EFFECT OF ETHER ANESTHESIA AND OF DRUG-INDUCED SLEEP ON DEVELOPMENT OF INFLAMMATION OF THE PHARYNGEAL MUCOUS MEMBRANES OF RABBITS

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Considerable attention has been paid in recent years to the study of the effect of the functional state of the nervous system on the evolution of inflammatory conditions. As a rule, the effect of ether anesthesia and of drug-induced sleep on the evolution of inflammatory conditions of different origins has been studied on the skin of experimental animals (cats, rabbits, guinea pigs), much less work having been done on these effects in mucous membranes. In particular, no work seems to have been done on the effect of the functional state of the nervous system on the evolution of inflammatory conditions in the pharyngeal mucosa.

Our experiments were done on rabbits. The first series of experiments was devoted to a study of the effect of drug-induced sleep and ether anesthesia on the permeability of the capillaries of the pharyngeal mucous membranes.

We applied the techniques used by S. I. Itkin [2] and K. F. Dogaeva [1] for the study of permeability of capillaries of rabbit and cat skin. Intravenous injections of 10 ml of 1% trypan blue per kg body weight were given by these authors, and permeability was estimated on the basis of the time elapsing between the injection of the dye and its passage through the capillaries, causing staining of the tissues (microscopic observation, in reflected light). Leakage of the dye from the capillaries was accelerated as their permeability increased.

Since the permeability of the capillaries of the pharyngeal mucosa exceeds that of skin capillaries we used lower dosages of dye, viz., 2 ml of 1% trypan blue in saline per kg body weight. The rabbits were immobilized on their backs, two jaw expanders were inserted into the mouth, and the mouth and throat were illuminated with a head lamp. Trypan blue was injected into a marginal ear vein, and the time of appearance of a blue discoloration of the pharyngeal mucosa was noted.

We first studied pharyngeal capillary permeability in a group of 15 normal rabbits (9 does, 6 bucks), weighing from 1.4 to 2.7 kg. In all cases the blue coloration began to appear 1 minute after injection of the dye, and gradually rose to a maximum at the sixth minute.

In the second group of experiments we studied capillary permeability in nembutal narcosis, on 14 rabbits (8 does, 6 bucks), weighing from 1.4 to 2.1 kg. Nembutal was given as 3% solution, at a dosage level of 2 ml per kg body weight, subcutaneously to 7, and intraperitoneally to the remaining 7 rabbits.

The rabbits became limp 15 minutes after introduction of nembutal, and lay on their sides, and were all unconscious after 30 minutes. The most profound level of anesthesia was found in animals given intraperitoneal nembutal (abolition of corneal reflexes). Trypan blue was injected while the rabbits were deeply anesthetized, 30 minutes after the nembutal injections. Blue staining of the pharyngeal mucosa appeared 3 minutes after the

injection of the dye in 13 cases, and 6 minutes after the injection in 1 case; it increased in intensity to a maximum 6 to 12 minutes after injection of dye.

In the third group we repeated the observations on animals in ether anesthesia, using 10 rabbits (3 does, 7 bucks) weighing from 1.4 to 2.1 kg. Ether was administered in the usual way for 15 minutes, after which a tracheotomy was performed, and a glass tube was inserted, connected by a rubber tube with a glass funnel containing cotton wool, into which ether was allowed to drip. This arrangement was necessary because of the need to observe the pharynx. The rabbits were deeply anesthetized after 30 minutes of ether inhalation, with abolition of corneal reflexes.

Trypan blue was injected while the animals were profoundly anesthetized, usually after 30 minutes. Staining of the pharyngeal mucosa was usually seen 6 minutes after injection of dye (8 animals), but the time was 7 minutes in one, and 7.5 minutes in another animal. In order to exclude the possibility that the effect was due to tracheotomy, 5 rabbits were tracheotomized, but were not given ether; discoloration of the mucosa was observed 2, 2.5, 3, 3, and 3.5 minutes after injection of dye.

It follows from this experiment that tracheotomy does have some effect on the permeability of the capillaries of the pharyngeal mucosa of rabbits, but the delay in appearance of staining (6 minutes, as compared with 1 minute for control animals) must be regarded as being due to ether anesthesia.

It follows from our experiments that therapeutic sleep and ether anesthesia cause a marked diminution in the permeability of the capillaries of the pharyngeal mucosa of rabbits.

We next attempted to determine the effect of inflammation of the mucosa on the permeability of its capillaries. With this object, xylene was applied to the pharyngeal mucosa of 8 rabbits, and the trypan blue test was done after development of inflammation. We were not, however, able to observe any effect on the time elapsing before appearance of staining, which is 1 minute in normal animals. It may be that this time is shortened for inflamed mucosa, but it is in any case so short that we could not register the difference.

In view of this we adopted a different procedure for studying the effect of ether anesthesia on the devlopment of the inflammatory process in the pharynx. Inflammation was initiated by placing 0.1 ml of xylene on the pharyngeal mucosa, and the development of inflammation was followed by microscopic examination of tissue specimens taken from the pharynx of 5 control and 5 experimental animals 30 minutes after application of xylene.

The inflamed mucosa sections showed edema and small hemorrhagic foci in the submucosal layer, and were markedly hyperemic. Stasis and clinging of leucocytes to the walls of the vessels were evident. Specimens taken from corresponding sites of mucosa not affected by the inflammatory process showed similar changes, to a smaller degree.

The effect of ether anesthesia on the evolution of inflammatory processes in the pharyngeal mucosa was studied on 3 groups, each of 10 rabbits.

The water content of the pharyngeal mucosa was taken as an index of the stage of development of inflammation, as was done by I. A. Oivin and L. L. Tseitlin [3] in their researches on the effect of ether anesthesia on inflammatory processes in the skin of rabbits. Edema develops more slowly in less acute inflammations, and hence the water content of the tissues is smaller than for more acute ones.

The water content of the biopsy specimens was determined by drying at 105°; the specimens (wet weight about 80 mg) were weighed on a torsion balance, accuracy up to 0.2 mg.

The first group consisted of control animals, for determination of the normal water content of the pharyngeal mucosa. The second group served for determination of water content 30 minutes after application of xylene. In the third group we determined the effect of ether anesthesia on development of inflammation. Ether was administered for 15 minutes, after which xylene was applied, and ether was continued for a further 30 minutes, when the biopsy specimens were taken; anesthesia was profound (abolition of corneal reflexes). A statistical evaluation of the results is given in the Table.

It appears from this that application of xylene to the mucosa, and the resulting inflammation, lead to an increase in its water content ($P < 0.001$). Application of xylene to ether anesthetized rabbits does not raise the

water content of the pharyngeal mucosa to a significant extent ($P > 0.05$); the differences between water content of the mucosa of rabbits after application of xylene to conscious and anesthetized animals was significant ($P < 0.05$).

TABLE

Water Content of the Inflamed Pharyngeal Mucosa of Rabbits

Statistical indices	Rabbits		
	Normal	with inflamed mucosa	
		without anesthesia	with anesthesia
M	78.6	81.4	79.7
m ±	0.38	0.35	0.54

Note: M is the arithmetic mean value, and m is the mean error ($\frac{\zeta}{\sqrt{N}}$ where ζ is the square of the deviations, and N is the number of rabbits)

It follows from our experiments that application of xylene to the pharyngeal mucosa of rabbits under ether anesthesia does not cause an inflammatory reaction. Profound inhibition of the central nervous system caused by ether anesthetization retards the evolution of the inflammatory process in mucous membranes as well as in the skin.

LITERATURE CITED

[1] K. F. Dogaeva, and S. I. Itkin, Problems of Clinical and Experimental Surgery, 2nd Edition, (In Russian) (Moscow, 1953) pp. 183-195.

[2] S. I. Itkin, ibid., pp 130-142.

[3] I. A. Oivin, Problems of Theoretical and Practical Medcine, in the Light of Pavlov's Teachings, (In Russian) (Stalinabad, 1954).