 2.

a) Changes in the number of leucocytes in the course of a day without administration of the stimulus; b), c), d), e), f) leucocytic reaction to injection of 1 ml of whole tuberculin (↓) into the thigh muscles of the hind limb; g), h) leucocytic reaction to injection of 1 ml of physiological solution (↓) into the thigh muscles of the hind limb.

The leucopenic phase of the reaction lasts 2-3 hours and is then replaced by a gradually increasing leucocytosis.

During administration of tuberculin simultaneously with Novocaine, and also during injection of tuberculin into a limb with all afferent nerves severed, the characteristic leucocytic reaction to tuberculin was absent; this indicated the natural-reflex nature of the described phenomenon.

These experiments showed that tuberculosis antigen is a stimulant of the nervous system. In connection with this, one more question remained to be solved: could the impulses from the receptors of the extremity, arising in connection with the action of tuberculosis antigen, reach the higher areas of the brain and produce changes in the content of the peripheral blood by this means also. For this purpose, it was necessary to develop a conditioned leucocytic reflex to the parenteral administration of tuberculin, combining repeated administration of tuberculosis antigen with any indifferent stimulus. It is known from the literature that the development of a conditioned leucocytic reflex to various kinds of stimuli is possible [1-7].

EXPERIMENTAL METHOD

We developed the conditioned leucocytic reflex to tuberculin in 5 healthy cats while maintaining strictly identical experimental conditions: the experiments were carried out in the same room by the same person. Tuberculin, which was administered in the quantity of 1 ml into the thigh muscle of a hind limb, alternating between the limbs, was used as the natural stimulus.

Blood was taken from the ear for investigation before administration of the antigen and 1/2, 1, 2, 3, 4, and 5 hours after the injection.

All the setting of the experiment and all the manipulations, as well as the prick and the injection of physiological solution into the thigh muscles of a hind limb, served as the conditioned stimulus.

Before initiation of the experiments, the background was determined: "spontaneous" fluctuations in the number of leucocytes in the peripheral blood in the course of a day. Usually they did not exceed 2,000 leucocytes per 1 mm³. 40 experiments were carried out; 6-7 observations were carried out in each, a total of 244 blood tests.

EXPERIMENTAL RESULTS

According to our previous data, the prick and the injection of physiological solution did not cause substantial changes in the number of leucocytes in the peripheral blood. In the present investigation, for example, cat No. 2 had 22,450 leucocytes before injection of 1 ml of physiological solution, 30 minutes after its administration — 21,750, after one hour — 22,250, after 2 hours — 23,750, after 3 hours — 22,500, and after 4 hours — 19,200.

In response to the unconditioned reflex stimulus — injection of tuberculin at intervals of 5, 8, and 10 days, we always observed the same type of leucocytic reaction, characteristic of tuberculin and described above.

After 4-5 repeated injections of tuberculin into the thigh muscles physiological solution was administered. In response to the action of a single conditioned stimulus, the same leucocytic reaction that occurred on injection of tuberculin (see diagram) took place in all 5 cats.

The data of the basic experiments are shown in the table.

As the table shows, in response to the injection of tuberculin, the number of leucocytes decreased by 23.9%-40% (an average of 30.2%) in comparison with the background in all the cats. Later, their number increased to the original level or higher. In experiments using a conditioned stimulus, the number of leucocytes decreased considerably also — by 17.4-28.2% (by an average of 22.5%).

From the data presented here, it follows that repeated parenteral administration of tuberculosis antigen (tuberculin) leads to the development of a conditioned reflex.

One of the proofs of the participation of the cerebral cortex in the reactions under study is the possibility of diminishing them and then reestablishing them by reinforcement with the natural stimulus — tuberculin.

No. of animal	Stimulus	Time of determination						
		before injection	after injection					
			30 minutes	1 hour	2 hours	3 hours	4 hours	5 hours
1	Tuberculin Physiological solution	19 700	15 000	15 050	16 200	18 600	24 900	—
		19 300	15 000	13 850	14 750	18 700	21 200	23 100
2	Tuberculin Physiological solution	27 550	21 800	21 850	19 500	20 250	28 650	33 400
		25 550	22 300	20 800	18 700	30 200	27 400	—
3	Tuberculin Physiological solution	30 250	21 450	20 200	30 300	33 500	31 400	—
		28 300	23 750	23 350	26 350	36 250	31 000	—
4	Tuberculin Physiological solution	22 100	15 700	15 700	14 450	13 250	23 800	—
		16 300	15 750	14 250	12 700	15 250	19 500	—
5	Tuberculin Physiological solution	30 350	27 450	23 100	27 200	27 200	36 950	—
		27 700	26 350	22 600	29 000	33 250	34 950	—

The conditioned leucocytic reflex formed in this way was unstable and disappeared after repeated administration of the conditioned stimulus alone. After 2-3 reinforcements with the natural stimulus, the conditioned reflex to administration of physiological solution was reestablished anew.

On the basis of the investigations which were carried out, it can be concluded that impulses from the peripheral receptors, arising under the influence of tuberculosis antigen (tuberculin), can reach the cerebral cortex. The conditioned reflex which was formed could reproduce the natural one, although it was very unstable in our experiments.

The facts which were established are an additional confirmation of the possibility of reflex influence on the blood by the metabolites of the tubercle bacillus.

LITERATURE CITED

- [1] Belenky, G. S., *Klinicheskaya meditsina*, 1950, No. 9, p. 52.
- [2] Voronov, A., and Riskin, I. *Russkaya Klinika*, 1925, V. III, No. 12, pp. 482-513.
- [3] Gartsshtein, N. G., and Schastny, A. I., In the book: Abstracts of Reports of the 7th Conference on the Problems of Higher Nervous Activity, Dedicated to the Memory of I. P. Pavlov, (Leningrad, 1940), pp. 23-24.
- [4] Ilyin, I. I., Materials for the Study of the Reflex Mechanism of Leucocytosis. (Author's abstract of dissertation), Leningrad, 1951.
- [5] Kiseleva, S. K., *Klinicheskaya meditsina*, 1951, No. 9, pp. 43-45.
- [6] Malysheva, K. G., in the book: Mechanisms of Pathological Reactions, 1950, Chptrs. 16-20, pp. 353-359, Moscow.
- [7] Ulyanov, M. I. *Klinicheskaya meditsina*, 1953, No. 9, pp. 52-56.
- [8] Shkolnikova, M. D., *Byull. eksperim. biol. i med.* 1952, Vol. XXXIV, No. 12, pp. 24-26; 1953, Vol. XXXV, No. 6, pp. 22-24.