

THE EFFECT OF UNILATERAL NEPHRECTOMY ON THE SENILE ATROPHY OF THE KIDNEY IN THE WHITE RAT

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(Received for publication, October 26, 1929)

Arataki (1) has demonstrated that there is a decrease in the number of glomeruli in the kidney of the white rat in old age. According to Arataki (1) this senile loss of glomeruli begins after 350 days of age and reaches two-thirds of the adult value at 500 days of age. Since this atrophy is not accompanied by gross or histologic evidence of pathologic destruction of the glomeruli, we may tentatively consider it as physiologic.

Arataki (2), Jackson and Shiels (3) Moore (4) and others have demonstrated that unilateral nephrectomy during the growth period (1 to 150 days of age) has no effect on the total number of glomeruli in the adult kidney. We have found no published reports concerning the effect of unilateral nephrectomy on senile atrophy.

Method

Thirty-two white rats from the colony of the Dept. of Zoology of Yale University were used, and are designated as the Yale Strain.† All animals were 200 days of age at the beginning of the experiment. The right kidney was removed from 16 animals by the usual lumbar route, under ether anesthesia. The remaining 16 animals were used as controls. Two animals from each group were sacrificed by a blow on the head at intervals of 30 days and the left kidney was injected with Janus Green B according to the technique of Nelson (5). The right kidney of the control animals was fixed in Zenker formol, embedded in paraffin and sectioned for histologic examination and measurement of glomeruli.

The total number of glomeruli in the injected kidneys was counted according to the technique of Nelson (5). In all cases the counts are complete enumerations of the left kidney.

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† This designation is necessary, since in the quantitative studies on the kidney carried on in this laboratory, three strains of white rats have been used.

TABLE I
Nephrectomy at 200 Days of Age

Experimental			Control		
Rat No.	Count	Weight	Rat No.	Count	Weight
Sacrificed 230 days (Dec. 1-1928)					
		gms.			gms.
3	28,756	195	23	28,092	170
4	41,427*	215	18	40,369*	216
Sacrificed 260 days (Jan. 1-1929)					
1	28,142	195	20	24,299	193
2	26,000	182	17	25,745	185
Sacrificed 290 days (Feb. 1-1929)					
5	20,569	245	22	21,693	253
6	25,121	223	25	26,491	223
Sacrificed 320 days (Mar. 1-1929)					
7	18,549	248	24	17,272	225
8	22,687	200	29	21,541	200
Sacrificed 350 days (April 1-1929)					
9	21,870	210	27	24,093	210
10	22,333	205	18	24,538	205
Sacrificed 380 days (May 1-1929)					
11	22,723	185	26	22,591	185
12	21,504	185	19	22,526	200
Sacrificed 410 days (June 1-1929)					
13	17,727	153	30	23,727	157
14	28,967*	195	28	24,227	200
Sacrificed 440 days (July 1-1929)					
15	29,889*	158	32	22,939	158
16	21,725	180	31	22,116	177

* These animals are of a different strain. See discussion in the text.

RESULTS

The results may be divided into two series of observations, first, the total glomerular counts, and second, glomerular sizes.

Inspection of Table I and Fig. I reveals that control animals with a count of about 28,000 at 230 days of age gradually decline to a count of 18,000 to 22,000 at 320 days of age. After 320 days of age there is little further loss of glomeruli. This is in general agreement with the results of Arataki (1).

It is further quite evident that there is no significant variation between the control and experimental animals. The experimental method precludes any quantitative observations on increase in

TABLE II

Age	Size of glomeruli (microns)		
	Minimum	Maximum	Average
<i>days</i>			
230	70	123	95.2
440	38	157	103.6

TABLE III

Age	Average diameter of glomeruli (microns)	Total number of glomeruli	Total glomerular surface mm. ² ($4\pi r^2$ = surface)
Adult.....	95.2	28,092	799.7
Senile.....	103.6	22,527	759.6

weight, but on inspection, the left kidney of the experimental group was appreciably larger than the controls. These results force the conclusion, that despite increase in size, unilateral nephrectomy during adult life has no effect on the senile atrophy of the opposite kidney as expressed in renal units.

Variations in the size of glomeruli were determined by measuring in Zenker fixed, paraffin sections, the diameters of 200 glomeruli at hilus level, in one adult and one senile kidney. The results are shown in Table II and plotted as frequency curves in Fig. II. The glomeruli in the senile kidney average 8.5 microns larger and show greater

variation in size. If the total surface of the visceral layer of Bowman's capsule is calculated, (Table III) it is found that the loss in renal units is accompanied by an increase in size. That this glomerular enlargement is a true hypertrophy, is not apparent at this time, since there is no evidence that the larger glomerulus has a greater functional capacity. The finding of a greater variation in the size of the glomeruli in senile atrophy is not in harmony with the results of Karsner, Saphir and Todd (7) in cardiac atrophy. In an atrophic heart,

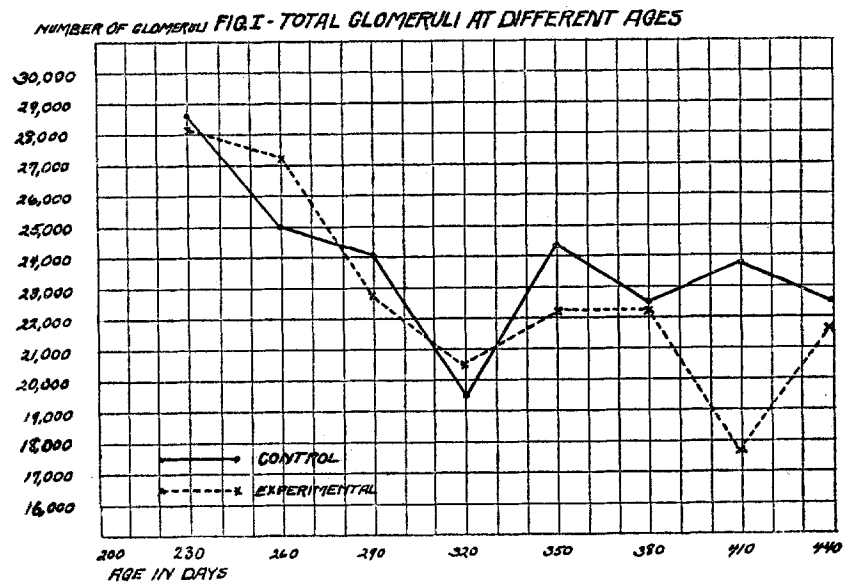


FIG. I

associated with tuberculosis, they found a greater uniformity in the size of muscle fibers than in a normal heart. This variation of morphology in two types of atrophy does not support the hypothesis of Bradley (8) of a single pathogenesis of decreased blood supply.

The method of disappearance of glomeruli in old age is interesting. As yet we have been unable to follow the process. Our present observations are confined to a complete serial section of the right kidney of a rat 440 days of age. In these sections there are insufficient fibrotic glomeruli to account for the total loss and we are inclined to

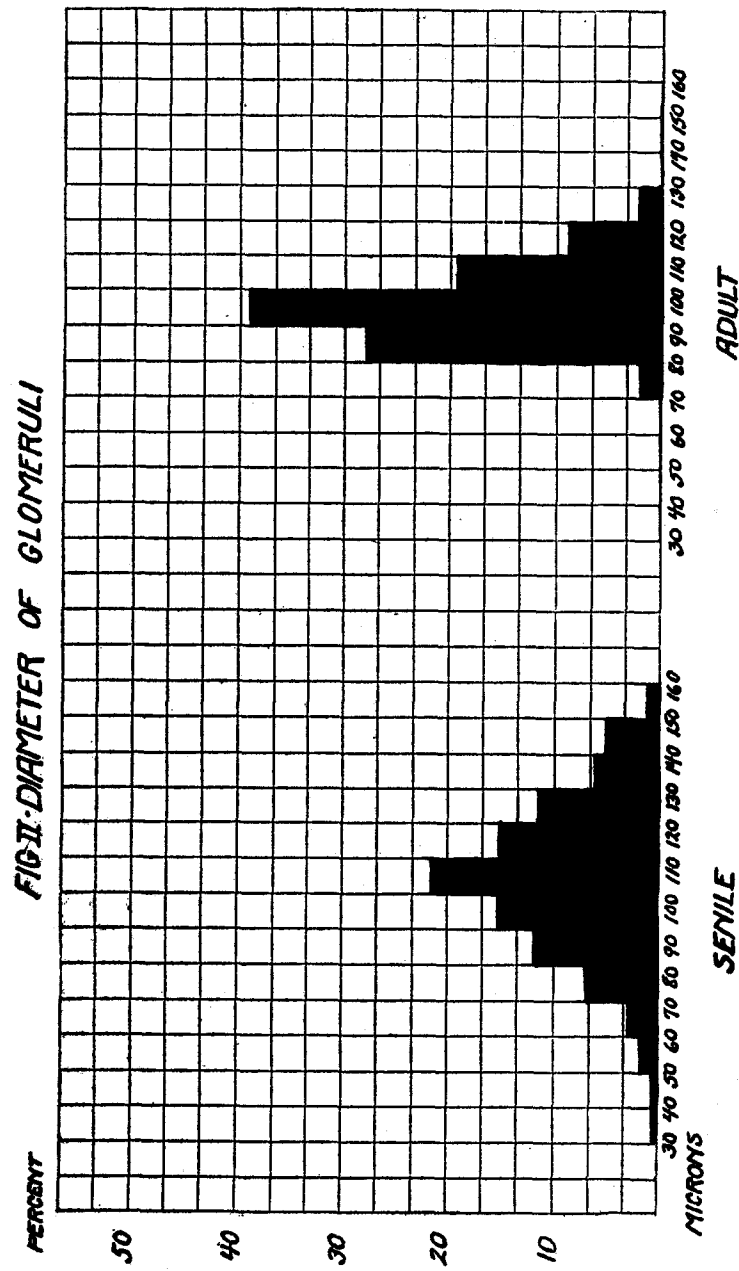


FIG. II

accept a process of gradual atrophy and complete disappearance as proposed by Chase (6) in *Necturus*.

The counts on rats No. 4, 14, 15 and 18 are worthy of further comment. The rats designated here as the Yale strain are a mixture of the Wistar rat and an ordinary wild rat. It is evident that this Yale strain is a hybrid stock composed of two substrains, one with 40,000 and the other with 30,000 renal units. This finding together with the possible effect of heredity on the total number of glomeruli is under investigation at the present time.

DISCUSSION

The results here reported have significance in the interpretation of the remote effects of unilateral nephrectomy in man. The investigation of Hayman and Starr (9) and Moore and Lukianoff (10) have demonstrated that the fluid output of the kidney is dependent in general on the total number of open glomeruli and this latter factor is limited by the total glomerular units in the kidney. If we postulate that approximately 25% of the glomerular filtration space is necessary for basal demands, it follows that the removal of one kidney during adult life leaves a reserve of 100%, but as this same animal approaches senility, further glomerular units are lost and a reserve of only 33% remains. Since the kidney of man undergoes analogous senile changes, it may be safely assumed that a patient under similar circumstances, would develop renal insufficiency after a kidney injury, innocuous to a patient with both kidneys.

The conclusions arrived at in this paper add quantitative support to the doctrine that "old age is inevitable." The senile loss of glomeruli proceeds at the usual rate and to the same extent despite the absence of one kidney. The relations between the total glomerular units and the number of open glomeruli in senile kidneys and the changes in circulation dependent on senility are under investigation in this laboratory.

Arataki (1) found that senility in the Wistar rat occurred after 350 days of age, while our observations place the time at about 300 days. It is possible that senility occurs at different ages in different strains of the same species. Unpublished observations from this laboratory indicate a wide variation in the age period of senile glomerular loss in the human kidney.

CONCLUSIONS

1. In senility in the white rat there is a decrease in the total number of glomerular units.
2. The decrease in glomerular units is associated with an increase in the average diameter and a greater variation in size, of the remaining glomeruli.
3. Unilateral nephrectomy during adult life has no effect on these senile changes.

We wish to thank Dr. Howard T. Karsner for aid in the preparation of this paper, and Dr. J. S. Nicholas for the use of his laboratory for the investigation.

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