ARTERIAL HYPERTENSION IN RATS

II. Effects on the Kidneys

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Plates 13 to 16

(Received for publication, February 9, 1942)

The exact relation between disease of the renal arterioles and arterial hypertension is not understood. It is not known whether the observed sclerosis and necrosis of the arterioles of the kidneys cause renal ischemia and therefore hypertension or are merely a consequence of elevation of the blood pressure. In some animals the evidence gained in experiments suggests, however, that the appearance in the renal arterioles results from hypertension. By partially constricting one renal artery in rats Wilson and Byrom (1) were able to bring about elevation of blood pressure and necrotizing arteriolitis in the vessels of the other kidney, indicating that in rats, at least, arteriolar disease is occasioned by hypertension. Their work has not received the notice it deserves. If their findings were substantiated in other animals and in man, some of the factors contributing to arterial hypertension would be made more clear. Unfortunately the experiment cannot be performed in dogs, as chronic hypertension does not usually result from affecting one kidney when the other is intact.

It appeared rewarding, on the plan of Wilson and Byrom, to attempt to ascertain further the relation of arteriolar disease to arterial hypertension in rats and to observe the effects upon one kidney of various kinds of injury to the other. It has been shown that unilateral renal injury results in cardiac hypertrophy, an indication of the presence of hypertension (2). The current study deals with changes in the renal arterioles associated with the latter condition.

Methods

The left kidneys of 80 rats were injured either by partial constriction of the renal artery, by the production of hydronephrosis, by trauma, or by placing cellophane around them (2). Eighteen more rats were injected with adrenalin in oil or pitressin and estradiol, and six with other substances (renin, dihydroxyphenylalanine, tyrosinase).

The animals were killed, after a suitable interval, the hearts weighed as previously described (2), and the kidneys fixed in Zenker acetic acid solution. Sections were stained either with eosin-methylene blue, hematoxylin and eosin, or Mallory's connective tissue stain. They were then examined by one of us who had had no previous knowledge of which of the rats had exhibited arterial hypertension. The degree of the following anatomical changes in each kidney was estimated and recorded in terms

of one to four plus: the presence of hyalinization of the glomeruli singly or in groups, proliferation of the parietal layer of Bowman's capsule (crescent formation), infiltration of the interstitial tissue by round cells, atrophy of the tubules, and replacement fibrosis. The condition of the vessels was estimated in a similar manner by ascertaining the presence or absence of the following: intimal proliferation of the arterioles, necrosis of their walls, hypertrophy of their muscles, hyaline degeneration, hyperplasia of the internal elastic membrane of the small arteries, and hyalinization of their walls. The presence of small hemorrhages in the substance of the kidney was noted, as was any other abnormality. A decision was then made as to the resemblance of these kidneys to those found in arterial hypertension particularly in so far as vascular change was concerned. The results of the microscopic examination were then compared with data obtained during the life of the animals, and with such changes as had taken place in the weights of their hearts.

RESULTS

The pathological findings were used to group the rats into two general classes. In the one, arteriolar lesions, including marked hypertrophy of the muscle, narrowing of the lumen, and partial to almost complete necrosis of the wall were the predominating features. These lesions bore a close resemblance to the arteriolar changes in the kidneys of rapidly progressive hypertension in human beings. In the other, arteriolar lesions were either non-existent or limited to variable but slight hypertrophy of the muscle. In this group the predominating pathological features were confined to the glomeruli, which showed thickening of the parietal layer of Bowman's capsule and various stages of hyalinization. Only the kidneys exhibiting arteriolar changes were believed to represent those of hypertensive animals. How closely this division according to pathological findings alone corresponded with other signs of hypertension such as the level of the blood pressure and cardiac weight found postmortem will now be described.

Fifty-nine rats exhibited cardiac hypertrophy. The kidneys of 51 (86 per cent) showed changes in the renal arterioles of various degrees and in 3 others slight lesions were noticed. In 45 cases there was no cardiac hypertrophy; in 36 there were few or no renal arteriolar lesions (Tables I to V).

When one kidney was injured by hydronephrosis, by partial constriction of the renal artery, by trauma, or by cellophane, arteriolar changes occurred in the opposite kidney with great regularity (Figs. 1 to 13). Of 52 rats so treated which exhibited cardiac hypertrophy, renal arteriolar lesions occurred in 47. Cardiac hypertrophy did not occur in the cases of 25; yet in the unaffected kidneys of 9 of these similar lesions were seen in the arterioles (Tables I to IV).

Rats given various chemical compounds (in an attempt to induce hypertension) and exhibiting cardiac hypertrophy developed renal arteriolar lesions with less regularity (Table V). Of 2 injected with pitressin and estradiol benzoate, renal changes occurred in 1. Of 4 injected with adrenalin in oil,

TABLE I

Effects of Unilateral Hydronephrosis

Rat No.	Change in heart weight*	Blood pressure‡	Time after injury	Kidney examined	Anatomical changes in kidneys									Remarks
					Arterioles			Change in arteries§	Tubular atrophy	Glomerular hyalinization‖	Small hemorrhages	Interstitial tissue**	Kidney hypertensive‡‡	
					Muscular hypertrophy	Hyaline degeneration	Necrosis of wall							
	per cent	*mm. Hg*	*days*											
H 96	+35	140/110	15	Both	++	+			+	+			Yes	Slight hydronephrosis
H 99	+31	167/112	23	R	++	+			+	+			Yes	Slight hydronephrosis
H 150	+31	148/112	23	L	++				++	+++		F		Moderate hydronephrosis
				R	++								Yes	
H 95	+27	140/105	15	Both	++	+			+	+			Yes	Slight hydronephrosis
H 97	+25	170/135	30	Both	++	+			+	++			Yes	Slight hydronephrosis
H 94	+18	150/120	28	Both	++	+			+	++			Yes	Slight hydronephrosis
H 100	+15	148/112	27	L	++	+		++	+++	++	+	F		Slight hydronephrosis
				R	++	+		+	++	+		F	Yes	
H 148	+14	168/122	109	L	++	++	++		++++	++++		F and R		Destruction of kidney
				R	++	++	+++		+	+++			Yes	
H 93	+12	168/128	22	Both	++	+			+	++			Yes	Slight hydronephrosis
H 149§§	+6	105/60	33	L			++++		++++	++		F and R		Destruction of kidney
				R	+					+			No	
H 147§§	+3	100/58	33	L		++++	++++		++++	++++		F and R		Destruction of kidney
				R	+				+	+			No	
H 143§§	−1	90/52	42	L					++	+++				Marked hydronephrosis
				R						+			No	
H 141§§	−3	95/60	42	L					++	+++		F		Marked hydronephrosis
				R						+			No	
H 145§§	−3	100/62	33	L					+++	+		F		Destruction of kidney
				R					+	+			No	
H 146§§	−6	100/58	33	L					++	+++				Marked hydronephrosis
				R						±			No	

§§ Total ureteral occlusion.

In the tables the significance of the symbols is as follows:

* = based on the formulas of Rytand (5).

‡ = measured by Hamilton's optical manometer. The first figure represents the systolic, the second the diastolic pressure.

§ = *i.e.* proliferation of internal elastic membrane, hyalinization of walls, muscular hypertrophy.

‖ = *i.e.* singly or in large foci.

** = F indicates fibrosis, R indicates infiltration by round cells.

‡‡ = an estimation of the general appearance of the kidney and its resemblance to those observed in hypertensive animals.

Changes are indicated by a plus (+) sign, and their degree estimated on the basis of one to four plus. When no symbol is given, there were no lesions.

they were present in 2. The kidneys were essentially normal in 10 of 12 animals failing to develop cardiac enlargement.

TABLE II

Effects of Unilateral Trauma

Rat No.	Change in heart weight*	Blood pressure†	Time after injury	Kidney examined	Anatomical changes in kidneys									Remarks
					Arterioles									
					Muscular hypertrophy	Hyaline degeneration	Necrosis of wall	Change in arteries§	Tubular atrophy	Glomerular hyalinization‖	Small hemorrhages	Interstitial tissue**	Kidney hypertensive††	
	per cent	*mm. Hg*	*days*											
I 21	+31		24	L	±	±								Hemorrhages
				R	±	±							No	
I 19	+23	148/112	30	L	±				+	+				No gross lesions
				R	±				+	+			No	
I 9	+21	160/112	120	L	++	++			+	±		F and R		
				R	++	++			+	±			Yes	
I 10	+18	95/72	122	L	+	+		+	+	+		F		
				R	+			+	++	+			Yes	
I 20	+7	120/84	24	L	±				+++	++++		F and R		Split and scarred
				R	±					±			No	
I 11	+5		122	L					+	+				
				R					+	+			No	
I 2	+4	130/95	9	L										Grossly scarred
				R					+	+			No	
I 5	+2	100/80	7	L										Necrotic and infarcted
				R	+	+			++	++		F	No	
I 4	−1	125/100	35	L					+	+				Contracted and scarred
				R									No	
I 17	−2	135/100	84	L					+	+		F and R		Scarred
				R						+			No	

Two were given dihydroxyphenylalanine, 1 renin, 3 tyrosinase. The arterioles of their kidneys were unchanged. No lesions were found in the kidneys of 10 normal rats.

There was a very rough correlation between degrees of cardiac hypertrophy and changes in the renal arterioles induced by the several varieties of unilateral renal injury. The most marked renal lesions were in general associated with the greatest cardiac hypertrophy, but there were many exceptions. An at-

tempt was made to find whether there was a relation between the degree of renal damage in the untreated kidney and the number of days after the other was injured. Marked changes occurred as early as 7 to 14 days. Five animals developing "malignant hypertension" (1) were allowed to survive for 2 months or more and their kidneys were more severely damaged.

When elevation of the blood pressure was considered an indication of the hypertensive state, about the same relative number of animals (88 per cent) developed changes in their kidneys as when cardiac hypertrophy was taken as the sign (Table VI). Single estimations of blood pressure have little value, especially when the pressure is normal or low in the presence of cardiac hypertrophy, since a state of shock is easily induced when such a condition obtains. But of the 32 animals which exhibited elevation of blood pressure 28 developed renal vascular lesions, and in 12 these included necrosis. Of 8 rats with normal hearts and elevated blood pressures, they were present in 6. When cardiac hypertrophy and elevation of blood pressure were considered together, roughly the same proportion (85 per cent) exhibited renal lesions and a similar one, necrosis of arterioles. Renal lesions were found in only 5 animals with normal hearts and normal blood pressures—all in rats subjected to partial constriction of a renal artery (Table VI).

The survival of renal tissue in the injured kidney at death was not always necessary for the development of hypertension or vascular lesions. The affected kidney was atrophic in 13 animals in which the renal artery had been constricted; 7 of these developed cardiac hypertrophy and 9 arteriolar lesions. On the other hand functioning of a partially injured hydronephrotic kidney seemed to be necessary for the development of hypertension and arteriolar lesions (Table I, Figs. 1 to 7).

Cardiac hypertrophy occurred in 3 cases when the left kidneys had been injured and the right ones remained normal. In 1 rat the injured organ was completed atrophied, in 1 full of hemorrhagic areas, and in the other the renal tubules were atrophied. In 2 cases after adrenalin, and 1 after pitressin and estradiol had been given, cardiac hypertrophy was found in the presence of normal kidneys.

Renal arteriolar lesions occurred without cardiac hypertrophy in 11 animals. The blood pressure was elevated in all but 5 in which renal arteries were constricted. It was elevated without cardiac hypertrophy in only 2 instances when the kidney was considered normal.

Although in most instances glomeruli showed hyaline degeneration, in only 3 was there seen proliferation of the parietal layer of Bowman's capsule (crescent formation), such as occurs in glomerulonephritis. On the other hand, necrosis of the walls of arterioles was common, being found in 34 animals. Five of these did not exhibit cardiac hypertrophy although the blood pressures of 3 were elevated.

TABLE III

Effects of Partial Constriction of One Renal Artery

Rat No.	Change in heart weight*	Blood pressure†	Time after injury	Kidney examined	Anatomical changes in kidneys									Remarks
					Arterioles									
					Muscular hypertrophy	Hyaline degeneration	Necrosis of wall	Change in arteries§	Tubular atrophy	Glomerular hyalinization‖	Small hemorrhages	Interstitial tissue**	Kidney hypertensive‡‡	
	per cent	*mm.Hg*	*days*											
174	+77		59	L	+	+++	++	+	+++	+++		F		Partially atrophic
				R	+	+++	+++	+	+++	++		F	Yes	
158	+75	168/135	35	L	+	++	+++	++	+++	+++		F		
				R	++	+	++++	+++	++	++		F	Yes	
151	+52	110/80	35	L	++	++	++	+	++++	++++		F		
				R	+++	++++	++++	++	+++	++		F	Yes	
121	+48	118/90	10	L	++	+	+		+++	+++	+	F and R		
				R	+++	+	+				+	R	Yes	
103	+48		11	L	+++	++	+	++	+++	++	+	F		
				R	+++	+		++	+++	+	+	F	Yes	
107	+46	88/58	7	Both	+	++	+	+	+	+	+	F and R	Yes	
156	+37	80/49	14	L					++++	+++	++++	F		Partially atrophic Enlarged
				R	+	++	++		+	+			Yes	
168	+37	40/22	61	L	+++	+		+	++++	+++		F and R		
				R	++++	+++	++++	++	+++	++	+	F	Yes	
123	+36	120/104	16	L										Completely atrophic
				R	++	+	+			+	+		Yes	
110	+35	130/106	41	L										Completely atrophic
				R	++	+							Yes	
106	+32	148/105	7	L	++	++		++	+	+		F		
				R	++	+		++	++	+			Yes	
175	+28	170/122	68	L										Completely atrophic
				R	+	+++	++	++		+	+		Yes	
154	+28	138/90	9	L	+	+	+		+	+	+			
				R	++	+			++	++			Yes	
115	+27	146/120	7	Both	+++	+	++		+++	++	+	F and R	Yes	
108	+26	110/64	12	L	++	++	+	+	++	++	+	F		
				R	++	++	+	++	++	+			Yes	
112	+26	72/62	4	L										Completely atrophic
				R						+			No	
116	+26	110/98	20	L										Almost completely fibrotic
				R	++	+		+	+	+			Yes	

TABLE III—*Concluded*

Rat No.	Change in heart weight*	Blood pressure‡	Time after injury	Kidney examined	Anatomical changes in kidneys									Remarks
					Arterioles									
					Muscular hypertrophy	Hyaline degeneration	Necrosis of wall	Change in arteries§	Tubular atrophy	Glomerular hyalinization‖	Small hemorrhages	Interstitial tissue**	Kidney hypertensive‡‡	
	per cent	*mm. Hg*	*days*											
122	+25	150/112	14	Both	++	+	+		+	+			Yes	
167	+24	50/28	61	L										Uremia. Completely atrophic
				R	+++	++	+++	++	+	+	+	F	Yes	
170	+18	140/100	61	L										Completely atrophic
				R	+					+			No	
104	+18	160/134	32	Both	++				++	+		F and R	Yes	
126	+15	112/80	8	L	+	+	+		++++	++++	+	F and R		
				R	++	+	+				+		Yes	
152	+13	140/102	30	L		++		+	+++	+++		F		
				R	+++	++	++	++	+	+			Yes	
176	+11	132/92	68	L										Atrophic
				R	+++					+	+		Yes	
118	+8	120/82	12	L										Atrophic
				R					++	+			No	
169	+5	178/128	61	L										Atrophic Enlarged
				R									No	
172	+2	110/60	75	L										Atrophic
				R	+++	+++	++	+	+	++			Yes	
162	+1	160/122	7	R	+++	+	+	+	+++	+		F	Yes	
161	+1	160/130	70	L										Atrophic
				R	++	+++	+	++	++	++			Yes	
153	−1	120/82	35	L	+	+++	++	++	++++	++++		F		
				R	+++	++		++	+	+			Yes	
160	−2	150/102	7	R	+++					+			Yes	
166	−2	132/96	56	R	+++	++			++	+			Yes	
164	−5	88/42	56	L										Atrophic
				R						±			No	
GN140§§	+22	162/128	5	L	++	++				±			Yes	

§§ Opposite (right) nephrectomy performed.

TABLE IV

Effects of Unilateral Cellophane Perinephritis

Rat No.	Change in heart weight*	Blood pressure†	Time after injury	Kidney examined	Anatomical changes in kidneys									Remarks
					Arterioles			Change in arteries§	Tubular atrophy	Glomerular hyalinization‖	Small hemorrhages	Interstitial tissue**	Kidney hypertensive‡‡	
					Muscular hypertrophy	Hyaline degeneration	Necrosis of wall							
	per cent	*mm.Hg*	*days*											
C 9	+66	98/55	59	R		+++	+		+++	++	+	F	Yes	
C 20	+38	142/102	36	R	++	++	+		+	±			Yes	
C 6	+37	120/60	36	L										Infection
				R	+++	++	++	+	+++	++		F	Yes	Large cortical hemorrhage
C 5	+36	162/80	21	R	+++	++			+	+			Yes	
C 8	+33	160/120	73	L										Infection
				R	+	+++			+	+			Yes	
C 19	+27	62/28	33	R	+	+++	++	+	++	++		F	Yes	
C 7	+25	120/86	60	L										Slight infection
				R	++	+	+++	+	+	+	+		Yes	Cortical hemorrhages
C 3	+24	170/106	27	L					++++	++++		F & R		Infection
				R		++	+++	++	++	+++	++	F	Yes	Hydronephrotic
C 10	+24	90/70	16	R	++	++	+		++	+++		F	Yes	
C 12	+23	172/98	16	L										Severely scarred
				R	++	+++	+++	+	+	+		F	Yes	
C 13	+20	160/130	31	R		+++	+++	+	++++	+++	+++	F	Yes	
C 14	+19	160/102	44	L	++	+++	++++	+	+	+				
				R	+	+++	+		+	+			Yes	
C 15	+18	178/117	58	L										Infection
				R	++	+	++++	++	+	++	+		Yes	
C 1	+17	145/102	59	L										Infection
				R	++	+++	+++	+	+++	++		F	Yes	Hydronephrotic
C 17	+16	190/150	31	L	+++	++	+		++++	++++		F		
				R	+++	++	++		++	++			Yes	Cortical hemorrhages
C 4	+6	160/106	28	L	++	+	++		++	++				Infection
				R	+++	+			+	+			Yes	
C 11	+5	150/90	38	R						±			No	
C 16	−1	165/128	31	R	++	++			+	±			Yes	
R 24	+6	148/106	60	L										No fibrous capsule
				R		+			+	++		F	No	
R 23	−6	112/78	60	L										No fibrous capsule
				R						±			No	
R 26	−7	130/102	60	L										No fibrous capsule
				R	±					±			No	

C = cellophane capsule. R = rayon capsule.

TABLE V

Rat No.	Change in heart weight*	Blood pressure‡	Time after injury	Kidney examined	Anatomical changes in kidneys									Remarks
					Arterioles									
					Muscular hypertrophy	Hyaline degeneration	Necrosis of wall	Change in arteries§	Tubular atrophy	Glomerular hyalinization‖	Small hemorrhages	Interstitial tissue**	Kidney hypertensive‡‡	
Effects of pitressin														
	per cent	*mm. Hg*	*days*											
P 21	+25	174/124	70	Both	+++	+		++	+	+		F	Yes	
P 18	+18		7	L R						±			No	
P 13	+11	125/75	10	R						±			No	
P 7	+6	110/70	4	R						±			No	
P 16	+4	170/122	40	Both	+	+			+	+++			Yes	Cortical scars
P 14	−1	130/90	9	R						±			No	Cortical scars
P 17	−8	140/98	10	R						±			No	
P 19	−13	142/88	16	R						±			No	
Effects of adrenalin														
A 20	+30		1	L	++	++			++	+			Yes	Small cortical hemorrhages
A 13	+25		1	L	++	+		+		±			Yes	
A 17	+16		14	L						+			No	Small cortical hemorrhages
A 14	+13	162/124	14	L						±		F	No	
A 22	+6		1	L	±					±			No	
A 21	+1		1	L	±								No	Small cortical hemorrhages
A 18	+1	134/104	14	L									No	
A 19	0		1	L	+					+			No	Small cortical hemorrhages
A 15	−1	158/119	16	L R	± +					±			No	Small cortical hemorrhages
A 16	−3	155/116	16	L	++	+				+			Yes	
Effects of miscellaneous substances														
N 33	−9	122/108	23	Both								F	No	Given tyrosinase
N 34	−1	90/79	16	Both					+	+		F	No	Given tyrosinase
N 43	+7	128/80		Both	+				+++	+		R	No	Given tyrosinase Spontaneous pyelonephritis
N 47	+15	144/106	26	Both	±					±			No	Given renin
N 70	−7	140/92	9	Both						±			No	Given dopa
N 71	+4	116/75	9	Both						±			No	Given dopa

The injured kidney appeared to be included in the hypertensive process along with the uninjured. This was to be expected in the cases of those animals with kidneys affected by hydronephrosis, by trauma, and by cellophane perinephritis (Figs. 12 and 13), exposed as they were to the elevated blood pressure. When the renal artery was partially constricted, however, the affected kidney should theoretically have been "protected" by the constriction. This was not the case (Figs. 8 and 9). Of the 28 of 33 animals developing

TABLE VI

Summary of Results in 104 Rats

Type of injury	No. of animals	Cardiac hypertrophy			Elevation of blood pressure			Cardiac hypertrophy or elevation of blood pressure			No cardiac hypertrophy or elevation of blood pressure		
		No. of cases	Renal arteriolar disease	Necrotic lesions	No. of cases	Renal arteriolar disease	Necrotic lesions	No. of cases	Renal arteriolar disease	Necrotic lesions	No. of cases	Renal arteriolar disease	Necrotic lesions
Hydronephrosis	15	9	9	1	8	8	1	9	9	1	6	0	—
Trauma	10	4	2	0	2	1	0	4	2	0	6	0	—
Partial constriction of renal artery	34	24	22	17	9	8	6	28	25	19	7	5	1
Cellophane perinephritis§§	18	15	15	13	8	8	5	17	17	13	1	0	—
Rayon sac	3	0	0	—	0	0	—	0	0	—	3	0	—
Adrenalin in oil	10	4	2	0	3	1	0	6	3	0	4	0	—
Pitressin and estradiol	8	2	1	0	2	2	0	3	2	0	5	0	—
Miscellaneous	6	1	0	—	0	0	—	1	0	—	5	0	—
Total	104	59	51	31	32	28	12	68	58	33	37	5	1
Per cent			86	61		88	43		85	57		14	20

§§ In this series a diastolic pressure of > 100 mm. Hg was considered to indicate hypertension when the systolic was > 150 (2). In all other cases 110 mm. Hg was taken as the upper limit of normal.

renal arteriolar changes, the affected kidneys were atrophic in 10, in 3 they were not examined, and in only 2 of the remaining 15 was there any marked difference in the arterioles of the injured and the uninjured sides (Figs. 10 and 11). One animal subjected to partial constriction of the left renal artery and right nephrectomy is included; lesions were present in the affected kidney (Table III).

DISCUSSION

In the light of these experiments it is clear that when one kidney of a rat is damaged by one of several methods renal vascular lesions occur with great

regularity in the opposite one when signs of arterial hypertension result. It is probable that vascular disease of this nature can, therefore, be caused by one of two factors; elevation of the blood pressure or some harmful substance released by the injured kidney. There is considerable difficulty in deciding which is responsible for the changes observed and what is the sequence of events. Injury to one kidney may cause the release of some pressor substance which raises blood pressure. The vessels of the other kidney may then be included in a general process of vasoconstriction, and respond by becoming hypertrophied. Or, injury to one kidney may cause the release of some vascular toxin which occasions lesions in both; ischemia then itself results in releasing pressor substances which raise blood pressure. Or perhaps indeed, the injured kidney may release two or more substances—pressor substances and vascular toxins. In that event arterial hypertension results from one, and renal arteriolar lesions from others. Clearly, situations may then arise in which only one substance is released. The experiments of Winternitz (3) point to this possibility.

In most instances renal vascular disease in rats is closely associated with the hypertensive state, and results from procedures which occasion arterial hypertension. From these observations it is impossible to be certain whether vascular lesions themselves are the cause or the result of elevation of the blood pressure. Their presence (5 cases) when both indices of the hypertensive state were absent, and their absence when one was present (8 cases) suggest that more than one process is at work. The most likely explanation is that arteriolar lesions are caused by the same disturbance whch results in hypertension and are merely a manifestation of its existence. That they in turn contribute toward the maintenance of renal ischemia and therefore hypertension, is probable. In those cases in which one kidney was completely destroyed by infection, trauma, or infarction, and in which hypertension persisted, ischemia may have been maintained by the renal vascular disease present in the other. Removal of an injured kidney in rats need not accordingly cause hypertension to disappear (4).

It is difficult to explain why kidneys made ischemic by partial constriction of renal arteries were included in the vascular process. This is not the case in dogs. A circulating vascular toxin may have affected the arterioles of both kidneys. Perhaps rats are more susceptible to vascular damage than are other animals.

These results differ from those found by Wilson and Byrom (1), although the conclusions to be drawn are similar. They report few lesions in kidneys affected by partial constriction of a renal artery; many were found in this study. Glomerular changes were common in their animals; less so in ours. The syndrome "malignant hypertension" described by them was encountered only 5 times, and then only when a renal artery had been constricted.

One difficulty has been the lack of reliable indices to establish the presence of the hypertensive state. Attempts have been made (2) to learn the normal blood pressure of rats and so to ascertan the development of hypertension. To this end greater emphasis was placed upon the presence of cardiac hypertrophy than upon elevation of the blood pressure, since this was known to be easily influenced by environmental factors and by stages in the disease itself (1). If renal vascular disease is also an expression of arterial hypertension, it becomes obvious that there is no single reliable way of establishing the existence of the hypertensive state. One or more of the phenomena, in all combinations, cardiac hypertrophy, elevation of blood pressure, and renal vascular disease occurred in a small proportion of the animals. Perhaps the best index of the hypertensive state is the presence of two of these three.

SUMMARY AND CONCLUSIONS

1. When rats developed cardiac hypertrophy or elevation of blood pressure as a result of one of several methods designed to bring about arterial hypertension, renal vascular disease occurred frequently.

2. When injury to one kidney was followed by cardiac hypertrophy or elevation of blood pressure, vascular lesions were found with considerable regularity in the opposite one, as well as in the one injured.

3. Renal lesions rarely occurred in the absence of cardiac hypertrophy or elevated blood pressure.

4. Renal vascular lesions in rats are occasioned, therefore, by injury to one kidney and are usually associated with, and dependent on, the presence of arterial hypertension.

BIBLIOGRAPHY

1. Wilson, C., and Byrom, F. B., *Lancet*, 1939, **1**, 136.
2. Schroeder, H. A., *J. Exp. Med.*, 1942, **75**, 513.
3. Winternitz, M. C., Nylon, E., Waters, L. L., and Katzenstein, R., *Yale J. Biol. and Med.*, 1940, **12**, 623.
4. Friedman, B., Jarman, J., and Klemperer, P., *Am. J. Med. Sc.*, 1941, **202**, 20.
5. Rytand, D. A., *J. Clin. Inv.*, 1938, **17**, 391.

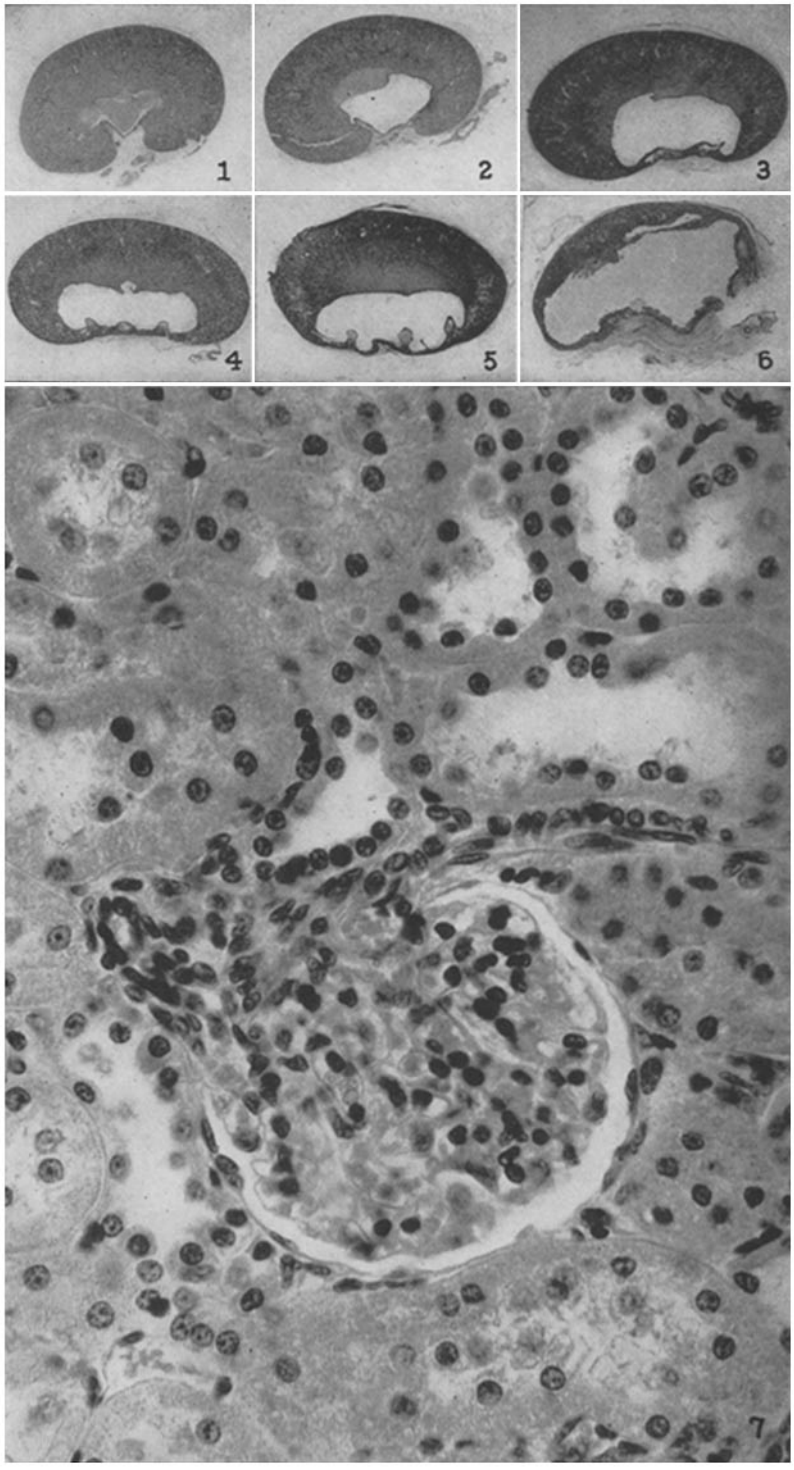
EXPLANATION OF PLATES

These photographs were made by Mr. Joseph B. Haulenbeek.

PLATE 13

FIGS. 1 to 6. Photographs of sections of the left kidneys of rats exhibiting hydronephrosis. Fig. 1, normal kidney; Fig. 2, rat H 94; Fig. 3, rat H 97; Fig. 4, rat H 100; Fig. 5, rat H 150; Fig. 6, rat H 147. The kidneys of all except that of No. H 147 functioned. Arterial hypertension was exhibited by all animals except No. H 147. Hematoxylin and eosin stain. × 2.

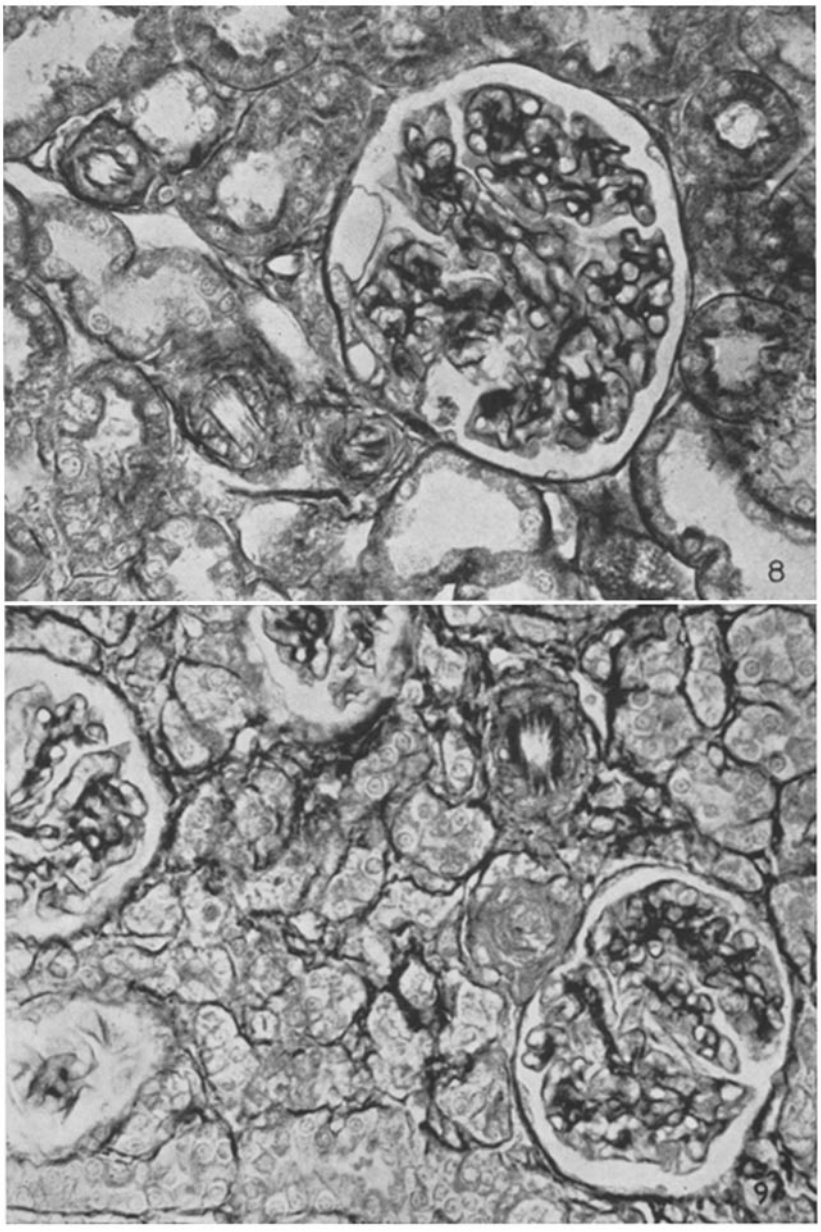
FIG. 7. Photomicrograph of right kidney of rat H 96, of which the left was hydronephrotic. Arterial hypertension was present. The glomerular arteriole is diseased, its wall thickened. Hematoxylin and eosin stain. × 500.



(Schroeder and Neumann: Arterial hypertension in rats. II)

PLATE 14

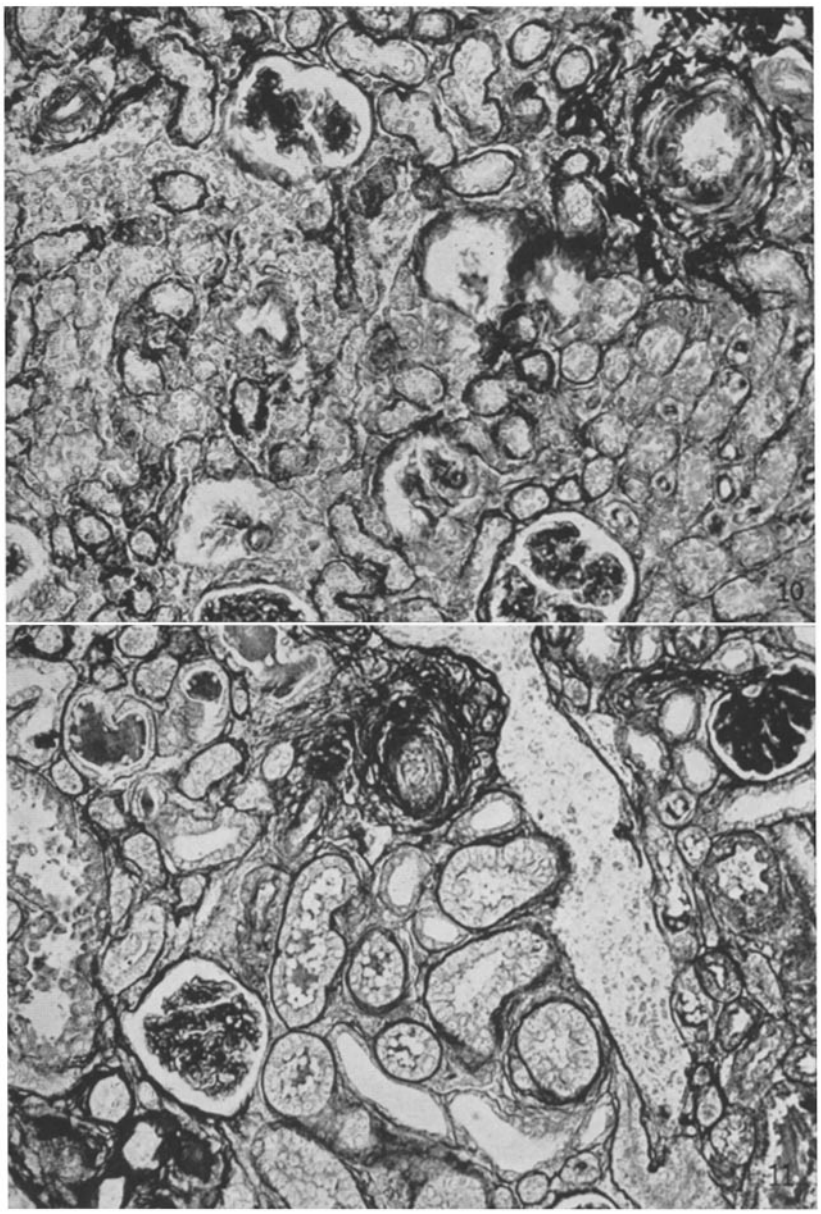
FIGS. 8 and 9. Fig. 8, photomicrograph of section of right kidney, and Fig. 9, of left kidney of rat G 158. The left renal artery had been partially constricted 35 days previously, and the rat exhibited arterial hypertension. Vascular changes, hyaline degeneration, hypertrophy of muscle, and necrosis are present in the arterioles of both sections to a similar degree. Mallory connective tissue stain. × 400.



(Schroeder and Neumann: Arterial hypertension in rats. II)

PLATE 15

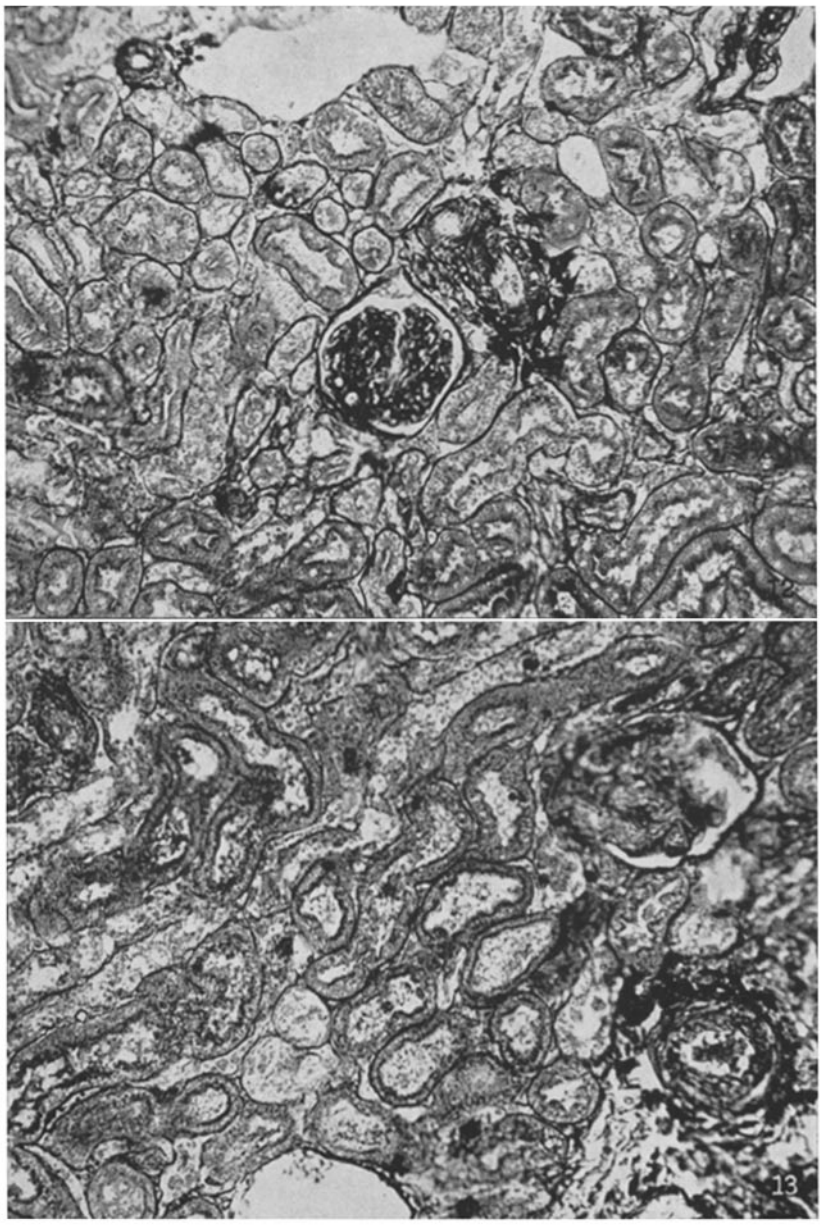
FIGS. 10 and 11. Fig. 10, photomicrograph of left kidney and Fig. 11, of right kidney of rat G 168. The left renal artery had been partially constricted 61 days previously. The animal exhibited cardiac hypertrophy, loss of weight, and convulsions before death. In the left kidney there are moderate changes in the arterioles, in the right marked. Necrosis of the walls of the arterioles is present only in the right kidney. Mallory connective tissue stain. × 200.



(Schroeder and Neumann: Arterial hypertension in rats. II)

PLATE 16

FIGS. 12 and 13. Fig. 12, photomicrograph of section of left kidney, and Fig. 13, of right kidney of rat C 17. Cellophane perinephritis had been induced about the left kidney 31 days previously. The animal exhibited arterial hypertension. Vascular changes occurred in both kidneys to a similar degree. There is hyaline degeneration of the walls of the arterioles in both sections. Mallory connective tissue stain. × 200.



(Schroeder and Neumann: Arterial hypertension in rats. II)