MECHANISM OF THE RESPIRATORY PARALYSIS IN BOTULISM, TETANUS, AND DIPHTHERIA

V. V. Mikhailov and S. D. Mikhailova

Department of Pathological Physiology (Head, Professor V. V. Mikhailov), Astrakhan Medical Institute
Presented by Active Member AMN SSSR, A. V. Lebedinskii
Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny, Vol. 57, No. 1, pp. 36-40, January, 1964
Original article submitted July 10, 1962

Clinical and experimental investigations [1-4, 6, 7, 10, 12] have revealed considerable changes in the function of the respiratory apparatus in botulism, tetanus, and diphtheria. It has been suggested that the cause of death in these neurotoxicoses is paralysis of the respiratory centers. Meanwhile, it has not yet been explained whether neurotoxins have a paralytic action on the cells of the respiratory centers. The mechanisms of their action on the conducting pathways and on the motor neurons of the respiratory muscles have been studied even less adequately.

The object of the present study was to investigate the pathogenic action of the toxins of botulism, tetanus, and diphtheria on the various links of the nervous apparatus of respiration: on the respiratory centers with the descending conducting pathways and on the spinal motor centers of the respiratory muscles.

![Fig. 1. Absence of paralysis of diaphragm on the side of hemisection of spinal cord in a cat poisoned with botulism toxin. Marked paralytic syndrome. Contraction of cupola of the diaphragm before (A) and after (B) hemisection of the spinal cord on the left side. The arrow indicates division of the right phrenic nerve. Below) time marker (5 sec).]

EXPERIMENTAL METHOD

Experiments were performed on cats and dogs poisoned with the toxins of botulism type A (1 MLD for mice, 0.00001 mg dried toxin), tetanus (1 MLD, 0.000081 mg), and diphtheria (1 MLD for guinea pigs, 0.003 ml). A generalized neurotoxicosis was obtained in cats by intravenous injection of the toxins in the following doses: botulism 0.05-0.1 mg/kg body weight, tetanus 0.1-0.5 mg/kg, and diphtheria 0.001 ml/kg. "Local" lesions to one cupola of
the diaphragm were produced by intramuscular injection of the toxins in the following doses: botulism 0.05-0.1 mg/kg body weight, tetanus 0.1-0.5 mg/kg and diphtheria 0.001 ml/kg. In dogs, local forms of neurotoxicosis were obtained by injection of the toxins into the nerve trunk in the following doses: botulism 0.05-0.1 mg/kg body weight, tetanus 0.05-0.08 mg/kg.

Acute experiments were carried out on poisoned and nonpoisoned animals under urethane anesthesia (1 g/kg). The respiratory movements were recorded by means of a Marey's capsule connected to a cuff or to the tracheotomy tube. The contractions of the cupolas of the diaphragm were recorded separately by means of two isotonic myographs. Respiratory reflexes were evoked by stimulation of the central end of the divided vagus nerve in the neck with rectangular pulses of current from a generator (length of pulses 0.65 millisec, frequency 1-500/sec). The crossed phrenic phenomenon was evoked by the method described in many previous papers [11-16].

Altogether 116 cats and 50 dogs were used in the experiments, 15 of the cats and 21 of the dogs acting as controls.

Fig. 2. Absence of paralysis of diaphragm on the side of preliminary hemisection of the spinal cord in a cat poisoned with botulism toxin. Generalized paralytic syndrome. A) Paralysis of cupola of diaphragm on intact side; B) contractions of cupola of diaphragm on the side of preliminary hemisection of the spinal cord. Below) time marker (5 sec).

EXPERIMENTAL RESULTS

After hemisection of the spinal cord above the nuclei of the phrenic nerve the contractions of the paralyzed cupola of the diaphragm could be restored by blocking or dividing the phrenic nerve on the opposite side. This restoration is the result of the bringing into play of crossed connections between the intact inspiratory reticulospinal fibers and the motor nucleus of the phrenic nerve on the side of the hemisection [11-16]. This phenomenon, the crossed phrenic phenomenon, was used to analyze the mechanism of action of the bacterial neurotoxins on the various links of the nervous apparatus of respiration. In the first series of experiments we investigated the functional state of the respiratory center and conducting pathways on the side of a local lesion of the diaphragm caused by the toxins of botulism, tetanus, and diphtheria. For this purpose, to obtain the crossed phrenic phenomenon, hemisection of the spinal cord was performed on the sound side and division of the phrenic nerve on the affected side.

In 13 experiments on cats and dogs carried out on the fifth-twenty-first day after poisoning with botulism toxin no change was found in the function of the respiratory center and the conducting pathways on the side of the paralyzed cupola of the diaphragm: a crossed phenomenon was observed in every experiment.

The results of the other 49 experiments on cats and dogs with local tetanus of the diaphragm showed that the crossed phrenic phenomenon readily occurred on the sixth-seventh day after poisoning, and, as a rule, disappeared later.