PROTECTIVE AND ADAPTATIONAL REACTIONS OF THE ANIMAL BODY TO THE INJECTION OF SMALL DOSES OF FOREIGN BLOOD

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The study of the protective reactions of the body in response to the action of pathogenic stimuli is of great importance. In the present paper we describe the results of an investigation of the protective and adaptational reactions arising after injection of small doses of foreign blood into animals (white rats).

EXPERIMENTAL METHOD

The investigation was carried out on the model which we have devised to reproduce heterotransfusional shock accompanied by acture pulmonary edema. In numerous experiments a variety of substances and agents (adrenalin, calcium chloride, potassium chloride, calcium chloride with glucose or adrenalin, quinine, atropine, novocain, various narcotics, novocain block of the vagus and sympathetic trunks in the neck, division of the vagus nerves in the neck or below the diaphragm, section of the spinal cord between the first and second thoracic vertebrae and so on) has been tested without showing any marked effect on the course of the shock. The only factor found to be effective was the preliminary intravenous injection of ox blood (plasma or serum) in doses which did not produce signs of shock. The mechanism of this phenomenon was the subject of our investigation.

EXPERIMENTAL RESULTS

If a few minutes before the infusion of a lethal dose of ox blood (plasma or serum) into a rat, a small dose of the same blood (plasma or serum), causing no perceptible disturbances of function of the animal, is injected intravenously into the rat, the subsequent injection of the foreign blood is tolerated by the animals in the majority of cases without any signs of shock; only a well-marked hemoglobinuria is observed.

A similar phenomenon after the injection of incompatible blood or serum was observed in dogs [10, 11 and others], cats [11], rabbits [3, 13], and also in man [2, 6, 12, 16 and others]. A rapid protective reorganization was also observed during the action on animals of microorganisms and their toxins [1, 7, 8 and others], tissue extracts [13, 14] and also of certain other protein and nonprotein substances. These phenomena have been described under various names ("tachyphylaxis", "allergization," "desensitization" and so on). We shall call the phenomenon which we observed tachyphylaxis [4, 7].

The phenomenon of tachyphylaxis appeared in our experiments after a preliminary injection of ox blood in doses of 0.5 ml/kg and over. Usually we employed doses of 2 to 3-5 ml/kg. Without causing signs of shock, as a rule these doses were sufficient to preserve the rats from shock after the subsequent injection of shock-producing doses of ox blood (Figs., 1 and 2).

Known shock-producing doses of foregin blood were injected into rats from 5 minutes - 1 hour after the injection of protective doses in 86 experiments. In 44 animals shock did not develop, 9 animals died from shock with acture pulomary edema, and in the remaining experiments only slight manifestations of shock were observed.

Of the 9 experiments which terminated fatally, in four the ox blood possessed very high shock-producing powers, and the severity of the shock was not reduced by two or three preliminary injections of small doses of the same blood. In a number of experiments it was demonstrated that the absence of tachyphylaxis depended on the individual reactive peculiarities of the rats.

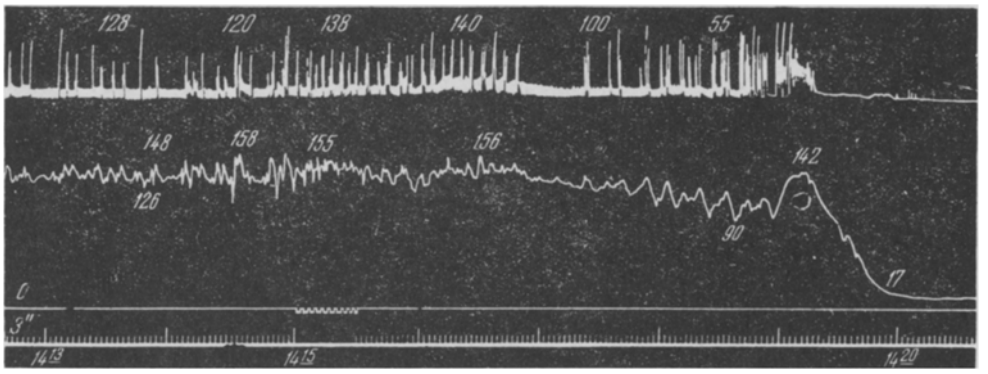

Fig. 1. Changes in the respiration and arterial pressure after injection of a lethal dose of ox blood into a white rat. Significance of the curves (from above downwards): respiratory movements (the figures indicate the number of respirations in one minute); arterial pressure (the figures indicte the height of the arterial pressure in mm of mercury); zero line and stimulation marker – injection of ox blood in a dose of 15 ml/ kg; time marker (3 seconds). Weight index of the lungs, determined after the death of the rat, 18.6.

We may note specially that in 2 experiments in which the arterial pressure and respiration were registered, after the injection of the "prepared" rats with a lethal dose of ox blood, not only did the arterial pressure not fall after the usual initial phase of elevation, but it considerably increased (to 200 and 210 mm of mercury). In some experiments, besides registration of the arterial pressure and respiration, a record was made on the drum of the kymograph of the volume of the kidney, by means of an oncometer. The experiments showed that the preliminary injection of small doses of blood protects the renal vessels from the constriction observed during shock.

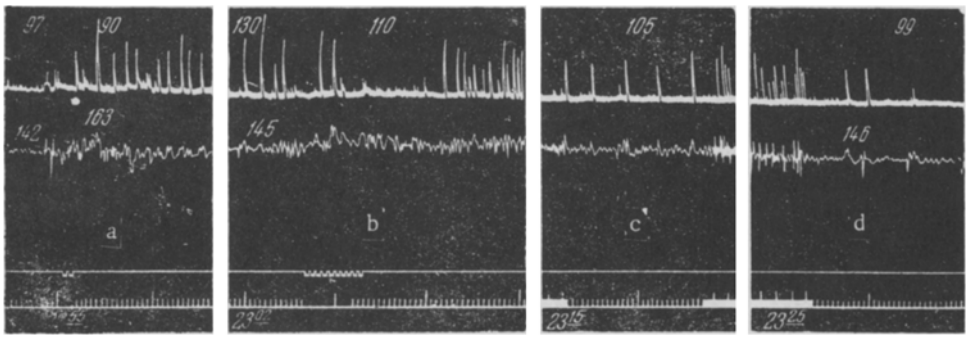

Fig. 2. Changes in the respiration and arterial pressure after injection of a white rat with a lethal dose of ox blood (15 ml/ kg) after the preliminary injection of a small dose (2 ml/ kg) of the same blood. Significance of the curves the same as in Fig. 1. Weight index of the lungs, determined after death of the animal, 6.1.

Thirty rats in which fatal shock did not develop were killed in order to determine the weight index of the lungs. On the average this amounted to 7.7, varying between 4.9 and 9.5, i. e. it was considerably lower than that observed in animals dying from shock (from 10.2 to 38.7). Histological investigations showed that the appearance of a certain degree of edema was often found in lungs which hardly differed from normal in their weight and external appearance.

In order to discover the duration of action of the protective and adaptational reorganization which we were studying, in 38 experiments white rats were injected with a lethal dose of ox blood from 2-7½ or from 50 minutes to 6 hours 55 minutes after injection of the small dose. Only 3 minutes after injection of the small dose of ox blood it was possible to observe the protective action, preventing death of the animals after the subsequent injection of blood. This action continues for 1½ hours. Some of our experiments on rabbits and dogs, and also clinical observations, when compared with the experiments and clinical observations of other authors [2, 3, 4, 6, 10, 11, 12 and others], show significant species differences in the ability of the animal to reproduce tachyphylaxis during infusions of foreign blood.

We also attempted to study the specificity of tachyphylaxis. Workers who have dealt with this problem [11, 14, 15 and others] are inclined to deny its existence. In 2 experiments, in one of which a record was made of the arterial pressure and respiration, tachyphylaxis was induced by human blood in a dose of 5 ml/kg given 10 minutes before the injection of ox blood. Tachyphylaxis did not develop. In 10 experiments tachyphylaxis was induced by dogs' blood in a dose of 1.35-15 ml/kg, given 10-16 minutes before the injection of ox blood. In 6 experiments the shock reaction was clearly diminished and in four tachyphylaxis was not observed. No direct connection could be observed between the size of the dose of the first injection and its effectiveness in these experiments. In 11 experiments, in seven of which records were made of the arterial pressure and respiration, rabbit blood was used in a dose of 1.5-5.9 ml/kg in order to produce tachphylaxis. Ox blood was infused 8 minutes 45 seconds -- 16 minutes 21 seconds after the injection of rabbit blood. In two of these experiments the injection of the small dose (2 and 5 ml/kg) diminished the shock reaction and the rats tolerated the injection of the lethal doses of ox blood. In the remaining 9 experiments no perceptible protective action was found and the rats died.

Thus, specificity of tachyphylaxis is observed in white rats but it is very relative. Consequently our experiments lead to the conclusion that the injection of small doses of ox blood into white rats evokes the development of protective and adaptational reorganization, preventing shock and acute edema of the lungs after the subsequent infusion of large doses of the same blood.

SUMMARY

The author has studied a number of medicines which prevented hemotransfusional shock and acute pulmonary edema in white rats. Preliminary intravenous administration of low doses (from 2 to 5 ml per kg of body weight) of cattle blood was the most effective. It was established that in only 3 minutes after the injection of low doses of blood the animal is protected from death, provided further injection of large doses of blood is effected. This phenomenon is relatively specific.

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