

THE MECHANISM OF DEVELOPMENT OF GAS GANGRENE

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The study of the general and special features of the development of a toxemic condition is of great importance in analysis of the mechanisms of the disease and in the search for methods of experimental therapy.

In recent years these problems have been the subject of systematic investigation in our laboratory. Particular attention has been devoted to the study of the role of reflex mechanisms in the process of development the course and the outcome of experimental gas gangrene [1-4]. As a result of these investigations the importance of pathogenic stimuli and the mechanisms which mediate them was revealed, both in relation to the disease and to the increase in the resistance of the body to the toxemic stimulus.

When studying the pathogenesis of gas gangrene we were confronted with the necessity of evaluating the role of two mechanisms in determining the development of the pathological process: the reflex and the "automatic" action of the toxins. It was necessary to take into consideration the fact that in the conditions of development of gas gangrene, besides pathogenic stimulation of the corresponding nerve endings in the affected focus, there also occurs a release of toxin into the internal media of the body, into the blood stream and the central nervous system. The question arose, what part did these mechanisms play in the general pathogenesis of the disease.

It had to be remembered that the degree of involvement of the reflex and the "automatic" components in the pathogenesis of the disease may differ and may vary depending on many factors, in particular on the stage of development of the infection.

In our previous research we observed that the reflex component of the disease plays an important part, especially in the first stages of development of the illness. In these stages it is possible, in the majority of cases, to prevent the development of the pathological process by measures directed toward changing the reactivity of the nervous system (novocain, interruption of the reflex arc in its afferent, efferent and central links, and so on). A later stages these measures, as has been shown experimentally, are incapable of arresting the development of the disease, evidently on account of the exclusion of mechanisms acting on the "automatic" principle.

The work of A. N. Aliev [1] showed that the pathogenetic importance of these two components may vary in accordance with the actual conditions of development of the toxemia. A subthreshold dose of the toxin of vibron septique, injected directly into the substance of the cerebral hemispheres, produced a threshold effect only in association with the repeated injection of fractionated doses of the toxin intramuscularly. In other words, the preliminary summation of pathogenic stimuli, which in themselves did not cause toxemia, was able to increase to a considerable degree the reactivity of the central nervous system to toxin injected directly into the brain. When the same experiment was carried out, but with the order of carrying out the procedures changed, no effect was found on the course of development of the toxemia.

TABLE 1

The Effect of Decortication of White Rats on the Development of Toxemia after the Administration, by Various Methods, of Lethal Doses of Toxin of Vibrion Septique

Group No.	Experimental conditions	Animals	Number of animals in the experiment	Number of animals	
				dying	surviving
1	Injection of toxin into the brain	Experimental	23	21	2
		Control	23	16	7
2	Intravenous injection of toxin	Experimental	8	8	0
		Control	8	7	1
3	Fractionated injection of toxin into the limb muscles	Experimental	8	1	7
		Control	8	7	1

TABLE 2

The Effect of Changes in the Reactivity of the Central Nervous System on the Therapeutic Action of Specific Antiserum

Group No.	Experimental conditions	Number of animals in the experiment	Number of animals	
			dying	surviving
1	Intravenous injection of specific antiserum	19	10	9
2	Intravenous injection of specific antiserum in association with sodium amytal narcosis	24	6	18
3	Control	43	43	0

To continue our analysis of these two components of the mechanism of development of gas gangrene infection and toxemia, we attempted to find conditions in which their action could be disassociated within certain limits, and their importance in the pathogenesis of the disease individually assessed. In our experiments [5] it was found that after decortication of white rats, gas gangrene did not develop in response to inoculation of a lethal dose of a culture of vibrion septique into the muscles of the limbs; nor did toxemia develop in the animals after repeated fractional injection of the toxin of the same microorganisms into the muscles.

The question arose, did decortication affect the reactivity of the central nervous system only in relation to stimulation coming from the periphery, or could such a procedure alter the reactivity of the animal also in relation to toxin, acting according to the so-called automatic principle. In order to analyze this problem we carried out the experiments described below.

Three weeks before injection of the toxin, the cerebral cortex of white rats was extirpated in areas (frontal, parietal, temporal) accessible for operation. The animals undergoing operation were divided into 3 groups. Control animals were selected by weight to each group.

The first group of experimental and control animals was injected with toxin of vibron septique (series 406) in a dose of 0.1 mg (2.5 MLD for mice) in the substance of the parietal region of the left cerebral hemisphere, the second group received a dose of 0.3 mg (7.5 MLD for mice) intravenously; and the third group of animals received a dose of 8 mg of toxin (200 MLD for mice), by fractionated injection of 10 MLD every 30 minutes, into the muscles of the hindlimb.

As may be seen from Table 1, the decorticated animals (with the exception of one rat) did not die after fractionated injection of the toxin into the muscles in doses causing the death of control animals (third group), whereas after injection of toxin into the brain of decorticated animals (first group) or into the blood stream (second group), the majority of them died from toxemia, just as did the control animals in these groups. Summation of pathogenic stimuli, taking place according to the reflex principle, was thus not observed after decortication, despite the fact that the reactivity of the animal to the automatic action of the toxin was not changed.

This showed that a change in the functional state of the central nervous system could entail dissociation of the reactions of the animal to the action of a toxin when administered by various methods. The consideration of this possibility and the discovery of the conditions in which this dissociation could be produced are of great importance in both the analysis of the pathogenesis of the infectious process and the study of the mechanisms by which the infection may be prevented.

We carried out a therapeutic experiment in gas gangrene, taking these findings into consideration.

When gas gangrene had already developed, and procedures directed towards removal of pathogenic stimuli were in themselves ineffective, and when specific forms of treatment (therapeutic serum) were also relatively ineffective, good results might have been expected from combined methods based on the above-mentioned features of the pathogenesis of toxemia in gas gangrene.

White rats (86 in number) were inoculated in the muscles of the hindlimbs with 0.1 ml of a suspension of vibron septique organisms, diluted 1:1000, in a 5% solution of calcium chloride (prepared from a standard glycerol suspension of microorganisms containing 6×10^9 organisms per ml). The original suspension was diluted before the experiment with sterile physiological saline. 6 hours after inoculation the first group (19 rats) was injected intravenously with specific antiserum (0.1 ml 25 antitoxin units); the second group (24 rats) received injections of serum after 6 hours during narcosis with sodium amytal, and the third group (43 rats) remained as controls.

The results of this experiment are shown in Table 2.

As may be seen from Table 2, the action of specific serum in association with sodium amytal narcosis (lowering the reactivity of the central nervous system to the pathogenic stimulus) had a favorable effect on the course of the disease.

Whereas the dose of serum chosen by itself could prevent death of only half the animals from gas gangrene, the same dose of serum in conjunction with sodium amytal narcosis was considerably more effective and preserved the lives of the majority of the animals. It must be remembered here that the animals were inoculated (as may be seen from the control group) with an absolute lethal dose of microorganisms.

A combination of pathogenetic measures, directed on the one hand toward decreasing the reactivity of the nervous system towards the action of pathogenic stimuli and on the other hand to the action of the specific stimulus itself, was found to be more effective than each of these procedures carried out separately. This conclusion became still more obvious when it was remembered that, by itself, sodium amytal has no essential effect on the disease at this stage of its development, and is able only to prolong the life of the animals. Nor does it have any effect, as shown by S. V. Magaeva's experiments, on the reactivity of the animal to vibron septique toxin injected directly into the brain.

The consideration of both components of the pathogenesis of toxemia in gas gangrene thus enables more effective methods of combined treatment of this disease to be designed.

SUMMARY

It was possible to reveal the dissociation between the reflex and the "automatic" actions of the vibron septique toxin in decorticated animals. In these conditions the white rats perished when the toxin was injected into the brain or blood. In repeated intramuscular injection of the toxin in fractional doses the process of summa-

tion of the pathogenic stimuli was absent and the animals did not die from intoxication.

The pathogenetic experimental therapy of gas gangrene was conducted with consideration of this regularity when coupled with the barbamy sleep, which decreases the reactivity of the animals to the pathogenic stimulation. The specific serum gave a better effect, than the separate use of these components.

LITERATURE CITED

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