

MICROBIOLOGY AND IMMUNITY

THE EFFECT OF ANTIGEN ON THE CAROTID SINUS RECEPTORS WITH REFLEX PRODUCTION OF ANTIBODIES PHARMACODYNAMICALLY ANALYZED

A. N. Gordienko, V. I. Kiseleva, B. A. Saakov,

I. M. Bondarev, and L. I. Zhigalina

From the Department of Pathological Physiology (Chairman: Prof. A. N. Gordienko),
Rostov State Medical Institute, Rostov-on-Don

(Received February 3, 1956. Presented by Academician A. D. Speransky)

In a previous study, we proposed a new method of isolating the carotid sinus. This method tests the completeness of isolation by the injection of radioactive phosphorus in large doses. The experiments conducted showed that the method we proposed guarantees complete isolation of the carotid sinus, so that radioactive phosphorus injected into the sinus does not appear in the blood. Having developed this method, we attempted once more to verify the possibility of the reflex production of antibodies; we showed that the injection of antigens into an isolated carotid sinus caused, as a rule, the production of antibodies. Antibodies were produced to the antigens injected into the carotid sinus, but did not form to antigens closely related to the antigen injected.

In the same investigation, we established that preliminary sectioning or ligation of the sinus nerve considerably reduces the production of antibodies, sometimes even eliminating it.

In this investigation, we decided to trace the production of antibodies by injecting an antigen previously treated with various substances into an isolated carotid sinus.

EXPERIMENTAL METHODS AND RESULTS

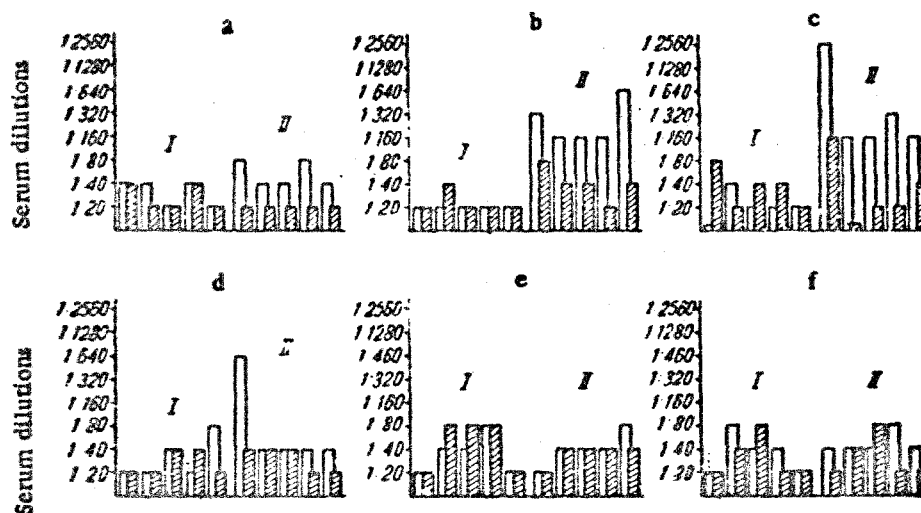
In the first series of experiments, the isolated carotid sinus was preliminarily treated with a physiological solution, and no antigens were subsequently injected. This experimental series showed the effect of operative intervention and of mechanically stimulating the carotid reflexogenic zone on the titer of antibodies present in the blood of each animal. In these and other experiments, we determined the titer of antibodies to the bacilli *Bact. typhi abdominalis* and *Bact. paracoli*. The experiments conducted on 5 dogs showed that the titer of antibodies remained practically the same under these conditions.

Therefore, one could affirm that operative intervention alone does not materially affect the titer of antibodies, which remains constant.

In further experiments, also on 5 dogs, we studied the effect of the preliminary action of sodium fluoride on the production of antibodies with the antigen injected into the isolated carotid sinus. The carotid sinus was isolated by our method and then treated with 5% sodium fluoride. Thirty minutes after repeated treatment of the carotid sinus with sodium fluoride, we injected the typhoid vaccine into the sinus. Seven days later, the titer of antibodies to the typhoid bacillus and to the paracollitis bacillus was determined. The experiments showed that the titer of antibodies to the typhoid bacillus had increased rather considerably. If the original titer of antibodies to the typhoid bacillus did not exceed a dilution of 1:20, then immunization increased the titer in two animals to 1:160, in one animal to a dilution of 1:320, and in the other two animals, to a dilution of 1:640; the titer to the paracollitis bacillus did not change in several cases, although it increased by one dilution in two cases.

These data suggest that preliminary treatment of the carotid sinus with sodium fluoride has no effect on the production of antibodies and, probably, that the action of the antigen on the receptors is not realized through change in the carbohydrate metabolism.

In a third series of experiments on 5 dogs, we studied the effect of Novocain on the reflex production of antibodies. The isolated carotid sinus was first treated with a 3% solution of Novocain, which, like the sodium fluoride, was injected into the sinus, where it remained for 20 minutes. After this, the Novocain was extracted and replaced by an injection of the typhoid bacillus. Subsequent determination of the titer 7 days later showed that preliminary treatment of the sinus with Novocain does not check the production of antibodies to the typhoid bacillus; in three animals, the titer of antibodies increased to dilutions of 1:160, in one animal it increased to a dilution of 1:320 and in the last animal it reached a dilution of 1:2560. There was no material change in the titer of antibodies to the paracollitis bacillus.



Change in the titer of antibodies with the antigen injected into a carotid sinus treated with various pharmacological substances.

a) Physiological solution, b) sodium fluoride, c) Novocain, d) Dicaine,* e) cocaine, f) Sovcaine; *I) original titer; II) after 7 days; white columns - Bact. typhi abdominis; striped columns - Bact. paracoll.

The results we obtained showed that the preliminary injection of Novocain does not materially affect the reflex production of antibodies. This is explained by the fact that Novocain in the concentration used has not the ability to cause terminal anesthesia and therefore, when injected into the sinus, did not materially affect the subsequent action of the antigen on the receptors.

Having established this, we decided to use substances causing surface analgesia. Among these are cocaine, Dicaine and Sovcaine.

In one series of experiments, we isolated the carotid sinus in the animals and then injected a 3% solution of Dicaine into it. Fifteen minutes later, the Dicaine was withdrawn, and the typhoid bacillus vaccine, diluted with Dicaine, was injected into the sinus. The results showed that the titer of antibodies increased to a dilution of 1:640 in only one animal, remaining the same in two animals, while in the fourth animal, the titer was reduced, and, in the last case, it increased by one dilution. The titer of antibodies to the paracollitis bacillus was almost unchanged.

This data indicates that, in an absolute majority of cases, preliminary treatment of the sinus with Dicaine checked the subsequent antibody production in the majority of animals. The increase in the titer of antibodies which occurred with one animal we believe to be due to the fact that the carotid sinus receptors were insufficiently anesthetized.

* Russian trade name.

We studied the effect of anesthetizing the carotid sinus receptors with cocaine on 5 animals. In these cases, the sinus was isolated by the method described above, and then 5% cocaine was injected into its cavity. Twenty minutes later, the cocaine was withdrawn, and the typhoid vaccine, diluted with a solution of cocaine, was injected into the sinus. In 4 of the 5 animals of this experimental series, the titer of antibodies in the blood was completely unchanged, and in the other animal it increased to a dilution of 1:80 (the titer of antibodies to the paracolitis bacillus also increased in this animal). Therefore, cocaine, like Dicaïne, in the majority of cases checks the production of antibodies caused by the action of antigens on a carotid sinus anesthetized by these two substances. Cocaine is known to cause blood vessels to constrict and, therefore, causes the capillaries along the nerve to contract when injected into the carotid sinus.

In order to exclude this possibility, we used Sovcaine in the next experimental series, as it does not cause capillaries to contract, but rather has the ability to dilate them. In this series, as in the others, we isolated the carotid sinus and then injected 5% Sovcaine into it; 15-20 minutes later, the Sovcaine was withdrawn, and the typhoid vaccine, diluted with the same solution of Sovcaine, was injected into the sinus. Seven days later, we determined the titer of antibodies in these animals and found that there was no increase in the titer of antibodies, except for an increase of one dilution in some animals which can be discounted, since a similar change had also been observed in the control experiments. Nor did the titer of antibodies to the paracolitis bacillus change. Therefore, the carotid sinus receptors lose their sensibility when preliminarily treated with Sovcaine and do not react to antigenic stimulation. The result of this is that the antigen injected into the isolated carotid sinus does not cause the titer of antibodies to rise.

All our experiments show that operative intervention and the action of a physiologic solution on the receptors of an isolated carotid sinus do not materially change the titer of antibodies, although the titer did increase by one dilution in some animals. Nor does treating the sinus receptors with sodium fluoride affect the reflex production of antibodies. The titer of antibodies increased in these animals to the same extent as in the animals not preliminarily treated. The action of Novocain on the carotid sinus receptors has little effect on the reflex production of antibodies; the receptors treated with Novocain remain sensitive to antigenic stimulation, and the action of the antigen causes increased production of antibodies. This is explained by the fact that Novocain does not cause terminal anesthesia in the concentration we used.

A completely different picture was observed when the receptors of an isolated carotid sinus were treated with Dicaïne, cocaine and Sovcaine — substances which, in the concentrations we used, could definitely cause terminal anesthesia. The receptors treated with these substances lost their sensitivity to antigens. The subsequent injection of the antigen into the isolated carotid sinus did not cause the titer of antibodies to increase (see Figure).

The data obtained further convince us that the action of antigens on the carotid sinus receptors causes the reflex production of antibodies.

All this further confirms the part of a reflex mechanism in the production of antibodies from the carotid sinus receptors.

SUMMARY

An operation of isolation of the carotid sinus with the following introduction of the physiologic saline into the carotid sinus has almost no effect on the titer of antibodies in the blood.

Preliminary treatment of receptors of carotid sinus by Novocain and by sodium fluoride does not change its sensitivity to the antigenic stimulation. Introduction of antigen on this background brings about production of antibodies, the titer of which reaches the same level as in antigenic stimulation without preliminary treatment by these substances.

Treatment of receptors of the isolated carotid sinus by cocaine, Dicaïne and Sovcaine causes disappearance of the excitability of receptors to the antigenic stimulation. Introduction of typhoid vaccine into the carotid sinus which had been treated by cocaine, Dicaïne and Sovcaine does not induce antibody production. The latter supports the view of the reflex mechanism of production of these antibodies.

LITERATURE CITED

- [1] A. N. Gordienko, V. I. Kiseleva, B. A. Saakov, I. M. Bondarev, E. I. Nekrashev, Byull. Eksptl. Biol. i Med., 1956, Vol. 42, No. 11, pp. 70-72.*

* Original Russian pagination. See C.B. Translation.