MORPHOLOGY AND PATHOMORPHOLOGY

THE EFFECT OF NOVOCAIN UPON THE COURSE OF ALLERGIC REACTIONS IN PREGNANT ANIMALS

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(Received August 31, 1957. Presented by Active Member Acad. Med. Sci. USSR S. V. Anichkov)

In previous studies [7] we established that the allergic reaction produced by the booster dose of a specific antigen when given to a sensitized, pregnant animal will, in all instances regardless of site, lead to termination of the pregnancy.

In view of the fact that at the present time numerous authors [1, 8] regard allergy as a reaction of the organism to a specific antigen and regulated by the nervous system, the question arose as to whether it may be possible to affect certain divisions of the nervous system in such a manner as to avert the onset of the reaction which manifests itself in these animals by termination of the pregnancy.

N. V. Kaverina and A. N. Poskalenko [10, 16] have shown experimentally that novocain can block stimuli in afferent pathways and diminish the vasomotor response to sympathetic impulses. For this reason we decided to employ novocain.

We took into consideration the work of M. A. Petrov-Maslakov [15] in which he showed that the solar plexus is the pathway mediating trophic influences in the higher divisions of the nervous system upon the internal sex organs.

In view of the opinion of A. V. Vishnevsky and A. A. Vishnevsky [4, 5], namely, that novocain block removes powerful nervous irritants and thus facilitates both the establishment of favorable trophic activities and also the formation of a barrier to pathological conditions, especially those produced by increased permeability (allergic states, edema, and others), we decided to novocainize the region of the solar plexus in our experiments.

The present investigation was undertaken to determine the effect produced in pregnant rabbits by novocain injection into the area of the solar plexus during the course of allergic reactions.

EXPERIMENTAL METHODS

In the first series of experiments, 15 rabbits were sensitized five times at 5-day intervals by intravenous injection of an extract prepared from homologous placental protein secreted from the horns of a pregnant uterus. The solution was injected into the ear vein and the quantity was such that 10 g of placental tissue was dissolved in 90 ml of Ringer-Locke solution; the protein content fluctuating within limits of 0.5-0.7%, the pH being 6.6-7.0.

19 to 23 days after the female had been mated, a midline abdominal incision was made under ether anesthesia, the intestine pushed into the right fossa and the area between the left kidney and adrenal thus becoming exposed, there could be seen medially through the serosa the solar plexus shaped like a small triangular plate.

Into this region, through the serosa, we injected 2 cc of a 0.25 % solution of novocain following which we injected into the vessels leading to the uterine horn 2 ml of the homologous placental protein, this being the booster dose of the allergic reaction.

EXPERIMENTAL RESULTS

Twelve of the rabbits went to term and gave, in the overwhelming majority of cases, living young; the average duration of the pregnancies in these animals being 29-33 days. The young were born 8-12 days subsequent to the booster injection of the antigen. However, 2 rabbits died 4 days and 4 rabbits died 23-26 days after delivering.

In two experiments a biopsy was performed within 3-6 days and in four more experiments — 2–2 ½ months after delivery.

On the 2nd day after the booster dose of antigen 3 of the pregnant rabbits were sacrificed.

The results of the microscopic studies of the organs in the animals (liver, kidneys, brain, uterus) may be divided into 4 groups.

In the first group are 2 experiments, in which the animals died 4 days after delivering, and 2 experiments in which the biopsy was performed 3-6 days after delivery. The organs of these animals showed marked vasomotor disturbances which manifested themselves as hemorrhages with necrotic foci (Fig. 1).

Fig. 1. Severe circulatory disturbances within the liver with extensive hemorrhages, necrotic foci and the beginning of thromboses.

In the second group of experiments, in which the animals died 20-25 days after delivery, microscopic studies showed degenerative changes and a definite proliferative connective tissue reaction.

In the thrid group, the animal biopsies were done 2– 2½ months after delivery. Microscopic studies of the liver and uterus showed only slight degenerative alterations.

The fourth group of 3 rabbits is particularly interesting as these does were sacrificed 2 days after the booster injection while the pregnancy was continuing. These animals had no macroscopic alterations. Histologic studies of the liver and uterus also failed to reveal changes. One doe only had within the liver small hemosiderin deposits with some proliferation of the Kupfer cells and slight accumulations of lymphoidal cells. The presence of these old liver vessel changes indicates that the five-fold sensitization with the homologous placental protein had left its traces within the animal.

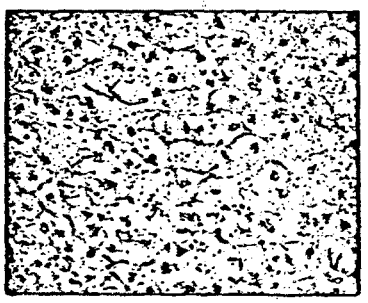

Fig. 2. Liver tissues almost unaltered.

Thus, the first series of experiments showed that novocainization of the solar plexus regularly prevented premature deliveries in pregnant rabbits which had been sensitized to homologous placental protein.

It may be thought that the delivery is a decisive event as, only after that event, does there develop in the doe the typical vascular reaction. However, the vessel reaction after the delivery is much weaker than the one seen in animals which had had no injection of novocain into the solar plexus.

To clarify the question as to whether the role played by the novocain in preventing abortion is a local or an absorptive effect, it was decided to perform a second series of experiments in which the novocain was given intravenously.

In this series 10 does received the homolgous sensitizing placental protein extract five times. Then the animals were mated. 19-22 days after the establishment of the pregnancy the animals received in the ear vein 2 ml of the 0.25 % novocain, this being followed through the same needle by 2 ml of the antigen (the booster injection).

1-2 days later all the animals underwent termination of pregnancy, mostly dead fetuses being aborted.

Two does died 1-3 days after the abortion, the rest surviving. 3 does had biopsies done 16-28 days subsequent to the abortion.

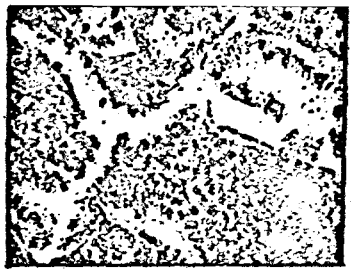

Fig. 3. Severe vascular disturbances within the kidney with vessel dilatation, stasis and numerous hemorrhages.

In those instances when the animals died within several days of the abortion, microscopic studies revealed vascular disturbances accompanied by numerous hemorrhages, stases and thromboses. (Figs. 2, 3, 4).

The picture was somewhat different in those instances when the animals survived and biopsies were taken from the liver and uterus 16-18 days after the abortion. Microscopic studies of the organs of these animals revealed only some limited old hemorrhages, atrophic foci and a small cell infiltration with a beginning of regenerative processes.

Thus, intravenous injection of the novocain does not interrupt the course of the allergic reaction which leads to the abortion and is accompanied by marked morphological alterations within the organs of the animals.

Then, how are we to explain the blocking action of the novocain infiltration of the solar plexus preventing the abortion while intravenous injection of the same amount of novocain fails to exert any effect?

Fig. 4. Severe hemorrhage within the musculature and mucous membrane of the uterus.

It has to be assumed that novocainization of the solar plexus produces such a concentration of the substance there that conduction of impulses both centrally and peripherally is blocked so that not only the sensory but also the motor fibers cease to conduct.

The therapeutic action of the novocain block is based, primarily, upon the afferent impulses of the reflex pathways being interrupted, this assuring the rest of the fulfilling organs, in this instance, the uterus.

In the opinion of S. V. Anichkov [2, 3] the therapeutic use of novocain block of sensory conductors and reflexogenic zones is predicated upon the basic situation in which there occurs inhibition of the stimulative processes because of the interruption of afferent impulses.

It is important to remember that the local anesthetic effect of novocain has a not insignificant action in excluding the reflexes.

The general resorptive action of novocain produced by its being diffused into the blood leads to a weakening of the conductivities at the various central, ganglionic and peripheral synapses. In addition, the resorption of the novocain increases cerebral cortical activity [12], it being especially important to note the vascular dilatation and relief of spasm [13].

Intravenous injection of the novocain produces only the resorptive effect if the slight vasospasm at the site of the injection is discounted.

The absence of a reaction following the intravenous injection of the novocain may also be due to the fact that maximal effects are produced immediately and the influence is exerted for only a short while because the novocain is destroyed within the blood with relative speed. With the blocking action, the resorptive action of the novocain manifests itself very gradually and lasts for a much longer time than does the intravenous injection.

SUMMARY

It was experimentally established that the allergic reaction, which brings about abortion in sensitized animals,

may be prevented. This prevention is carried out by introduction of 2 ml of 0.25 % novocain solution into the solar plexus directly before the booster dose.

No specific morphological changes are revealed in histological examination of a number of organs of these animals.

LITERATURE CITED

[1] A. D. Ado, Arkh. Patol. 3, 3-16 (1951).

[2] S. V. Anichkov, in the book: Maintenance of Health in Soviet Estonia,* Symposium 3, Tallin, 112-123, 1955.

[3] S. V. Anichkov, Scientific Theses of the 9th General Session of the Acad. Med. Sci. USSR,* Moscow, 54-57, 1955.

[4] A. V. Vishnevsky, in the book: Nerve Trophism in the Theory and Practice of Medicine.* Moscow, symposium 2, 15-21, 1936.

[5] A. V. Vishnevsky and A. A. Vishnevsky, Novocain Block and Oil-Balsam Antisepsis as a Special Form Pathogenic Therapy,* Moscow, 1952.

[6] M. M. Voropaev, Problems of Clinical and Experimental Surgery,* Moscow, section 2, 121-129, 1953.

[7] Ia. A. Dul'tsin, Biull. Eksptl. Biol. i Med. 7, 30-33, (1956).**

[8] P. F. Zdrodovsky, Problems of Reactions in the Study of Infection and Immunity,* Moscow, 1950.

[9] S. I. Itkin, in the book: Problems of Clinical and Experimental Surgery,* Moscow, section 2, 130-142, 1953.

[10] N. V. Kaverina, Farmakol. i Toksikol. 15, 2, 17-22 (1952).

[11] M. V. Kirzen, O. R. Kol's and A. M. Zukerman, in the book: Problems of Clinical and Experimental Surgery,* section 2, 82-99, 1953.

[12] T. M. Kucherenko, Farmakol. i Toksikol. 19, 2, 8-12, (1956).

[13] N. I. Leporsky and T. T. Karakulina, Transactions of the Military Naval Medical Academy,* Leningrad, 39, 50-58, 1952.

[14] O. L. Nemtsova, in the book: Problems of Clinical and Experimental Surgery,* section 2, 159-165, 1953.

[15] M. A. Petrov-Maslakov, Neurogenic Dystrophies of the Female Sex Organs,* Leningrad, 1952.

[16] A. N. Poskalenko, Farmakol. i Toksikol. 18, 5, 8-13, (1955).

[17] E. I. Shur, in the book: Problems of Clinical and Experimental Surgery,* section 2, 165-176, 1953.

[18] A. S. Ershtein, in the book: Problems of Clinical and Experimental Surgery,* section 2, 176-183, 1953.

* In Russian.

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