THE EFFECT OF LARGE DOSES OF RAT GAMMA
GLOBULIN ON NEPHRECTOMIZED RATS

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THE EFFECT OF LARGE DOSES OF RAT GAMMA
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In the recent literature there are references to the claim that
massive doses of heterologous gamma-globulin (bovine) are able to induce
nephrectomized rabbits diffuse but transitory glomerulonephritis (Bowen
and Janeway, 1947; Moore and co-workers, 1949).

The aim of the present work is the determination of the influence
of massive doses of homologous gamma-globulin on nephrectomized animals.

The experiments were conducted on 14 rats with unilateral nephrec-
tomy. On the fifth day after surgery, rat 6.5% gamma-globulin in a dose
of 0.5 ml per 100 gr. of weight was introduced intravenously to the
animals every other day. Gamma-globulin was isolated from serum by
means of the rivanol method of Korshak. The purity of the gamma-globulin
was checked by means of electrophoresis on paper; the addition of other
protein fractions did not exceed 2% (Fig. 1). Each rat received from 2
to 9 injections of gamma-globulin.

On the 6th-9th day after the last injection, albuminuria and hematuria
originated in the rats; on 10-14th day, cylindruria. 11 rats perished on
9-30th day after the last injection, at the time of death the amount of re-
sidual blood nitrogen in them equaled 156-400 mg% (the 14th rat died of an
accidental cause). Upon dissection, ascitis and hydrotorax were dis-
covered in five rats; in all rats the kidneys appeared considerably en-
larged with a grayish-yellow anemic cortex and brightly-pink medullary
substance. Microscopically, in the kidneys a picture was discovered
which recalls proliferative intracapillary glomerulonephritis with sharp
swelling of vascular loops, protein exudate into the cavity of Bowman's
capsulae (Fig. 2 and 3); in 3 rats which survived until the 30th day, rich
desquamation of peritubular loops and considerable swelling of the
cells of epithelium of the capsule on the side contralateral to the neck
of the glomeruli were noted (Fig. 4). From the sides of the epithelium
of convoluted tubules, granular degeneration and hyalin-droplet degener-
ation of protoplasm was noted, in the lumen of straight and convoluted
tubules, homogenous albumin masses and hyalin cylinders.

In the given series of experiments 14 rats with unilateral
nephrectomy served as control, at the same times and in the same doses,
rat serum without gamma-globulin was introduced to them (Fig. 5). In
these animals, insignificant albuminuria (0.09-0.12%) appeared, which
disappeared soon after the termination of injections.

40 days after the last injection of serum all rats were sacri-
cificed. The residual nitrogen of the blood by this time equaled 36-42
mg%. In dissection the kidney appeared somewhat enlarged, the cortex
and medulla substance were of the usual color. Under microscopic exami-
nation the glomeruli appeared somewhat enlarged, the lumen of capsules
appeared free, in vascular loops with the usual density of nuclei place-
ment, granular degeneration was observed from the side of the convoluted
tubules (Fig. 6).

We also have investigated microscopically the kidneys of rats with
unilateral nephrectomy (on 25-30th day after surgery), which were not sub-
jected to any influences. No changes were discovered in these kidneys,
extcept for insignificant increase in size of glomeruli.

On the basis of clinical and pathomorphological data concerning
rats to which hemologic gamma-globulin was introdused intravenously, it
is possible to assume in them proliferative intracapillary glomerulone-
phritis.

CONCLUSION

Proceeding from the concept of glomerulonephritis as an allergic
organic reaction, it is also possible in the described experiment to
find the realization of a peculiar allergic mechanism, namely: that with
rat gamma-globulin, either ready antirenal antibodies have been intro-
duced, or, under the conditions of unilateral nephrectomy, the introdused
gamma-globulin assumes nephrotoxic properties.

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Fig. 1. The curve characterizes the content of admixtures in the introduced gamma-globulin of veronal-medinal buffer; pH = 8.6. At the bottom electrophrogram: wide dark band corresponds to the fraction of gamma-globulin.
Fig. 2. Intracapillary productive glomerulonephritis; death on 16th day after the last introduction of gamma-globulin (staining with hematoxylin-eosin. X 200).

Fig. 3. Fibrinoid swelling and homogenization of the glomerular loops. Death on 7th day after the last introduction of gamma-globulin (staining with hematoxylin-eosin. X 200).
Fig. 4. The beginning of the formation of a crescent (left segment of glomerulus). Death on 28th day after last introduction (staining with hematoxylin-eosin. X 200).
Fig. 5. Solid line—serum deprived of gamma-globulin; the upper electrophoregram corresponds to it; dotted line—normal rat serum; the lower electrophoregram corresponds to it. The conditions of electrophoresis are the same.
Fig. 6. The kidney of a rat from the control group - certain increase of glomeruli size, granular dystrophy of epithelium of convoluted tubules; 40 days after the last introduction (staining hematoxylin-eosin. X 200).