

THE PHAGOCYTIC ACTIVITY OF THE LEUCOCYTES IN EXPERIMENTAL DIABETES AND RADIATION SICKNESS

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In a paper devoted to the subject of the glycogen content of the leucocytes, Hoppe-Selyer wrote: "The process of breakdown of glycogen taking place in a working muscle is carried out in just the same way as in moving protoplasm". Later, K. Voskresenskii pointed out: "Glycogen is an indication of the special vital activity of the mobile blood cells, the leucocytes. The body reacts to pathological conditions of a certain intensity by a morphological increase in the mobile blood cells and by the appearance of glycogen in these cells. Leukocytosis is the reaction of the body to the introduction of infection; glycogen is the reaction of the leucocyte to the same factor" [1]. It was shown, in research by N.V. Puchkov, that the injection of small doses of adrenalin into the blood stream increases the phagocytic activity of the blood, and that in response to the action of substances interfering with glycogenolytic processes (monoiodoacetate, arsenate, phloridzin), the phagocytic reaction of the leucocytes is paralyzed although under these circumstances the leucocytes themselves remain viable and continue to absorb oxygen and to excrete carbon dioxide [4]. The action of phloridzin is particularly demonstrative, for in a concentration of 1/500 M it completely suppresses the phagocytic activity of the leucocytes and the formation of lactic acid by these cells, although respiration is completely preserved. In our investigations [5], we were able to show that a 5% solution of glucose, to which had been added 1.6 I.U. of insulin, causes an increase in phagocytosis, whereas glucose and insulin, given separately, do not produce this effect but, on the contrary, may even lower the phagocytic activity of the leucocytes. In other experiments, we suppressed glycolysis in the leucocytes with monoiodoacetic acid, which led to a decrease in phagocytosis; the subsequent addition of lactic acid restored this activity to its normal level. At the same time, when glycolysis is present, lactic acid brings about a fall in the phagocytic activity of the leucocytes in precisely the same way.

There is, therefore, no doubt that the phagocytic activity of the leucocytes and, consequently, the cellular component of immunity, depends on the carbohydrate metabolism of the phagocytes themselves. Evidently this, in turn, depends on the carbohydrate metabolism as a whole.

It may readily be understood from the foregoing why characteristic signs of diabetes, in which there is a severe disturbance of the carbohydrate metabolism, are furunculosis and an increased tendency towards infections. Ehrlich [6] pointed out long ago that, in spite of the high blood sugar concentration in diabetics, their leucocytes contain hardly any glycogen. All these facts seemed to justify the performance of experiments in which we investigated the relationship between the phagocytic activity of the leucocytes in dogs in various stages of experimental diabetes and in radiation sickness; we chose the latter because, in this condition the islet apparatus of the pancreas is affected [3] and phagocytosis is severely impaired [2]. With the same object, we investigated the effect of insulin, injected into animals, on the phagocytic activity.

EXPERIMENTAL METHOD

Experiments were carried out on 6 dogs, in three of which $\frac{2}{3}$ of the pancreas had been removed operatively, and to the other three a single lethal or sublethal dose of x-rays had been given.

The system of investigation was as follows: the first 3-4 days the phagocytic reaction of the blood (by the usual method) and the blood sugar concentration (by the Hagedorn-Jensen method) were determined in the animal. The blood sugar of the healthy animals was found to be 85-120 mg%, and the phagocytic activity 25-35%. On the 4-5th day, the operation was performed or the animal was irradiated. After 24 hours, the determinations of the blood sugar and phagocytic activity of the leucocytes were resumed. Blood was taken from the subcutaneous vein of the thigh during the morning hours.

EXPERIMENTAL RESULTS

The trend of the changes found in the dogs as a result of pancreatectomy is shown in Fig. 1. As the diabetic hyperglycemia developed, the phagocytic activity of the blood was lowered, although no directly proportional relationship was found: regardless of to what level the blood sugar rose (300, 600, 900 mg%), the phagocytic index always fell very sharply. On the 6-7th day, subcutaneous injections of insulin began (2 I.U./kg body weight). At this period, the value of the blood sugar and phagocytic activity of the blood was estimated twice a day — in the morning and 2 hours after injection of insulin. Concurrently with a fall in the blood sugar concentration to its original level, 2 hours after the injection of insulin, the phagocytosis was restored almost to normal. After 24 hours, i.e., when the effect of the insulin ceased, with the recurrence of hyperglycemia a fall in the phagocytic activity of the leucocytes was once again observed. A further injection of insulin led to a repetition of the same picture. The experiments were repeated many times on each animal and always with the same result.

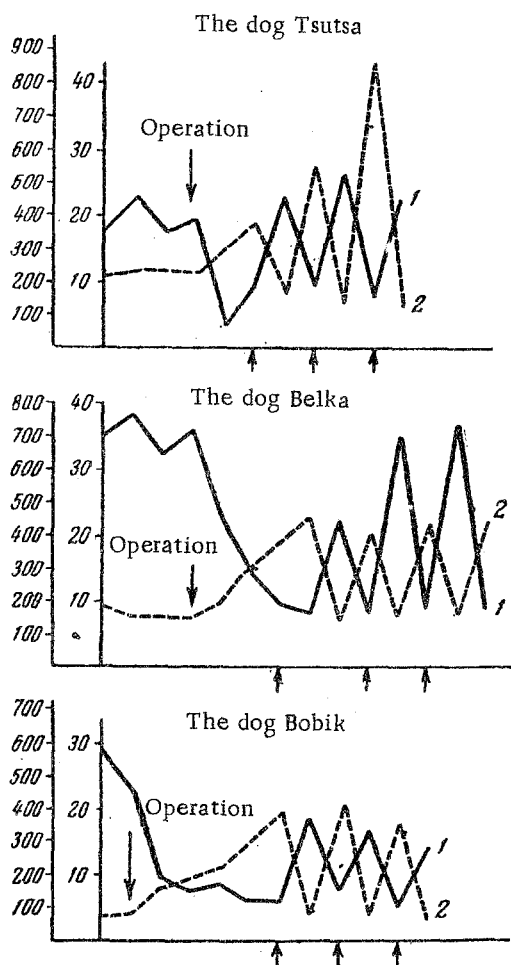


Fig. 1. Changes in the phagocytic activity of the leucocytes and in the blood sugar concentration in experimental diabetes. 1) Phagocytic activity of the leucocytes; 2) blood sugar concentration; \uparrow) injection of insulin.

The changes in the blood sugar level and the phagocytosis in dogs during radiation sickness are shown in Fig. 2. In these experiments, we also counted the leucocytes.

In the dog Seryi, irradiated with a sub-lethal dose (400 r), hyperglycemia developed slowly, and on the 22nd day the blood sugar was 650 mg%. At this time, the phagocytosis had fallen to 10% and the leucocyte count to 8000. On the 23rd day, daily injection of insulin began; under these circumstances, as in the experimental diabetes, each injection of insulin led to restoration of the phagocytosis almost to the normal value at the same time as the blood sugar level fell. With daily injection of insulin, the clinical features of radiation sickness cleared up 1½ months after irradiation. The blood sugar concentration, the leucocyte count and the phagocytic activity of the leucocytes returned to normal at this time.

One of the two dogs (Ryzhik) irradiated with a lethal dose of x-rays (600 r) reacted to irradiation by the rapid development of radiation sickness and it died on the 14th day. On the 6th day, the blood sugar concentration in this dog had risen from 95 to 180 mg%; the leucocyte count had fallen from 16,000 to 6000 and the phagocytic activity from 29 to 10%. Injection of insulin to this dog caused the blood sugar level to fall, but had only a slight effect on the phagocytic activity of the leucocytes — although in the same direction as in the experimental diabetes. In the third dog — Mishka — which also received a lethal dose of radiation (600 r), the disease

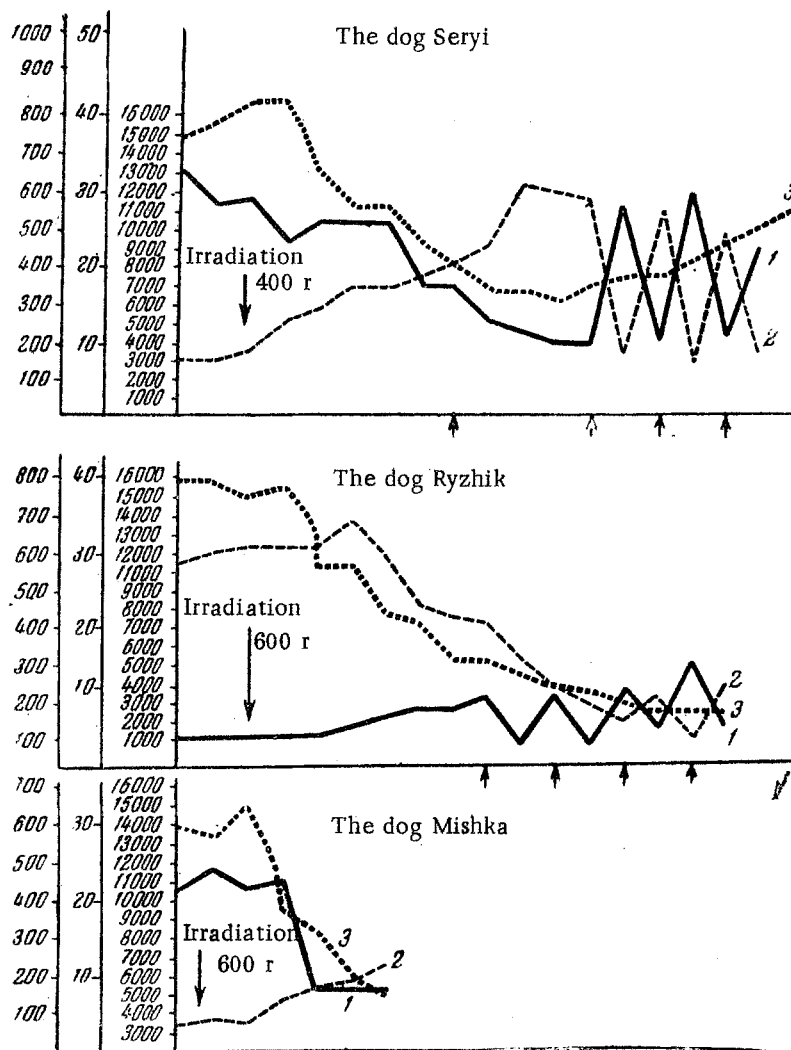


Fig. 2. Changes in the leucocyte count, in the phagocytic activity of the leucocytes and in the blood sugar concentration during radiation sickness. 1) Phagocytic activity; 2) blood sugar content; 3) leucocyte count; \uparrow - injection of insulin.

developed very quickly and the animal died on the 7th day. In this case, no insulin was injected. The changes in the blood sugar, the leucocyte count and the phagocytic activity of the leucocytes were the same as in the other irradiated animals, but they developed much more quickly.

It follows from the foregoing that a definite correlation existed between the blood sugar concentration and the phagocytic activity of the leucocytes. This was shown by the fact that in hyperglycemia from various causes (experimental diabetes, radiation sickness), the cellular phagocytosis was severely disturbed. Administration of insulin normalized, at the same time, both the blood sugar and the phagocytic activity of the leucocytes. Confirmation was thus obtained of our findings *in vitro*, published in a previous paper, with the exception that the experiments described were carried out on the intact animal. It may thus be asserted that the phagocytic activity of the leucocytes is not determined by the glucose concentration in the blood alone but by the relationship between the glucose and insulin of the blood; in other words, the phagocytic activity depends not only on the supplying of glucose to the leucocytes but also on their normal ability to utilize the glucose.

SUMMARY

Hyperglycemia in experimental diabetes and radiation sickness in dogs is associated with diminished phagocytic activity of leucocytes. Subcutaneous injection of insulin results not only in the decrease of the blood

sugar level, but leads at the same time to the recovery of the phagocytic activity. Such dependence of the phagocytic activity on the relationship between glucose and insulin in the medium was formerly revealed by the author in vitro.

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