STUDY OF CHEMOCEPTION IN EXPERIMENTAL TUBERCULOSIS

PART II. MECHANISM OF RECEPTION OF TUBERCULOSIS ANTIGEN

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(Received September 19, 1953. Presented by V. N. Chernigovskii, Member of the Acad. Med. Sci., USSR)

In our studies on the effect of the toxin of the tuberculosis bacillus on the individual links of the interoceptive reflex arc we showed that tuberculin exerts a stimulation action on the interoceptors of the small intestine.

We have attempted in the present paper to show that the stimulating action of tuberculin on a loop of small intestine not in vascular connection with the organism is a result of stimulation of its chemoceptors, and to elucidate the mechanism of this effect.

EXPERIMENTAL METHODS

We performed 32 experiments on cats with isolated ileal loops, by Chernigovskii's procedure. The animals were anesthetised (intravenous urethane), and a section of ileum 20-30 cm in length was isolated and perfused with Ringer-Locke solution saturated with oxygen and maintained at 38-40°. The sensitivity of the chemoceptors was deduced from the strength of the reflex blood pressure and respiratory changes. The chemical stimulant (tuberculin and nicotine) was injected into the perfusion fluid stream. Stimulation of receptors by carbonic acid was effected by substituting Ringer-Locke solution saturated with carbon dioxide for the oxygenated fluid.

EXPERIMENTAL RESULTS

According to present-day concepts, stimulation of chemoceptors depends on biochemical metabolic processes which are initiated by the action of the chemical stimulant. Our earlier results [1], which showed that the nature of interoceptor reflexes changes when the chemoceptors of the small intestine are subjected to the prolonged action of tuberculin, provided evidence that the stimulatory action of tuberculin was related to its effect on tissue metabolism.

Two series of experiments were performed with the object of verifying this hypothesis. In these experiments sensitivity to tuberculin was tested under conditions of impaired tissue metabolism, due to the action of monoiodoacetic acid, an enzyme poison interfering with carbohydrate metabolism, and of mercuric chloride, which eliminates sulphydryl compounds from metabolism.

Monoiodoacetate was used as 0.01 N solution, 5 to 25 ml of which was introduced into the perfusion fluid. Sensitivity to tuberculin of the chemoceptors was then tested, and compared with that found under similar conditions with known stimulants, viz., carbonic acid, nicotine, and acetylcholine. Altogether 17 experiments were performed in this series.

The action of monoiodoacetate on small intestine chemoceptors is to evoke a marked pressor reaction and a sharp increase in frequency and amplitude of respiration. At the same time the stimulability of the

receptors falls appreciably. It is in most cases possible to observe a regular sequence in change in stimulability of the chemoceptors, consisting in lowering of sensitivity, transition from pressor to depressor reflexes, and in some cases, total abolition of reflexes.

Comparison of the reactions to tuberculin and to carbonic acid shows that the reflexes due to these stimulants acting on iodoacetate-poisoned intestine do not always change in the same way. In some cases the changes are parallel, but in most cases sensitivity to tuberculin persists longer, and is still retained after sensitivity to carbonic acid and other stimulants has disappeared. Thus in Exp. 123 the nature of the reflex to tuberculin is unchanged, whereas it is inverted with carbonic acid. In Exp. 122 all reflexes except that due to tuberculin have been abolished. In one experiment only (No. 166) is the reaction to tuberculin totally abolished, as well as to other stimulants (Fig. 1).

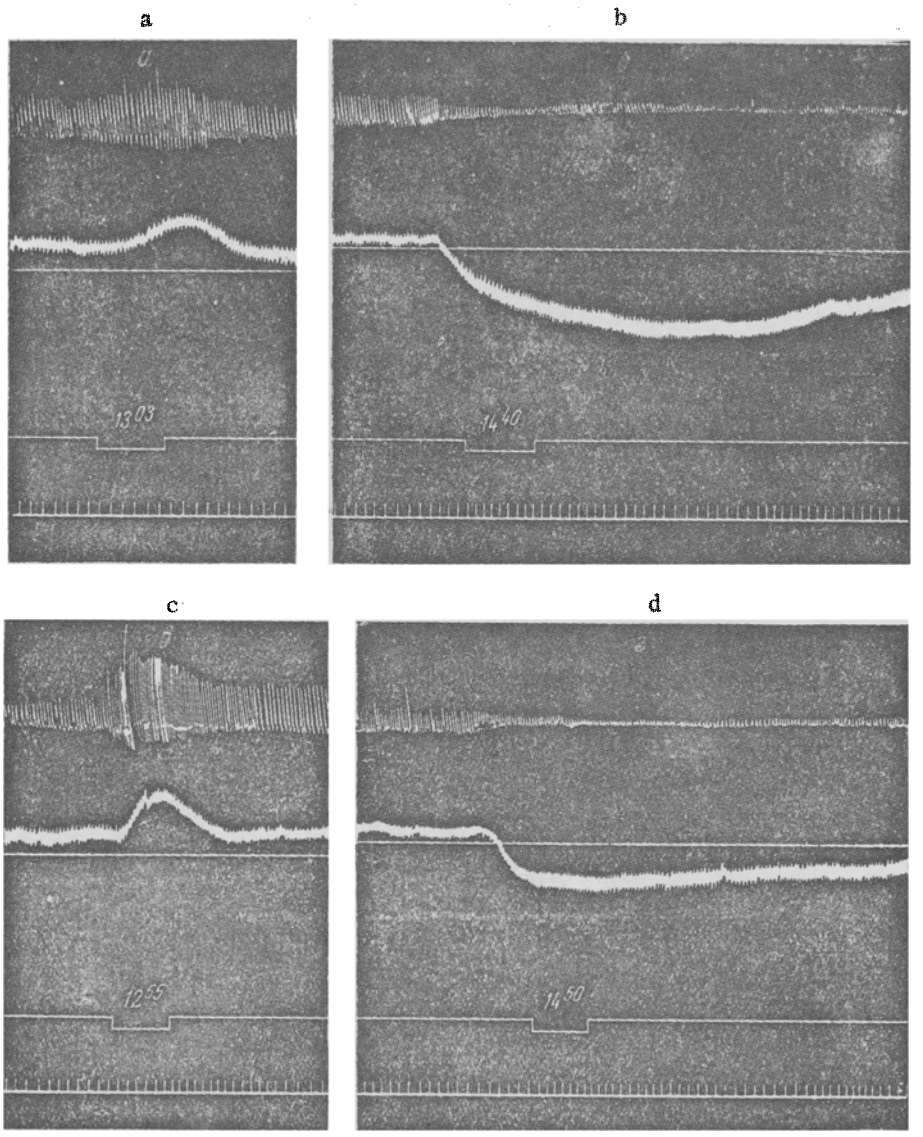

Fig. 1. Vasomotor and respiratory reflexes from ileal chemoceptors before and after perfusion of the blood vessels with a solution containing 5 ml of 0.01 N monoiodoacetate. a) reaction to tuberculin (1:50) before introduction of $CH_2I \cdot COOH$; b) inverted vasomotor reaction (from pressor to depressor) to tuberculin (1:50) after introduction of $CH_2I \cdot COOH$; c) reaction to carbonic acid before introduction of $CH_2I \cdot COOH$; d) inverted vasomotor reaction (from pressor to depressor) to carbonic acid after introduction of $CH_2I \cdot COOH$. Exp. 166. Explanation of tracings, from above down: respiration, blood pressure in the carotid artery, signal showing time and duration of stimulation, time base (5 seconds).

It might be thought from these experimental results that the mechanism of the stimulatory process initiated in the intestinal chemoceptors by tuberculin involves the participation of the latter in the carbohydrate metabolism of the tissues. They also suggest, however, the presence of some other mechanism by means of which tuberculin can also exert its stimulating action.

The differences between the mechanism whereby tuberculin and carbonic acid exert their stimulating action are also apparent in the second series of experiments, in which the effect of mercuric chloride on the sensitivity of the chemoceptors to these stimulants was studied.

We introduced 0.1% mercuric chloride in 5 ml portions into the perfusion fluid. This caused a marked fall in arterial (carotid) pressure. Subsequent introduction of all the stimulants showed that the sensitivity of the ileal chemoceptors was lowered.

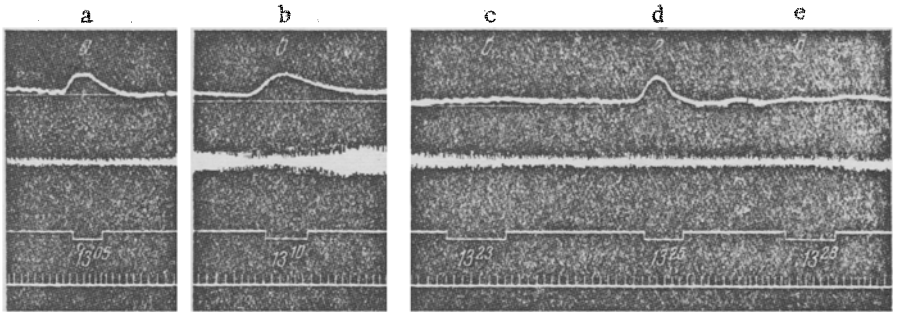

Fig. 2. Reflexes from ileal chemoceptors before and after perfusion of the blood vessels with a solution containing 5 ml of 0.1% mercuric chloride. Reaction to carbonic acid (a) before, (d) after perfusion with $HgCl_2$; Reaction to tuberculin (1:50) (b) before, (c), (e) after perfusion with $HgCl_2$. Exp. 155. Explanation of tracings (from above down): arterial (carotid) pressure, respiration, signal showing time and duration of stimulation, time base (5 seconds).

In contrast to the preceding series of experiments, sensitivity to tuberculin fell to a greater degree than to carbonic acid. The reaction was abolished earlier, and reappeared much later than for carbonic acid (Fig. 2).

Mercuric chloride, which combines with sulphydryl groups, affects the sensitivity of the chemoceptors to tuberculin in a different way, suggesting that the mechanisms of the stimulating action of tuberculin and carbonic acid are not the same.

It thus appears from the results of the two series of experiments that the mechanism of the stimulating action of tuberculin is connected with metabolic biochemical processes in the tissues in which the chemoceptors are situated. The experiments do not, however, indicate that there is more than a connection between the stimulatory action of tuberculin and metabolic processes of the chemoceptors. It is intended in further experiments to make a more profound study of the problem.

LITERATURE CITED

[1] F. A. Levtova, Bull. Exptl. Biol. Med., 1952, 7, 35-39.