ANALYSIS OF INTEROCEPTIVE REFLEXES IN EXPERIMENTAL TUBERCULOSIS

Article III

THE EFFECT OF TUBERCULIN UPON REFLEXES FROM THE CHEMORECEPTORS OF AN ISOLATED LOOP OF THE SMALL INTESTINE IN HEALTHY CATS

V. A. Strelets

From the Department of Experimental Pathology and Therapy (Head – Candidate of Medical Sciences, G. S. Kan), Leningrad Institute for Tuberculosis Research (Director – Prof. A. D. Semenov, Research Consultant, V. N. Chernigovsky, Active Member of the Academy of Medical Sciences, USSR)

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In works published earlier, we presented data regarding the effect of tuberculin on reflexes from carotid sinus receptors and from the mechanoreceptors of the internal gonads [1,2]. We established that the reflexes from the carotid sinus receptors on the blood pressure were more sensitive to the toxic effect of tuberculin on animal bodies than were the reflexes from the mechanoreceptors of the gonads. We suggested that this difference was caused by the fact that both the baroreceptors of the carotid sinus and the chemoreceptors of the carotid plexus participated in the reaction to pressure on the carotid artery.

The purpose of the present work was to prove the hypothesis that the reflexes from the chemoreceptors are less resistant to the toxic effect of tuberculin than are the more stable reflexes from the mechanoreceptors.

EXPERIMENTAL METHODS

The method we used consisted of perfusing an isolated loop of the small intestine. The experiments were done on cats under urethane anesthesia.

After the celiac cavity had been opened, the small intestine was freed, and a loop of it near Bauhin's valve 20-25 cm long was isolated from the rest of the intestine, immersed in a vessel with Tyrode's nutritive solution and heated to a temperature of 37°. A glass tube was inserted into the distal end of the isolated intestinal loop in order to remove the intestinal contents. Then the neurovascular plexus was freed from the surrounding tissues. The nerves entwining the artery were carefully freed, and the vein and artery ligated. All the surrounding tissues, including the mesenteric glands, were ligated. A cannula was inserted into the artery in order to introduce the previously heated, oxygenated Tyrode's solution. The solution was withdrawn through a cannula inserted into the vein. Therefore, the only way in which the isolated intestinal loop was still connected with the body was through the nerves.

The condition of reflex excitability of the chemoreceptors in the perfused portion of the intestine was determined by the blood pressure and respiration reactions which were effected by adding to the Tyrode's solution 1 ml of a nicotine solution (10^{-5}) or 1 ml of an acetylcholine solution (10^{-3}, 10^{-4}), and also by the temporary replacement of the oxygenated solution with a solution containing carbon dioxide.

The blood pressure in the carotid artery was recorded with a mercury manometer, and the respiration, by means of a Marey capsule, which was connected to the animal's trachea by a glass T-tube.

After a background of the original blood pressure and respiratory reflex reactions caused by the introduction of acetylcholine, nicotine or carbon dioxide into the intestinal perfusion current had been established, the animal was intramuscularly injected with tuberculin. Old Koch's tuberculin was injected in a dose of 4-10 ml

– 8-15 mg of a purified dry preparation diluted with 8-12 ml respectively of a physiological solution. A total of 18 experiments were done. In three experiments, the reflex reactions from the chemoreceptors in response to the three kinds of stimulants – acetylcholine, nicotine and carbon dioxide – were examined. In five experiments, they were activated by two stimulants – acetylcholine and nicotine or acetylcholine and carbon dioxide. In the other ten experiments, either acetyldholine alone or carbon dioxide alone were used as the stimulants. The reflexes from the bladder mechanoreceptors were also examined in three experiments. Such composite experiments made it possible to compare the effect of tuberculin on the reflex excitability of the basomotor and respiratory centers with the stimulants coming from different kinds of receptors under the same experimental conditions.

EXPERIMENTAL RESULTS

After the tuberculin injection, in 17 experiments the degree of the reflexes from the chemoreceptors on the blood pressure either decreased (by 14.2-87.5%), or the reflexes totally disappeared (5 experiments). Only in one experiment using carbon dioxide as the stimulant did the reflex on the blood pressure increase after the tuberculin injection by 22.2%.

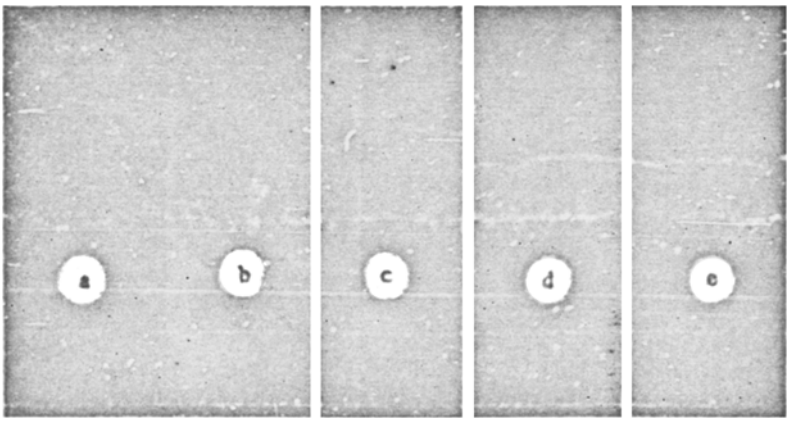

Fig. 1. Inhibition of reflex from small intestine chemoreceptors and sharp decline of average level of blood pressure after intramuscular injection of 9 ml of tuberculin, with the introduction of a 10^{-4} solution of acetylcholine.
a,b) original reflex; c,d,e) reflex after 10 minutes, 30 minutes and 1 hour following the injection of tuberculin. The curves from top to bottom signify: blood pressure, respiration, indication of stimulation, indication of time (in 5 second marks).

The decrease or disappearance of the reflexes most frequently occurred during the first 10-30 minutes after the tuberculin injection (in 14 out of 17 experiments). In 9 experiments, no greater inhibition of the reflexes from the chemoreceptors than that which occurred during the first 10-30 minutes was observed. The reflex either remained decreased to almost the same degree for the 1-$1\frac{1}{2}$ hour observation period after the tuberculin injection (Fig. 1) or increased, sometimes even reaching the original level. In 5 experiments out of 14, the reflexes which had decreased during the first 10-30 minutes after the tuberculin injection showed an even greater tendency to decrease during the subsequent observation (Fig. 2).

In 3 experiments out of 17, the reflexes from the chemoreceptors only became inhibited an hour after the tuberculin injection. Up to this time, the reflexes either remained the same as before the tuberculin injection or even slightly increased.

The arterial pressure level did not change much in the majority of experiments. A sharp decline of the average blood pressure was observed shortly after the tuberculin injection in only 2 experiments – 45% in both cases (see Fig. 1).

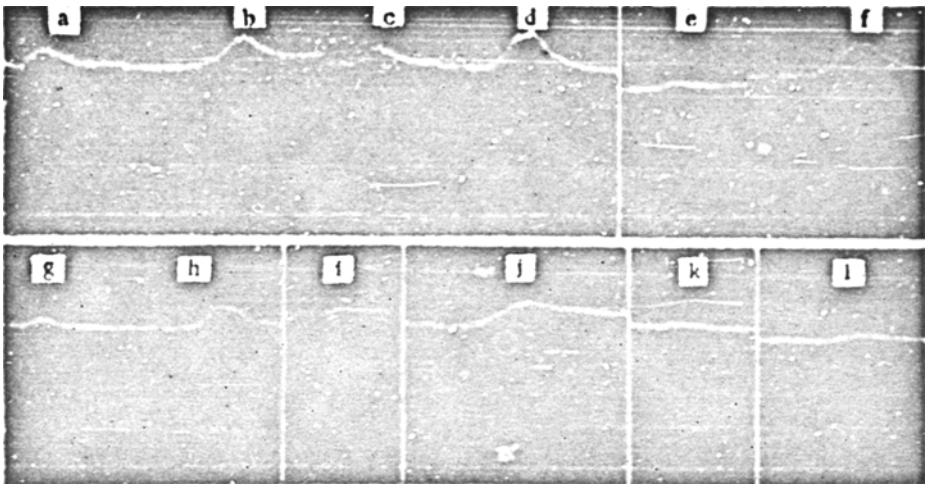

Fig. 2. Decrease in reflexes from the small intestine chemoreceptors after intramuscular injection of 4 ml of tuberculin.
a,b,c,d) original reflexes; e,f,g,h,i,j,k,l) reflexes after tuberculin injection; 1) with introduction of 10^{-4} acetylcholine; 2) with introduction of CO_2. The Curves are the same as in Fig. 1.

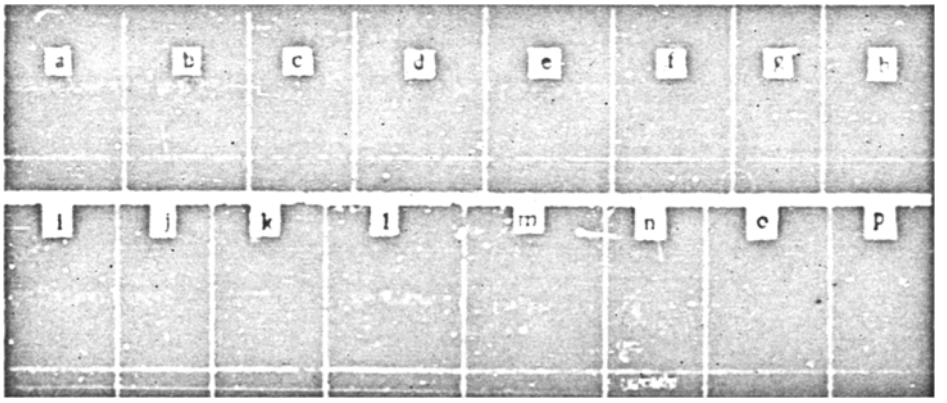

Fig. 3. Decrease of reflexes from small intestine chemoreceptors and increase of reflexes from bladder mechanoreceptors after injection of 5 ml of tuberculin.
a,b,c,d) original reflexes; f,g,h,k,l,n,o,p) reflexes from chemoreceptors after tuberculin injection; e,i,m) reflexes from mechanoreceptors after tuberculin injection. 1) reflexes from bladder when it was inflated under pressure of 90 mm of mercury; 2) with introduction of 10^{-4} acetylcholine; 3) with introduction of 10^{-5} nicotine; 4) with introduction of CO_2. The curves are, from top to bottom: blood pressure, respiration, indication of time (in 5 second marks), indication of stimulation.

In all of the experiments, the respiratory reflex reactions were either unchanged or very slightly inhibited.

The reflexes from the bladder mechanoreceptors increased in all 3 experiments in which they were examined after the tuberculin injection (Fig. 3) in contrast to the reflexes from the chemoreceptors.

The control experiments showed that the reflexes from the chemoreceptors, in 2 hours of observation, did not show such considerable oscillations as appeared after the tuberculin injection.

DISCUSSION OF RESULTS

The observations made from our first experimental series showed that tuberculin is far from inert in relation to the interoceptive reflexes. The most characteristic effect of tuberculin was that it first inhibited the reflexes from the chemoreceptors. This appeared most distinctly in the perfusion experiments on the intestine, as well as in the experiments with the carotid body reflex, which, with our method of stimulation, depended on stimulation of both the baroreceptors and the chemoreceptors. The effect of tuberculin on the reflexes from the bladder mechanoreceptors was much less inhibitory. This fact, we believe, indicates that tuberculin has an inhibiting effect on those central nervous elements in the afferent part of the reflex arc which are connected with the tissue chemoreceptors. This effect could not have been produced by the direct action of tuberculin on the chemoreceptors, as we know to be possible from the experiments of E. A. Levtova [3]. In our experiments, the reflex from the chemoreceptors was reproduced from the perfused loop of the small intestine, which had no humoral relations with the body, and was therefore not subject to the direct influence of the preparation.

The effect described was evidently not connected with a direct inhibitory effect of tuberculin on the efferent part of the reflex arc (vasomotor center and connection of this with the heart and vessels) nor on the effector mechanisms (heart and vessels). The absence of such an effect was especially evident when, under the same experimental conditions, the reflexes from the chemoreceptors were compared with those from the mechanoreceptors, which comparison showed that the former were inhibited considerably by tuberculin, while the latter not only were not inhibited, but often even increased. Therefore, while the impulses from the chemoreceptors to the effector organs (heart and vessels) became blocked, the impulses from the mechanoreceptors proceeded freely.

Therefore, tuberculin, penetrating the brain, acts electively in the subcortical region on the central nervous elements entering the afferent route from the tissue chemoreceptors. We propose that this effect is not realized in the cerebral cortex, since the experiments were conducted under anesthesia.

The inhibitory effect of tuberculin on the reflexes from the chemoreceptors appeared with the use of doses far greater than those used for diagnostic purposes in people and animals. Therefore, one could assume that it was simply a question of the toxic effect of the preparation. This must be clarified in the event of possible misunderstandings. In the control experiments, conducted on 4 cats, it was shown that the doses we used in the experiments studying interoceptive reflexes (3-10 ml) could not be considered vitally toxic to the experimental animals. The intramuscular injection of as much as 25 ml of tuberculin into the cats, with or without anesthesia, did not cause death in the experimental animals either during the first hours of observation or during subsequent days. It may only be a question of the elective toxicity typical to any poison or pharmacological substance. If, in the dose we used, tuberculin had had simply a toxic effect on the body, then the reflexes would have disappeared from the mechanoreceptors as well as from the carotid sinus receptors. This, however, was not the case in our experiments. Therefore, the inhibitory effect of tuberculin on the reflexes from the chemoreceptors is a manifestation of the elective toxicity inherent in the subject stimulant.

SUMMARY

It was shown that in its common effect upon healthy cats, tuberculin first of all inhibits reflexes arising from the chemoreceptors. This effect was most marked in perfusion experiments on the intestine, as well as in experiments with the carotid sinus reflex. Inhibition of reflexes from mechanoreceptors of the urinary bladder was less marked. The assumption is made that in its general effect, tuberculin inhibits the central neural elements of the afferent section of the reflex arc associated with tissue chemoreceptors.

LITERATURE CITED

[1] V. A. Strelets, Byull. Eksptl. Biol. i Med., 1953, Vol. 36, No. 9, pp. 22-25.

[2] V. A. Strelets, Byull. Eksptl. Biol. i Med., 1953, Vol. 36, No. 12, pp. 34-37.

[3] F. A. Levtova, Byull. Eksptl. Biol. i Med., 1952, No. 7, pp. 35-39.