Present Data on the Pathogenesis of Tetanus

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1 Introduction

Over the period of the last few years, studies on the pathogenesis of tetanus have led to numerous results and greatly advanced our knowledge of the mechanisms of the action of the tetanus toxin and of the development of this disease. In this report I shall attempt to present the main results of work carried out in this field and also to define some new problems and perspectives of research.

2 Pathways of Tetanus Toxin to CNS

After the fundamental works of MARIE and MORAX [56], MEYER and RANSÖM [62] and of the important studies of FRIEDEMANN et al. [17], D'ANTONA [11], WRIGHT et al. [81–83] recent works of FEDINEC [14–16], HABERMANN et al. [23–25] as well as of studies carried out in our laboratory [31–35, 46], we are justified in thinking that the neural transport of tetanus toxin to the central nervous system is proven.

The neural pathway of tetanus toxin into the central nervous system (spinal cord and the brain stem) has been established in animals of various species (mice, white rats, guinea pigs, rabbits, cats, dogs, donkeys, monkeys) and in all essential forms of tetanus-local, ascendens, blood-born tetanus [31, 34, 46]. There is a direct dependence between the species sensitivity of animals to toxin and the extent of the spread of toxin by a neural pathway between the species resistance to toxin and species barrier properties of the neural pathway in relation to toxin [32, 33].

Toxin spreads by the neural pathway with a definite rate depending on the

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quantity in the muscles, the particular features of the neural pathway and the muscle activity.

The neural pathway of toxin spread to the CNS consists of the following links: neural motor endings in muscles – muscle nerve – anterior roots – anterior horns of the gray matter of spinal cord or motor nuclei in the brain stem [32–34, 46]. It remains unclear whether toxin can spread along the sensory fibres. Toxin is revealed in the spinal ganglia which, possibly, play a role of barrier formations [32].

There exists a regional and general neural pathway of the toxin entrance into the CNS. The general neural pathway represents the sum of regional neural pathways from all muscles. The clinical picture of disease greatly depends on which neural pathways are involved in the process of toxin transport into the CNS. At the entrance of toxin only by the regional neural pathway there arises a local and ascendens tetanus in animals and partial tetanus in human. This situation occurs if the spread of toxin with blood is blocked by antitoxin. When toxin spreads with blood it enters initially into all muscles and then reaches CNS by the general neural pathway (30-called blood-born tetanus). Under these conditions toxin enters first into the motor nuclei of the shortest neural pathways – from the head and the face; as a result, there arises a trism and risus sardonicus; then toxin enters the CNS by the longer neural pathways (nerves of the neck and trunk) with the resulting opistotonus, etc. Thus there arises the so-called tetanus descendens. This term, apparently does not reflect the main point of the phenomenon since the matter is not of the descendant movement of toxin along the spinal cord but of the sequence of involvement of the motor nuclei into intoxication in relation to the length of the neural pathway [32, 35].

The findings obtained in experiments with radioactively labelled toxin [24, 25] show that toxin (label) can be retained in the spinal cord for a long time.

Intracisternal injection of tetanus antitoxin, ensuring the spread of the latter along the whole spinal cord and its penetration into the brain part of the neural pathways as well as presumably into the brain substance, can completely prevent the development of local and ascendant tetanus [45] and can also produce a therapeutic effect at earlier stages of disease [27, 45].

The question concerning the possibility of penetration of tetanus toxin into the brain tissue through the blood-brain barrier remains undecided.

3 Binding of Toxin by Brain Tissue

The physico-chemical receptor of tetanus toxin in brain substance is represented by gangliosides forming a complex with the cerebrosides [76–78]. An important role in this binding is played by the sialic acid of the gangliosides [60, 79]. In treatment of the complex protagon – tetanus toxin with neuraminidase sialic acid and tetanus toxin are released, a certain conformance of the