INTEROCEPTIVE CONTROL OF BLOOD COAGULATION

COMMUNICATION I. THE EFFECT OF REFLEXES FROM THE CAROTID SINUS CHEMORECEPTORS ON BLOOD COAGULATION

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Nervous regulation of blood composition was first suggested by S. P. Botkin in 1875. Exteroceptive influences on the process of blood coagulation have been established by many authors [6, 3, 2, 8]. Recently, A. A. Markosyan [4] has established the possibility of conditioned reflex change in the rate of blood coagulation.

Interoceptive regulation of the morphological composition of the blood has been examined in works by A. Lezner [9], V. N. Chernigovsky and A. Ya. Yaroshevsky [5] and others. Interoceptive regulation of the blood - coagulating system has not been investigated at all to date, unless the work of E. Perlik [11], studying the effect of reflexes from the carotid sinus pressoreceptors on certain aspects of blood coagulation, is counted, although the author did not treat coagulation as a whole.

Even before Perlik's article appeared, we had finished this present study, the purpose of which was to establish the possibility that blood coagulation is regulated by the reflexes from the carotid sinus chemoreceptors. The resolution of this question could shed some light on the pathogenesis and prophylactics of thrombo-embolic disease, which is now a question of real importance to practical medicine.

EXPERIMENTAL METHODS

24 experiments were done on dogs. The experiments were conducted under morphine-pentothal anesthesia. After tracheotomy, we began to prepare a preparation isolated vascularly, but with the nerve links of the carotid sinus angioreceptive field preserved by the method of Moiseev-Geimans-Anichkov. For this, all the vessels of the sinus region were ligated, while the nerve fibers were preserved and, as far as possible, left unharmed. A glass cannula was inserted into the peripheral end of the common carotid artery in order to introduce the Tyrode's solution, and a second, withdrawing cannula was inserted into the central part of the lingual artery. Perfusion was done at a rate of 50-60 drops per minute. The Tyrode's solution rinsing the sinus entered under 125 cm of water pressure, through a tube, into a coil placed in a water bath 38-40° in temperature: from the coil, the heated solution entered the sinus.

After the preparations were finished, the original rate of blood coagulation was determined before permanent results were obtained. Blood for examination was taken from the lower part of the femoral artery by our modification of Kennon's method. This method makes it possible to obtain fresh blood by means of paraffined cannulas without changing the properties of the blood and without the admixture of extraneous tissue elements, which occurs with the use of a hypodermic or pricking, which may alter the true rate of blood coagulation. The moment of the entrance of the blood into the cannula was recorded with a stopwatch; coagulation time was determined by Fonio's method.

After the original level of the blood coagulation rate had been determined, 0.25-2 ml of acetylcholine or nicotine, in dilutions of from 10^{-4} to 10^{-7} and preliminarily heated to the temperature of the perfusion fluid,

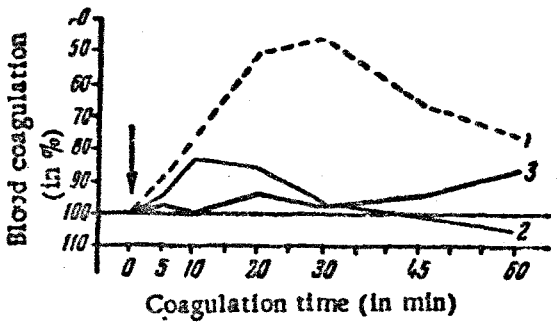
were introduced into the perfusion current (once, in some experiments, in others, two or three times). We gauged the preservation of the carotid sinus nerve links according to the reflex change in respiration, which was recorded on a kymograph tape.

The blood coagulation rate was again determined at intervals of 5, 10, 20, 30, 45, 60 and, in some experiments, 90 minutes after stimulation of the carotid sinus chemoreceptors.

EXPERIMENTAL RESULTS

In the first series of experiments, we examined blood coagulation after the nicotine and acetylcholine solutions had been introduced into the current perfusing the carotid sinus. Both stimulants gave approximately the same results. A more or less expressed shortening of blood coagulation time was observed in all cases. From the average curve shown in the graph, one can see that the coagulation time decreased by almost 50% after stimulation of the chemoreceptors. The greatest coagulation acceleration was obtained 20-30 minutes after stimulation and lasted about 1-1½ hours.

To prove the reflex character of the results we obtained, we conducted a second, control series of experiments with denervation of the carotid sinuses, in which the sinus nerve was cut, and the afferent part of the reflex arc thereby broken. In these experiments, no reflex change in the blood coagulation rate was obtained in response to the introduction of nicotine or acetylcholine into the perfusion current (see Figure).



Blood coagulation rate under different conditions: carotid sinus chemoreceptors stimulated with a solution of nicotine or acetylcholine (1), denervation of suprarenal glands (2), denervation of the carotid sinus (3).

In the same way, no change in the blood coagulation rate was observed with perfusion of the carotid sinus, with the sinus nerve intact, without the introduction of the chemical stimulants. As a rule, however, the coagulation time had gradually decreased by the end of the control experiment. This was evidently connected with the effect of the narcosis and the release of thromboplastin from the wounded tissues.

Starting from the works of Kennon [6], M. S. Klimova [3] and others, in which the influence of suprarenal gland adrenalin secretion on blood coagulation was shown, it was interesting to determine the importance of the adrenal system to the realization of the blood coagulation reflex from the carotid sinus chemoreceptors. For this purpose, the celiac nerves which are the secretory nerves for the suprarenals were transected under the diaphragm.

These experiments showed that, under conditions of suprarenal gland denervation, blood coagulation is very little affected by stimulation of the carotid sinus chemoreceptors, although this causes a marked respiratory reflex. In the experiments, blood coagulation time had decreased an average of 17.2% by the 10th minute, but then increased again, even exceeding the original level (by 4.7%, see graph) one hour after stimulation of the carotid sinus chemoreceptors.

The facts we have presented regarding the reflex acceleration of blood coagulation are especially interesting in connection with clinical observations on the relationship of unexpectedly developing thrombosis and the stimulation of sinocarotid zones of heightened excitability [7, 10]. Since nicotine caused the acceleration of blood coagulation, one must consider smoking to be forbidden to people threatened with thrombotic complications: such people include patients during pre- and postoperative periods, those with preinfarction conditions or diseases of the cardiovascular system, etc.

SUMMARY

Nicotine or acetylcholine stimulation of the carotid sinus in dogs shortens the coagulation time of the blood. The time of clotting is the shortest 20-30 minutes after the start of stimulation. Perfusion of the carotid sinus with the sinus nerve intact and no stimuli applied, as well as the injection into the denervated zone of nicotine or acetylcholine caused no reflex change of the clotting time. Experiments with the celiac nerve indicate

that the secretion of adrenalin by the adrenal glands is an important, though not the sole factor in the reflex effect of the carotid sinus chemoreceptors on the blood coagulation time.

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