EXPERIMENTAL STUDY OF THE PATHWAYS OF SPREAD OF TETANUS TOXIN

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Although many problems concerning the mechanisms by which tetanus toxin reaches the central nervous system are still unsolved, the neural route of toxin transport into the spinal cord can now be regarded as well established [1-8]. The existence of a neural route along which the toxin enters the central nervous system has been demonstrated in animals of different species with different forms of tetanus, and its pathogenic importance has been recognized [5-8]. However, the possibility that toxin from the blood may enter the neural route through the tissues has not previously been studied experimentally.

To examine this problem,experiments were carried out in which a limb, remaining in communication with the rest of the body through the nerves, was perfused with heparinized blood containing tetanus toxin, which was subsequently determined in the limb nerves.

EXPERIMENTAL METHOD AND RESULTS

Experiments were carried out on 15 dogs anesthetized intravenously with hexobarbital. The operation of disarticulation of the right hind limb was carried out, leaving intact the two main motor nerve trunks—femoral and sciatic. To prevent injury to the nerve trunks from trauma and the action of adverse factors, a layer of muscle about 0.5 cm thick immediately surrounding the nerve trunk was not divided. Continuous perfusion with heparinized blood from a donor dog was carried out by means of an extracorporeal circulation apparatus (the Soviet NIIKhAI Model). In these conditions the tissues of the disarticulated limb largely remained viable. The duration of perfusion of the limb was 4-10 h. The operation and perfusion usually led to the development of shock, and appropriate measures were taken to prevent this. After the beginning of perfusion, tetanus toxin (3 MLD for dogs) was injected into the system. The wound surfaces were carefully insulated by means of polyvinyl chloride covers to prevent the transfer of toxin by contact; for the same reason the stump wound (proximal) was sutured as far as the "neuromuscular bridge."

At the end of the experiment (perfusion) the "neuromuscular bridge" was divided, and the proximal portion of the sciatic nerve (i.e., above the level of amputation) was resected for a distance of 12-14 cm and divided into 4 equal segments in each of which the toxin was estimated. Macroscopic signs of moderate edema of the disarticulated and perfused limb were observed in five cases.

Histological examination of the tissues of the perfused limb showed that the limb remianed viable in these experimental conditions. No obvious signs of necrosis were seen.

The investigation showed that during 4-10 h of continuous perfusion the toxin spread along the nerve for a distance of 12 cm above the amputation site. It was detected in large quantities in the outer membrane covering the nerve trunk—the epineurium,—which has a relatively rich blood and lymphatic supply, and was less commonly found in that part of the nerve consisting of bundles of nerve fibers, perineurium, and endoneurium. In some experiments tetanus toxin was found in the blood taken from the vein of the ear, and this was most likely the result of transfer through the small layer of muscle left around the nerve. No clinical signs of tetanus, of either the generalized or the local form, were noted in any of the 11 surviving dogs. Hence, despite the non-physiological nature of the model used, and the immobility and edema of the disarticulated limb, toxin was found in the trunks of the motor nerve. These experiments cannot claim to solve the whole problem of the pathways of spread of tetanus toxin from the body and its entry into the central nervous system. Only one conclusion can be drawn from them; in these experimental conditions tetanus toxin circulating in the blood may enter the trunks of the motor nerves and travel along them towards the center.

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LITERATURE CITED

1. G. N. Kryzhanovskii, Byull. éksp. Biol., No. 1, 42 (1960).
2. G. N. Kryzhanovskii, L. A. Pevnitskii, V. N. Grafova, et al., Byull. éksp. Biol., No. 3, 42; No. 8, 31; No. 11, 35; No. 12, 30 (1961).
3. G. N. Kryzhanovskii, Tetanus, Problems in Pathogenesis, Doctorate Dissertation, Moscow (1963).
4. G. N. Kryzhanovskii, Recent Advances in the Pharmacology of Toxins, Oxford (965), p. 105.
5. E. A. Wright, R. S. Morgan and G. P. Wright, J. exp. Brit. Path., 32, 169 (1951).
6. Idem, Lancet, 2, 316 (1952).
7. G. P. Wright, Proc. roy. Soc. Med., 46, 319 (1953).
8. Idem, Pharmacol. Rev., 7, 413 (1955).