MICROBIOLOGY AND IMMUNITY

THE EFFECT OF CORTISONE AND DESOXYCORTICOSTERONE ON THE ACTIVITY OF THE ENDOTHELIAL-MACROPHAGAL SYSTEM

Z. A. Ertuganova and L. S. Ageeva

From the Department of Chemotherapy (Head – Corresponding Member of the Academy of Medical Sciences of the USSR, Professor Kh. Kh. Planelyes) of the Institute of Pharmacology and Chemotherapy (Director – Active Member of the Academy of Medical Sciences of the USSR, Professor V. V. Zakusov) of the Academy of Medical Sciences of the USSR, Moscow.

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In cases of acute bacterial and viral infections, the administration of cortisone not only does not improve, but on the contrary aggravates and accelerates the course of the infectious process and hastens the death of experimental animals and patients [3]; seeding of the stimulant is considerably greater from the blood of animals receiving cortisone and infected with fungi than among controls. The mechanism of this phenomenon has not been explained as yet.

Taking into account data in the literature and the results of our previous observations and the observations of Z. A. Popenengova [1], when it was found that cortisone administration speeds the death of experimental animals with pneumococcal infection, we decided to study, in order to discover the mechanism of this negative effect of the adrenal cortical hormones on the course of the infectious process, to what extent the indicated substance changes the phagocytic capacity of the endothelium blood vessels with relation to bacteria administered into the blood.

In the present paper are presented the results of studying the action of cortisone and desoxycorticosterone on the phagocytic activity of the endothelio-macrophagal system. In our experiments the methods were used which, in our opinion, made it possible to determine the functional activity of the indicated system as exactly as possible.

EXPERIMENTAL METHODS

The experimental animals (rabbits) were administered cortisone and desoxycorticosterone intramuscularly for a week, then a suspension of bacterial culture or a solution of Congo red intravenously. At certain intervals after infection, venous blood samples were taken. In one case, the blood was seeded in dishes with nutritive medium, in the other, the amount of Congo red was determined colorimetrically. The dishes were kept in thermostat about 24 hours, after which the number of colonies which grew was counted and compared with the number of colonies which grew in dishes seeded with the blood of control animals. The results of the colorimetry were compared with a standard.

In all, about ten experiments were carried out on 31 rabbits with the culture and on 18 rabbits with Congo red. The rabbits weighed 2-2.5 kg. Some rabbits received cortisone intramuscularly, 5 mg/kg of weight twice a day for 5-7 days. Others received desoxycorticosterone, also intramuscularly, 5 mg/kg twice a day for the same length of time. The latter group served as a control. On the day of the experiment, the same doses of the preparation were administered to the animals once more 30 minutes before infection.

As we already indicated, infection was carried out intravenously, by administering a suspension of a 24-hour culture of B. coli strain No. 613, using 10 billion microbial bodies per 1 kg of the animal's weight. One-half, 2,4, and 6 hours after infection, 0.1 ml blood samples were taken from the peripheral vein of the ear for seeding and diluted in 1 ml of simple bouillon containing 1% sodium citrate. Using a micropipette, 0.01 ml of diluted blood was taken and seeded in a Petri dish with Endo's medium. The dishes were placed in a thermostat for 20-24 hours, following which the number of colonies was counted. The growth of the colonies was compared with the seeded blood of the control rabbits.

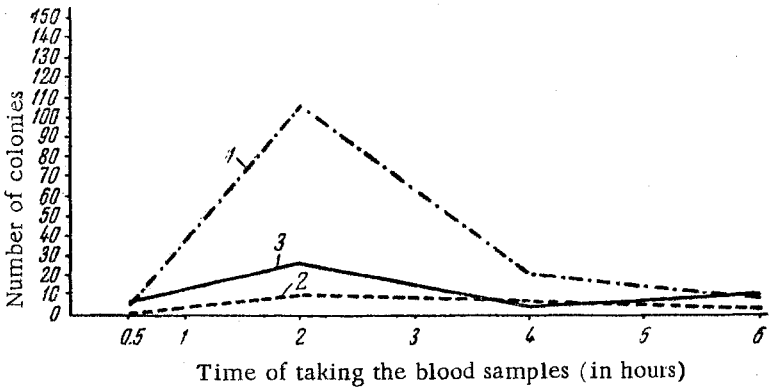

Fig. 1. Recovery of B. coli 613 from the blood of rabbits receiving cortisone (1) or desoxycorticosterone (2) and of control animals (3).

EXPERIMENTAL RESULTS

The results of the observations are shown in Fig. 1.

In Fig. 1 it is evident that, half an hour after infection, only a few bacteria were seeded with respect to the total number of microbial bodies administered. Thus, for example, after the administration of 100 million bacteria per 1 ml of the rabbits blood, on seeding, 6,000 bacteria were found in 1 ml of blood among the controls, 4,000 bacteria among the animals receiving cortisone, and 1,000 bacteria among the animals receiving desoxycorticosterone.

Thus, the disappearance of the administered bacteria from the blood occurred fairly intensively in all cases in the experiment, but most intensively when desoxycorticosterone was used. It is difficult to explain such a rapid disappearance of the administered bacteria from the blood by an increase in the bactericidal activity of the blood under the influence of the indicated preparations, since the same rapid disappearance was observed among the control animals also, if the small fluctuations in the number of seeded bacteria are not taken into account.

We observed a different picture 2 hours following infection. Now the recovery of B. coli from the blood of animals receiving cortisone was almost 4 times greater than from that of those receiving desoxycorticosterone.

The increased recovery of the stimulant from the blood of the control animals, not mentioning the animals receiving cortisone, can be explained by the situation described by V. K. Vysokovich. He wrote bacteria administered into the blood die partly under the influence of the bactericidal properties of the blood, and partly are consumed by the cells of the endothelio-macrophagal system. The bacteria which are consumed by the cells of the endothelio-macrophagal system are usually destroyed, while those which are not destroyed multiply and, returning to the blood, produce a wave of increased recovery from the blood.

Thus, it can be supposed that cortisone suppresses the ability of the cells of the endothelio-macrophagal system to destroy the engulfed bacteria, while desoxycorticosterone, on the contrary, stimulates this activity. In this connection, Mene [2] indicates that cortisone does not change the normal phagocytic functions of the reticuloendothelial cells of the systems already existing in the organism of the principle organs (liver, spleen, bone marrow, lymph nodes) and inhibits the replacement of the reticuloendothelial cells of the system, which are loaded with colloid, by new cells, thus, interfering with the reestablishment of the suspended phagocytic functions [3].

The increase in the number of live bacteria circulating in the blood 2 hours after infection can be explained by a fall in the ability of the phagocytes under the influence of cortisone to suppress the vitality of the bacteria engulfed by them or by the phenomenon of inhibition of the replacement of the phagocytic cells loaded with bacteria by new ones which assure the engulfment of bacteria which reenter the blood from the cells in which they could multiply. Gell and Hail indicate that cortisone has no direct effect on macrophagy.

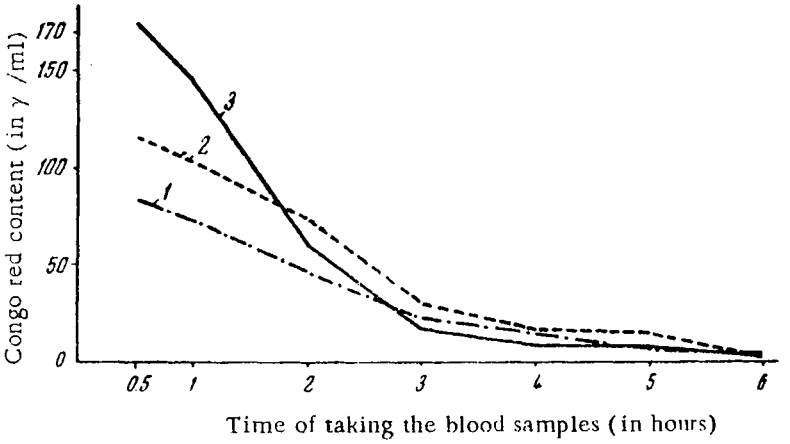

Fig. 2. Congo red content of the blood of rabbits which received cortisone (1) or desoxycorticosterone (2) and of control animals (3).

It should be noted that in our experiments almost all the experimental rabbits died by the end of the first 24 hour period, and some died during the experiment. All the dead animals were autopsied and the liver, spleen, lungs and urine were seeded. It was observed that the stimulant was recovered from all the organs and under all the conditions of the experiment in a fairly large number of cases.

As we indicated earlier, along with the experiments with live bacteria we carried out experiments with Congo red.

Congo red, 83 mg/kg each, was administered intravenously to rabbits which had been injected intramuscularly for 5 days with using cortisone or desoxycorticosterone 5 mg/kg of the animal's weight twice a day. Blood samples for photocolorimetric analysis were taken 30 minutes, 1, 2, 3, 4, 5 and 6 hours after the administration of the dye. In order to avoid its coagulation in the blood sodium oxalate was added, it was centrifuged, the top, transparent layer was decanted and analyzed photocolorimetrically. The figures from the apparatus were compared with the figures on a standard curve.

The results of these observations are shown in the form of curves in Fig. 2. As is evident from Fig. 2 when cortisone was administered, the Congo red content of the blood 30 minutes after the administration of the dye was two times less than that of the control and 1.4 times less than when desoxycorticosterone was used. Two hours after the administration of the dye, we observed an increase in concentration of Congo red in the blood of animals receiving cortisone, as occurred when live culture was used instead of dye. It is understood that in this case we should not expect a secondary wave of increased dye concentration, since cortisone does not decrease the engulfing capacity of the cells of the endothelio-macrophagal system, but decreases the ability of the indicated cells to destroy the engulfed bacteria or other particles. Thus, the second wave of bactermia in animals receiving cortisone can be explained by a depression of the ability of the cells of the endothelio-macrophagal system to destroy the engulfed bacteria, as a result of which bacteria multiply in them and, reentering the blood, cause a wave of bacteremia. Desoxycorticosterone strengthens not only the phagocytic function, but also the ability to destroy the engulfed bacteria by cells of the endothelio-macrophagal system.

SUMMARY

Cortisone injected intramuscularly in the dose 5 mg per 1 kg body weight of a rabbit, two times daily during 7 days did not suppress the phagocytic properties of the cells of endothelial-macrophagal system, but it suppressed the ability of these cells to lyse absorbed cells (B. Coli , strain 613), whereas desoxycorticosterone stimulated this activity.

LITERATURE CITED

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