CHANGES IN THE RATE OF EFFECTIVE PLASMA FLOW, THE RATE OF GLOMERULAR FILTRATION, AND THE FILTRATION FRACTION IN THE KIDNEYS DURING SERUM SENSITIZATION

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There are reports in the literature [4, 5, 12, 13, 14] that experimental nephritis and nephrosis produced in animals sensitized to foreign serum or to bacterial antigens are severer in degree than similar lesions of the kidneys in unsensitized animals. These findings are largely responsible for the statement [2, 8] that diffuse glomerulonephritis is a disease of allergic nature.

It may now be regarded as proved [1, 3, 7] that the injection of an assaulting dose of antigen into the renal artery of a sensitized animal causes the development of a hyperergic reaction similar to the picture of diffuse glomerulonephritis. This explains the attempts of research workers to define the morphological and functional characteristics of the kidneys during sensitization. We know that, in serum sensitization, changes may take place in the nitrogen-excreting capacity [11], as well as delay in the excretion of uric acid by the kidneys [1]; there are reports [6] of an increase in the rate of excretion in the urine of radioactive phosphorus P^{32}, injected parenterally into an animal.

In the light of the filtration—reabsorption—secretion theory of urine formation, modern methods of study of the functional powers of the kidneys enable the activity of different parts of the nephron to be investigated in detail.

The object of the present research was to study the rate of glomerular filtration, the rate of the effective plasma flow, and the magnitude of the filtration fraction in the kidneys of dogs sensitized to normal horse serum.

EXPERIMENTAL METHOD

The investigations were carried out on five dogs—females, weighing 14—19 kg—under chronic experimental conditions. One month before the beginning of the experiments, the ureters of each animal were transplanted to the skin of the abdomen by the Pavlov—Tsitovich method. The plan of the investigations was as follows: at 9-10 A.M. the dog was placed on the apparatus, in a fasting state; the urine was collected by means of a special funnel every 15 min; observations on the spontaneous diuresis were conducted for 30 min and then, by means of a gastric tube, the animal was given a high water intake of 60 ml/kg body weight. Next, into the dorsal lateral metatarsal vein, an infusion was given of physiological saline containinginulin (0.3 %) and cardiotrast (diotrast) (0.3 %). The concentration of inulin in the plasma under these conditions did not exceed 10 mg %, and the cardiotrast concentration—2 mg %. After perfusion had proceeded for 40-50 min, when the rate of diuresis had reached 5-8 ml/ min, the rate of the effective plasma flow and the rate of glomerular filtration were determined in two 15 min clearance periods.

The inulin in the plasma and urine was determined by Harrison's [10] method and the cardiotrast by the method of Rolf and White [15]. Experiments were performed once in seven days on each animal.

In the course of three weeks the background for each dog was determined, on the basis of six clearance periods, after which the animal was sensitized to horse serum in a dose of 0.2 ml/kg body weight, given by subcutaneous injection on three occasions on alternate days. In each animal the investigations were carried out on the 7th, 14th, and 21st days after the first sensitizing injection. The presence of sensitization was established retrospectively as a result of the development of anaphylactic shock in response to the injection of an assaulting dose of serum in a volume of 0.6 ml/kg body weight. The pattern of the anaphylactic shock was recorded by means of tracings of the arterial pressure and respiration.

The following were used in the experiments: horse serum prepared by the Moscow Mechnikov Institute, series No. 861; cardiotrast manufactured by the Lomonosov Chemopharmaceutical Factory; inulin of British manufacture.

The filtration fraction was expressed in per cent and was calculated by the formula :

$$\frac{C_{in}}{C_{ct}} \cdot 100 = FF$$

Changes in the Effective Plasma Flow, Glomerular Filtration, and Filtration Fraction during Serum Sensitization

	Background	Days of sensitization		
	average value and limits of variation	7	14	21
	Dog No. 1			
C_{ct}, ml/min	319,98 (274,95—354,00)	270,60	361,87	288,76
C_{in}, ml/min	69,05 (61,92—79,30)	73,72	89,21	80,09
FF %	21,70 (18,80—23,10)	27,26	24,66	27,73
	Dog No. 2			
C_{ct}, ml/min	249,28 (216,29—279,19)	165,65	265,22	347,38
C_{in}, ml/min	69,23 (57,11—87,88)	55,37	72,37	116,89
FF %	27,65 (22,71—32,57)	33,42	27,28	33,76
	Dog No. 3			
C_{ct}, ml/min	291,68 (285,31—297,99)	279,86	205,61	306,86
C_{in}, ml/min	76,71 (71,99—85,36)	78,45	102,47	85,91
FF %	26,30 (24,47—29,56)	28,23	49,85	27,90
	Dog No. 4			
C_{ct}, ml/min	324,85 (296,64—356,40)	244,28	172,50	179,57
C_{in}, ml/min	72,53 (62,95—77,63)	55,87	67,72	63,24
FF %	22,36 (21,22—23,39)	22,88	39,39	35,45
	Dog No. 5			
C_{ct}, ml/min	321,25 (300,00—341,25)	280,34	220,84	205,22
C_{in}, ml/min	75,38 (64,15—84,38)	86,76	71,62	83,47
FF %	23,53 (18,79—27,07)	30,99	32,46	40,67

The mean background value was calculated from three experiments; C_{ct}) effective plasma flow; C_{in}) glomerular filtration; FF) filtration fraction.

where C_{in} is the glomerular filtration; C_{ct}, the effective plasma flow; FF, the filtration fraction.

EXPERIMENTAL RESULTS

Thirty experiments were carried out on five animals (59 clearance periods, including 118 clearances of inulin and cardiotrast) and the results obtained were approximately the same (see Table).

The presence of serum sensitization in all the dogs was confirmed at the end of the experiments by the development of the usual picture of anaphylactic shock after the assaulting injection of antigen.

The effective plasma flow during the period of sensitization was characterized by a decrease of 4-46 % of the mean value of the "background" in ten of the 15 experiments. At the same time a relationship was found between the number of cases of a fall in the cardiotrast clearance and the day of sensitization. For instance, on the seventh day the cardiotrast clearance was reduced in all five animals, on the 14th day—in three animals, and on the 21st day of sensitization—in two animals. An increase of 5-39 % in the cardiotrast clearance was observed in one animal on the 14th day, and in two on the 21st day of sensitization.

On the whole the rate of glomerular filtration varied within the "background" limits. At individual moments of sensitization, however, a marked increase in the inulin clearance was observed. On the seventh day the glomerular filtration was increased in one animal, on the 14th day—in two animals, and on the 21st day of sensitization—in three animals. In dog No. 2, on the 21st day of sensitization, the inulin clearance was increased by 68 %. In two dogs, Nos. 2 and 4, on the seventh day of sensitization the inulin clearance was increased by 20 %.

In the majority of experiments (in 11 out of 15) the filtration fraction was increased in the period of sensitization. On the seventh day of sensitization an increase observed in three animals, on the 14th day—in four animals and on the 21st day— in four animals. The greatest increase in the filtration fraction (by 67-89 %) was observed on the 14th and 21st days of sensitization.

In the light of modern views on the system or regulation of the circulation of blood in the kidneys, the change in the rate of the effective plasma flow, which we observed in the serum sensitization experiment, may be explained as the result of a change in the size of the lumen of the arterioles of the glomerular apparatus. A decrease in the rate of the effective plasma flow may be connected with a reduction in the lumen of the afferent and efferent arterioles. With a constant or increased rate of glomerular filtration, however, a slowing of the effective plasma flow gives evidence of the predominant constriction of the efferent glomerular arterioles. The increase in the filtration fraction supports this explanation.

The appreciable increase in the rate of glomerular filtration in several of the sensitization experiments, with no change in or a slowing of the effective plasma flow indicates the increased permeability of the glomeruli.

From a comparison of the data on the effective plasma flow, glomerular filtration, and filtration fraction, it may be concluded that constriction of the efferent glomerular arterioles took place in the sensitization experiments (in 11 of 15 experiments). Meanwhile, in two experiments (dogs Nos. 2 and 4 on the seventh day of sensitization), constriction of the afferent arterioles took place, for a decrease in the inulin and cardiotrast clearances was observed. In the overwhelming majority of experiments, sensitization thus had a marked vasoconstrictor effect. From these results it is possible to suggest an explanation of the increase in the pressor vascular reaction in the kidneys of sensitized dogs under our experimental conditions. In connection with V. M. Khramov's findings [9], showing an increase in the pressor vascular reactions in rabbits sensitized to horse serum, while the region of the kidneys in the animals was simultaneously cooled, such a hypothesis appears to us to be justified.

It has been shown [3] by morphological investigations that, during sensitization of rabbits, hyperemia of a large proportion of the glomeruli is observed. This can be explained in the light of our experimental results as the result of constriction of the efferent arterioles.

SUMMARY

Experiments were performed on 5 male dogs with ureteric orifices exteriorized into the abdominal skin. The author studied the effect of serum sensitization on the effective plasma flow (determined by means of cardiotrast), on the glomerular filtration (determined by inulin), and on the filtration in the kidneys. A reduction of cardiotrast clearance was noted in the majority of the experiments; inulin clearance was changed within limits approaching normal values; however, in individual cases it was markedly increased and as a rule the filtration fraction showed a rise.

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