HISTOLOGICAL CHANGES IN THE RENAL GLOMERULUS IN ESSENTIAL (PRIMARY) HYPERTENSION *

A Study of Fifty-One Cases

Leone McGregor, M.D.
Fellow of the National Research Council
(*From the Pathological Laboratory of the Boston City Hospital, Boston, Mass.*)

Throughout this paper the term essential (primary) hypertension is used to include all chronic hypertension of unknown etiology. Although this is probably not a homogeneous group, most of the cases are similar clinically and pathologically. They are all characterized by (1) a persistent systolic blood pressure of 150 mm. or more, and (2) a definite left ventricular hypertrophy not associated with any of the diseases known to cause hypertrophy.

The object of this paper is to describe the histological picture of the renal glomerulus in essential hypertension.

The material consists of all the 1927 and 1928 Boston City Hospital autopsy cases which have a history of chronic high blood pressure. After excluding the cases of secondary hypertension due to glomerulonephritis, toxemia of pregnancy, urinary obstruction, nephrosis and aortic insufficiency, there remain fifty-one cases of primary hypertension. The series is subdivided according to the cause of death into (1) a cerebral group (apoplexy) of 16 cases, (2) a cardiac group (myocardial insufficiency and coronary disease) of 19 cases, (3) a renal group (uremia) of 14 cases, and (4) a miscellaneous group (rupture of aorta and diabetes) of 2 cases. The controls are kidneys from nine persons who died in the fifth, sixth, seventh and eighth decades and who were known to have had a normal blood pressure. The object was to determine the glomerular lesions due to age alone.

Before proceeding to a study of these cases, the general conception of the histological changes in the kidney in primary hypertension must be summarized. The work of Johnson,[1] Gull and Sutton,[2] Ziegler,[3] Jores,[4] Herxheimer,[5] Gaskell,[6] Volhard and Fahr,[7, 8, 9, 10, 11] Lohlein,[12, 13, 14] Evans,[15] Fishberg,[16, 17] Jaffe,[18] Bell and

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Clawson,[19] and Klemperer and Otani [20] has shown that the most conspicuous renal lesions are an arteriolosclerosis (a formation of hyalin under the endothelium of the afferent glomerular arterioles) and a hyperplastic elastic tissue intimal thickening of the walls of the small and medium-sized arteries.

In addition Löhlein described a dilatation of the afferent arteriole at its entrance to the glomerular tuft. This finding was confirmed by Fishberg and by Jaffé. Löhlein also observed hyaline areas in the glomeruli continuous with the hyalin of the arterioles. Jaffé suggested that the primary renal lesion be sought in the glomerular tuft where he noted a thickening and hyaline degeneration of the capillary walls.

Volhard and Fahr saw inflammatory glomerular changes in cases of essential hypertension with death from uremia. They believed that the inflammation superimposed on the arteriosclerosis caused the renal insufficiency. Löhlein, Jores and Herxheimer opposed this theory because they thought the glomerular damage was vascular in origin and not inflammatory. More recently Fahr described an acute arteritis of the afferent glomerular vessels as the cause of uremia. Volhard has lately explained the renal insufficiency on the basis of a general vasoconstriction which includes the glomeruli. Fishberg believed the glomerular lesions were non-inflammatory and that uremia was usually due to an acceleration of the arteriosclerotic process. Bell and Clawson found that patients with slowly developing uremia had at autopsy a simple glomerular and tubular atrophy from progressive narrowing of small arteries and arterioles, while those with rapidly developing uremia had a necrosis of arteries and arterioles producing small infarcts, infarcted glomeruli and rarely glomerulitis. Klemperer and Otani ascribed the glomerular changes to ischemia rather than to inflammation.

Technique: The tissues available had all been fixed in Zenker's fluid. The stain which proved most valuable was the Mallory-Heidenhain azan carmine.[21] Unless otherwise stated descriptions of glomeruli are made from this stain. Nuclei are red and all connective tissues including glomerular, capsular and tubular basement membranes are blue. Phosphotungstic acid hematoxylin, Weigert and Verhoeff's elastic tissue stains were used on some of the tissues.

Method of Studying Glomeruli: For practical purposes there are only three types of glomeruli seen in the primary hypertensive

kidney: (1) non-hypertensive glomeruli, some of which may show diffuse or focal inflammatory lesions, (2) hypertensive contracted glomeruli, a few of which may also contain diffuse or focal inflammatory areas, and (3) hyaline glomeruli.

One hundred consecutive glomeruli were counted in each section and classified as (1), (2) or (3). Subheadings under non-hypertensive and under contracted hypertensive were used to indicate the number of such glomeruli showing focal or diffuse inflammatory reactions.

Non-Hypertensive Glomeruli: This term is used to include (1) all normal glomeruli, and (2) all glomeruli which are normal except for focal or diffuse inflammatory lesions.

The reader is referred to a previous paper by the author [21] for a description of the histology of the normal glomerulus. Briefly, the glomerular epithelium and basement membrane are continuous with the tubular epithelium and basement membranes respectively. Likewise, the endothelium of the glomerulus is a continuation of the endothelium of the afferent and efferent vessels. The wall of the tuft contains three structures, which from within out are endothelium, basement membrane and epithelium. These are easily distinguished from one another with the Mallory-Heidenhain azan carmine stain (Figs. 1 and 3).

As Table VI shows, the average percentage of non-hypertensive glomeruli is 20 in the renal group, 44 in the miscellaneous group, 52 in the cardiac group, 63 in the cerebral group and 96.2 in the control group. In the hypertensive series many of these normal glomeruli are hypertrophied in an attempt to compensate for atrophied units.

The inflammatory lesions which occur may be diffuse and involve the whole tuft, or focal and involve only one or two loops. When the whole glomerulus is affected the lesion seems to be identical with that described by the author [22] for acute and chronic glomerulonephritis. However, only a very small number of glomeruli are involved. In early stages the glomerulus is enlarged, the capsular and glomerular epithelium proliferates and the capillary loops are occluded by inflammatory mononuclear cells, swollen endothelium and hyaline fibers (Fig. 5). The latter gradually contract and slowly obliterate the capillary lumen. The end result is a hyaline glomerulus.

Usually only a portion of a tuft is involved. The glomerular

epithelium around the loop, as well as the adjacent capsular epithelium, swells, proliferates and often undergoes hyaline granular degeneration. The lumen of the loop is occluded by fatty swollen endothelium, inflammatory cells, fibrin and hyaline fibers. These fibers, which become collagen, contract and destroy the function of the loop. The adjacent capsular epithelium may proliferate and form crescents. The lobule with the focal lesion often becomes adherent to the capsule during the inflammatory and healing processes.

Glomeruli with focal inflammation are more numerous than those with diffuse involvement. The cerebral group of hypertensives shows the fewest inflammatory lesions while the renal group shows the highest. Every uremic death in this series is associated with inflammatory glomeruli.

The Hypertensive Contracted Glomerulus: (Figs. 2 and 4.) This glomerulus is always smaller than normal, its diameter often being reduced one-half. The decrease in size of the glomerulus produces an apparent increase in the pericapsular connective tissue and gives it a lamellated appearance. The capsular basement membrane is thickened. Its epithelial lining is normal.

The normal glomerular tuft has multiple loops opening out of the main lobules. In a hypertensive glomerulus the original lobulation remains but the loops are decreased in number. This gives the glomerulus a simpler structure. Glomerular epithelium and endothelium are unchanged. The striking feature is a uniform thickening and wrinkling of the glomerular basement membrane. The process seems to proceed diffusely throughout the tuft. Normally the basement membrane is thin and not wrinkled. All transitions from normal are present in one section. In this study only glomeruli in advanced stages of the lesion are counted as hypertensive.

There is no intracapillary impediment to the circulation in such a glomerulus. The afferent arteriole, the capillaries of the tuft and the efferent vessel are always open. The afferent arteriole is not dilated or narrowed at its entrance to the glomerulus.

Occasionally a few of these glomeruli show focal and diffuse inflammatory lesions. The result is occlusion of the whole tuft or part of it and eventual hyalinization. The afferent arteriole usually shows lesions at the hilum of an inflammatory glomerulus.

The percentage of hypertensive contracted glomeruli is 47 in the renal and miscellaneous groups, 33 in the cardiac group, 24 in the cerebral group and 0.8 in the control group (Table VI).

The Hyaline Glomerulus: This type of glomerulus is usually the result of atrophy due to sclerosis of arteries or arterioles. Herxheimer has shown that a small percentage is congenital. The others are due to the healing of inflammatory processes. The latter explanation applies particularly to hyalinization of single loops or lobules.

Glomeruli which atrophy following disease of arteries are usually found in wedge-shaped cortical areas. Those which atrophy due to arteriolar disease are often scattered in groups throughout the kidney. All transition stages between hypertensive and hyaline glomeruli are found in one section. Anilin blue stains the thickened glomerular basement membrane in the midst of the hyaline mass.

The average percentage of hyaline glomeruli is 33 in the renal group, 8 in the miscellaneous group, 15 in the cardiac group, 13 in the cerebral group and 4 in the control group.

Renal Vessels: In this paper the term arteriole is used to indicate the afferent and efferent glomerular vessels, the former arising from the interlobular artery. Serial sections show that the efferent arteriole is normal. The condition of the afferent vessel varies along its course. A distal segment two to three hundred microns long, adjacent to the glomerulus is usually normal. The proximal portion of the arteriole may show an irregular subendothelial fatty hyaline deposit which narrows the lumen. Elastic tissue stains prove that such homogeneous material is internal to the elastic membrane. This type of arteriole may supply (1) an apparently normal glomerulus, or (2) an early hypertensive glomerulus, or (3) a typical hypertensive contracted glomerulus. The arteriolar lesion must then precede or be independent of the glomerular lesion. However, the serial sections show that every hypertensive glomerulus has an afferent vessel which is definitely narrowed and sclerosed in some portion of its course, usually at some distance from the hilum of the tuft. The arteriolar change must, therefore, be related to the basement membrane thickening and wrinkling. The lesions are similar in that the hyaline thickening is subendothelial in both arteriole and glomerulus. Apparently the arteriolar change takes place first.

A dilatation of the afferent arteriole at the entrance to the glomerulus in early cases of hypertension was described by Jaffé and Löhlein. According to my study all normal glomeruli in the control series show this dilatation and only the normal glomeruli in the hypertensive series.

TABLE I

Essential Hypertension (Cerebral Group)

Case number	Age	Sex	Cause of death	Blood pressure	Known duration of symptoms	Summary of history	Blood urea nitrogen	Blood non-protein nitrogen	Urine phenol sulphonephthalein	Heart weight
	years			*mm. mercury*			*mg. per cent*	*mg. per cent*	*per cent*	*gm.*
1	32	f	cerebral hemorrhage	235/125	9 years	9 years ago edema throughout first pregnancy. 5 years ago edema and high blood pressure with second pregnancy. From then on, edema, headaches, dyspnea and nausea. Fundi show exudate and old scars.	..	28	30	370
2	42	m	"	190/120	?	Sudden loss of consciousness.	..	..	..	350
3	43	f	"	270/130	6 months	Not well for past 6 months. 5 days ago became delirious then stuporous.	..	48	..	410
4	48	m	"	200/120	15 years	Cerebral shocks 15 years ago, 5 years ago and 4 days ago. Headaches and high blood pressure for years.	..	..	..	500
5	49	f	"	185/115	?	Sudden loss of consciousness.	..	..	..	400
6	53	f	"	230/130	?	Sudden loss of consciousness.	..	..	..	500
7	55	m	"	230/140	2½ years	Sudden loss of consciousness.	..	..	..	540
8	60	m	"	250/110	several years	High blood pressure for several years. 4 days ago a cerebral accident.	..	..	..	370
9	60	f	"	155/110	20 years	20 years of palpitation and dyspnea on exertion. 5 years of attacks of angina, failing vision and nocturia. 4 days of cyanosis, peripheral edema and coma.	..	..	..	530
10	65	m	"	150/95	?	Admitted comatose, cyanosed with edema of legs one day after cerebral accident.	..	..	..	550
11	68	f	"	245/120	3 years	3 years of treatment for high blood pressure. 2 weeks of weakness, dizziness and headaches. Vessels of fundi tortuous. One day ago a sudden cerebral accident.	..	..	..	420
12	70	f	"	high	3 years	3 years ago had high blood pressure and a cerebral shock. Admitted in coma.	..	..	..	350
13	71	m	"	220/140	10 years	10 years of periodic dyspnea and edema. 2 years ago high blood pressure and a cerebral accident. Admitted in coma.	..	37	..	500

TABLE I

Essential Hypertension (Cerebral Group)

Coronary sclerosis	Mural thrombosis	Weight of kidneys	Sclerosis small and medium-sized renal arteries	Sclerosis of renal afferent arterioles	Tubular atrophy	Glomeruli						
						Non-Hypertensive			Hypertensive contracted			Hyaline
						No inflam.	Focal inflam.	Diffuse inflam.	No inflam.	Focal inflam.	Diffuse inflam.	
		gm.				per cent	per cent	per cent	per cent	per cent	per cent	per cent
–	absent	210	+++	++++	++	44	..	..	30	..	..	26
–	absent	158	++	++	+	55	..	..	34	2	..	9
–	absent	310	++	++++	++	62	..	..	30	..	..	8
++++	present	240	+	+	–	80	..	..	15	..	..	5
+	absent	300	+	+	–	70	..	..	22	..	..	8
++	absent	200	+	++	+	77	..	..	21	..	..	2
–	absent	280	++++	+++	++++	27	..	..	29	..	1	43
–	absent	210	+++	+++	++	48	..	..	40	..	..	12
++++	present	270	+	+	++	34	..	..	30	2	..	34
–	absent	250	+	++	++	57	2	3	20	..	..	18
+++	absent	320	++	+++	++	62	11	..	22	..	..	5
++++	absent	200	++	+	–	75	..	..	20	..	..	5
++++	absent	240	++	+	++	77	..	..	13	..	..	10

TABLE I (*continued*)

Case number	Age	Sex	Cause of death	Blood pressure	Known duration of symptoms	Summary of history	Blood urea nitrogen	Blood non-protein nitrogen	Urine phenol sulphonephthalein	Heart weight
	years			*mm. mercury*			*mg. per cent*	*mg. per cent*	*per cent*	*gm.*
14	72	m	cerebral hemorrhage	180/90	15 years	15 years ago a cerebral accident. Two more while in hospital with erysipelas.	..	42.5	..	350
15	77	m	"	220/115	?	19 days ago a cerebral accident. Coma and hemiplegia since then.	..	..	..	390
16	80	f	"	210/100	1 year	1 year of high blood pressure, dizziness, nocturia and dyspnea.	..	..	..	320

TABLE II

Essential Hypertension (Cardiac Group)

Case number	Age	Sex	Cause of death	Blood pressure	Known duration of symptoms	Summary of history	Blood urea nitrogen	Blood non-protein nitrogen	Urine phenol sulphonephthalein	Heart weight
	years			*mm. mercury*			*mg. per cent*	*mg. per cent*	*per cent*	*gm.*
17	39	m	cardiac insufficiency	190/130	1 month	1 month of dyspnea, edema, nocturia and ascites. Decompensation.	..	..	..	660
18	39	f	"	210/170	7 years	7 years of high blood pressure. 1 month of dyspnea, cough, cyanosis and edema. Decompensation.	..	60	..	580
19	50	m	"	175/105	1 year	1 year of angina pectoris, dyspnea and pleural effusion. Decompensation.	..	..	..	760
20	54	m	"	162/120	1 year	1 year of high blood pressure, dyspnea, cough, edema and nocturia. Decompensation.	..	..	..	860
21	55	m	"	240/160	2 years	2 years of nocturia, dyspnea weakness and epistaxis. 6 weeks of palpitation and edema. Decompensation.	..	50	..	560
22	55	f	"	240/130	3 years	3 years of headache, blurred vision, palpitation, praecordial pain, edema and nocturia. Decompensation.	23.30	..	..	500
23	56	m	"	160/115	5 years	5 years of cough and epistaxis. 3 weeks of edema and dyspnea. Decompensation.	..	..	..	560

TABLE I (*continued*)

Coronary sclerosis	Mural thrombosis	Weight of kidneys	Sclerosis small and medium-sized renal arteries	Sclerosis of renal afferent arterioles	Tubular atrophy	Glomeruli						
						Non-Hypertensive			Hypertensive contracted			Hyaline
						No inflam.	Focal inflam.	Diffuse inflam.	No inflam.	Focal inflam.	Diffuse inflam.	
		gm.				*per cent*	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*
–	absent	320	–	–	–	65	..	..	15	..	..	20
++	absent	290	++	++	+	75	..	..	15	..	..	10
++	absent	320	–	–	–	91	..	..	4	..	..	5

TABLE II

Essential Hypertension (Cardiac Group)

Coronary sclerosis	Mural thrombosis	Weight of kidneys	Sclerosis small and medium-sized renal arteries	Sclerosis of renal afferent arterioles	Tubular atrophy	Glomeruli						
						Non-Hypertensive			Hypertensive contracted			Hyaline
						No inflam.	Focal inflam.	Diffuse inflam.	No inflam.	Focal inflam.	Diffuse inflam.	
		gm.				*per cent*	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*
+++	present	370	++	+	–	70	..	..	25	..	..	5
+	absent	290	++++	++++	++	34	1	1	46	2	2	14
+++	present	300	+++	+	+	47	2	4	37	..	..	10
?	absent	520	+	+	–	55	..	..	15	..	..	30
+++	absent	220	++++	++++	++	18	3	2	73	1	..	3
++	absent	270	++	+	+	42	..	..	40	..	..	18
–	absent	270	++	+	–	80	..	..	8	..	..	12

TABLE II (*continued*)

Case number	Age	Sex	Cause of death	Blood pressure	Known duration of symptoms	Summary of history	Blood urea nitrogen	Blood non-protein nitrogen	Urine phenol sulpho-neph-thalein	Heart weight
	years			*mm. mercury*			*mg. per cent*	*mg. per cent*	*per cent*	*per cent*
24	56	m	cardiac insufficiency	180/120	12 years	12 years ago two cerebral accidents. At that time, blood pressure 128/80, dizziness, dyspnea, edema and nocturia. 4 years ago blood pressure 170/80, headaches, nocturia, edema and ascites. Decompensation.	..	..	35	830
25	57	f	"	150/60	4 months	4 months of dyspnea, edema and weakness. Decompensation.	..	..	..	500
26	58	f	"	252/148	3 years	3 years of dyspnea and high blood pressure. 4 months of decompensation.	..	50	..	560
27	63	m	"	200/140	11 months	11 months of decompensation.	..	..	..	850
28	63	m	"	210/110	2 years	2 years of high blood pressure. 2 years ago a cerebral accident. Now angina pectoris and decompensation.	..	..	..	515
29	64	m	"	170/110	4 years	4 years of dyspnea, cough, nocturia and edema. Decompensation.	..	..	..	475
30	70	f	"	200/130	18 months	18 months of dyspnea. 1 month of angina pectoris and fibrillation.	..	..	..	520
31	70	f	"	200/?	9 months	9 months of weakness and dyspnea. 2 weeks of ascites and cyanosis. Decompensation.	..	..	..	520
32	74	m	"	140/80	6 years	6 years of dyspnea, edema and angina pectoris. Decompensation.	..	..	..	600
33	80	m	"	170/95	7 weeks	7 weeks of dyspnea, weakness, dizziness and edema. Decompensation.	..	45	..	600
34	80	f	"	160/110	9 years	9 years ago a cerebral accident. 5 years ago another. Decompensation.	..	..	..	400
35	82	m	"	170/110	3 months	3 months of edema and cyanosis. Tortuous retinal arteries. Decompensation.	..	82	..	750

TABLE II (*continued*)

Coronary sclerosis	Mural thrombosis	Weight of kidneys	Sclerosis small and medium-sized renal arteries	Sclerosis of renal afferent arterioles	Tubular atrophy	Glomeruli						
						Non-Hypertensive			Hypertensive contracted			Hyaline
						No inflam.	Focal inflam.	Diffuse inflam.	No inflam.	Focal inflam.	Diffuse inflam.	
		gm.				*per cent*	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*
++++	present	310	+++	++++	+	52	..	..	30	..	..	18
++	absent	185	++++	++++	++++	26	2	10	10	..	..	52
–	absent	small	++++	++++	++++	38	2	1	20	8	1	30
+	absent	410	++	+	+	68	..	..	18	..	..	14
++++	absent	240	++++	++++	++++	10	3	4	66	2	..	15
+	absent	310	+	+	+	57	..	..	23	..	..	20
++++	present	380	+	+	–	72	..	..	13	..	..	15
+++	absent	400	++	+	–	83	..	..	9	..	..	8
++++	absent	320	++	+	–	76	..	..	12	..	..	12
++	absent	400	++	+	–	75	..	..	17	..	..	8
++++	present	400	++	++	–	66	..	..	30	..	..	4
–	absent	290	++++	++	+	35	..	2	48	2	2	11

TABLE III

Essential Hypertension (Renal Group)

Case number	Age	Sex	Cause of death	Blood pressure	Known duration of symptoms	Summary of history	Blood urea nitrogen	Blood non-protein nitrogen	Urine phenol sulphonephthalein	Heart weight
	years			*mm. mercury*			*mg. per cent*	*mg. per cent*	*per cent*	*gm.*
36	34	f	uremia	280/150	3 years	3 years of headaches, dizziness, blurring of vision and epistaxis. Fundi show old hemorrhages. Uremia.	37.78	..	..	480
37	37	f	"	220/120	1 year	1 year of epistaxis, failing vision, polyuria, dyspnea and palpitation. 3 months of headache, edema and praecordial pain. Fundi show recent and old hemorrhages. Uremia.	58.26	..	0	542
38	46	m	"	227/140	3 months	3 months of praecordial pain, dyspnea dizziness, edema, nocturia and vomiting. Albuminuric retinitis. Uremia.	..	193	0	470
39	47	m	"	245/160	7 years	7 years of headaches, weakness and nocturia. 3 years of high blood pressure and impaired vision. Dyspnea and edema. Uremia.	200.4	..	23	775
40	50	f	"	260/?	3 years	3 years of high blood pressure, dyspnea, headaches and nocturia. 2 years ago a cerebral accident. Uremia.	..	111	..	485
41	50	m	"	high	3 years	3 years of heart trouble. A few weeks of dyspnea, cyanosis, edema and vomiting. Uremia.	..	..	..	640
42	52	m	"	240/150	1 year	1 year of high blood pressure, weakness, dyspnea and epistaxis. Cerebral accident with facial paralysis. Uremia.	..	135	20	570
43	53	m	"	208/126	3 years	3 years of palpitation, epistaxis and nocturia. 6 weeks of cough, dyspnea and praecordial pain. Fundi show exudate and old hemorrhages. Uremia.	135	..	..	520
44	57	m	"	236/144	6 years	6 years of nocturia. 8 months of headache, blurred vision, epistaxis, dyspnea and weakness. Fundi show old hemorrhages. Uremia.	69	..	..	510
45	57	m	"	230/170	3 years	3 years of high blood pressure, dyspnea, praecordial pain, nocturia and edema. Months of chronic uremia.	..	166	0	555
46	58	m	"	230/160	3 years	3 years ago a cerebral accident. Since then, angina pectoris, headaches, dyspnea, edema and chronic uremia. Fundi show new and old hemorrhages.	..	243	0	660
47	60	m	"	208/178	?	Semi-comatose with clinical uremia.	..	..	..	590
48	69	f	"	200/110	6 months	6 months of angina pectoris, weakness, palpitation and dyspnea. Fundi show old hemorrhages. Uremia.	..	300	..	390
49	71	m	"	high	2 weeks	2 weeks of cough, weakness, cyanosis, delirium and twitching. Uremia.	..	75	..	435

TABLE III

Essential Hypertension (Renal Group)

Coronary sclerosis	Mural thrombosis	Weight of kidneys	Sclerosis small and medium-sized renal arteries	Sclerosis renal afferent arterioles	Tubular atrophy	Glomeruli						Hyaline
						Non-Hypertensive			Hypertensive contracted			
						No inflam.	Focal inflam.	Diffuse inflam.	No inflam.	Focal inflam.	Diffuse inflam.	
		gm.				*per cent*	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*
++	absent	200	++++	+++	+++	25	2	2	62	6	1	2
++	absent	215	++++	++++	++++	46	..	..	66	3	2	23
?	absent	110	++++	++++	++++	..	..	..	27	3	..	70
+	absent	150	++++	++++	++++	4	2	1	47	2	4	40
–	absent	100	++++	++++	++++	10	8	..	44	5	..	33
+	absent	380	++++	+++	++++	20	10	2	7	6	..	55
+++	absent	300	++++	++++	++++	15	2	2	52	8	3	18
+	absent	165	+++	++++	++++	20	4	..	27	1	7	41
++	absent	285	++++	++++	++++	34	..	..	55	4	..	7
?	absent	195	++++	++++	++++	..	..	..	76	4	..	20
+++	absent	220	++++	++++	++++	14	1	..	46	5	1	33
–	absent	150	++++	++++	++++	6	1	..	8	9	3	73
+++	absent	80	++++	++++	++++	20	8	..	18	5	11	38
+	absent	288	++++	++++	+++	20	1	2	64	1	2	10

TABLE IV

Essential Hypertension (Miscellaneous Group)

Case number	Age	Sex	Cause of death	Blood pressure	Known duration of symptoms	Summary of history	Blood urea nitrogen	Blood non-protein nitrogen	Urine phenol sulpho-neph-thalein	Heart weight
	years			*mm. mercury*			*mg. per cent*	*mg. per cent*	*per cent*	*gm.*
50	47	m	rupture of aorta	242/140	6 years	6 years of headaches and dyspnea. 1 year of high blood pressure and edema. 3 days of acute abdominal pain.	..	..	..	1280
51	56	m	diabetes	208/104	several years	Diabetes for years. Admitted in coma and died in 3 days.	..	33	..	770

TABLE V

Control Group (Kidneys from Non-Hypertensives in the 5th, 6th, 7th and 8th Decades)

Case number	Age	Sex	Cause of death	Blood pressure	Heart weight	Coronary sclerosis	Mural thrombosis	Weight of kidneys
	years			*mm. mercury*	*gm.*			*gm.*
N 1	42	m	carcinoma stomach	120/80	255	–	absent	305
N 2	45	f	carcinoma breast	112/76	small	–	"	300
N 3	54	m	pulmonary tuberculosis	normal	340	–	"	480
N 4	55	m	carcinoma esophagus	105/75	260	–	"	380
N 5	58	m	chronic lymphatic leukemia	120/80	300	–	"	360
N 6	60	f	perforated gastric ulcer	normal	260	–	"	280
N 7	60	m	carcinoma esophagus	104/72	290	–	"	275
N 8	70	m	lobar pneumonia	110/80	310	–	"	250
N 9	80	f	mitral stenosis with decompensation	120/90	320	–	"	210

TABLE IV

Essential Hypertension (Miscellaneous Group)

Coronary sclerosis	Mural thrombosis	Weight of kidneys	Sclerosis small and medium-sized renal arteries	Sclerosis of renal afferent arterioles	Tubular atrophy	Glomeruli						
						Non-Hypertensive			Hypertensive contracted			Hyaline
						No inflam.	Focal inflam.	Diffuse inflam.	No inflam.	Focal inflam.	Diffuse inflam.	
		gm.				per cent	per cent	per cent	per cent	per cent	per cent	per cent
?	absent	490	++++	++++	+++	18	..	2	67	4	..	9
++++	absent	455	++	++	+	68	..	..	22	..	..	10

TABLE V

Control Group (Kidneys from Non-Hypertensives in the 5th, 6th, 7th and 8th Decades)

Sclerosis of small and medium-sized renal arteries	Sclerosis of renal afferent arterioles	Tubular atrophy	Glomeruli						
			Non-Hypertensive			Hypertensive contracted			Hyaline
			No inflam.	Focal inflam.	Diffuse inflam.	No inflam.	Focal inflam.	Diffuse inflam.	
			per cent	per cent	per cent	per cent	per cent	per cent	per cent
–	–	–	98	..	..	..	..	..	2
–	–	–	95	..	..	..	..	..	5
–	–	–	95	..	..	..	..	..	5
+	–	–	100	..	..	..	..	..	..
–	–	–	94	..	..	3	..	..	3
–	–	–	91	..	..	2	..	..	7
+	–	–	97	..	..	..	..	..	3
+	–	–	92	..	..	2	..	..	6
++	–	–	92	..	..	..	..	..	8

No one of the fifty-one cases happened to have the acute inflammatory arteritis described by Fahr or the arteriolar necrosis with glomerular infarction seen by Bell and Clawson. Inflammatory

TABLE VI

Summary of Glomerular Lesions

	Number of cases	Average age	Non-Hypertensive glomeruli	Hypertensive contracted glomeruli	Hyaline glomeruli
		years	*average per cent*	*average per cent*	*average per cent*
Non-hypertensive control group	9	58	96.2	0.8	4
Essential hypertension cerebral group	16	59	63	24	13
Essential hypertension cardiac group	19	55	52	33	15
Essential hypertension miscellaneous group	2	51	44	48	8
Essential hypertension renal group	14	52	20	47	33

glomeruli in my series usually have arterioles with a very marked degree of sclerosis or thrombosis extending up to or through the hilum.

Table V shows that there is no arteriolosclerosis in the control group. Two of the cerebral group also show no arteriolosclerosis (Table I, cases 14 and 16) although they have a small percentage of hypertensive glomeruli. This discrepancy may be due to the relative size of glomeruli and arterioles, the former being easier to find than the latter.

The interlobular, small and medium-sized arteries of the kidneys show the changes described by others, namely, intimal atherosclerosis and hyperplastic elastic tissue intimal thickening. As noted in Table V, four of the control series have a mild degree of this sclerosis.

DISCUSSION

The glomeruli in essential hypertension are usually described as normal. In my series of fifty-one cases the renal group averages only 20 per cent normal glomeruli, the miscellaneous group 44 per cent, the cardiac group 52 per cent and the cerebral group 63 per cent. Nine non-hypertensive controls from the fifth, sixth, seventh and eighth decades average 96.2 per cent normal glomeruli (Figs. 1 and 3).

All fifty-one cases show the presence of a typical glomerulus with a thickened wrinkled basement membrane (Figs. 2 and 4). The average percentage of such glomeruli is 48 in the renal and miscellaneous groups, 31 in the cardiac group and 25 in the cerebral group. In all except Case 16 these hypertensive contracted glomeruli are present in sufficient numbers to indicate the diagnosis. It is interesting that this case according to the data available is undoubtedly primary hypertension and yet there is no cardiac hypertrophy and no arteriolosclerosis.

Hypertensive contracted glomeruli are most numerous in kidneys with extensive arteriolosclerosis (Tables I, II, III and IV). Microscopically either lesion may be considered indicative of clinical hypertension. In early cases it is simpler to look for hypertensive glomeruli than for arteriolar disease.

The thickening of the glomerular basement membrane may be the result of a spasm of the tuft or of atrophy due to ischemia or to partial disuse. Serial sections show that sclerosed arterioles may lead to normal glomeruli but that hypertensive glomeruli always have narrowed arterioles. These two facts suggest that the arteriolar lesion precedes and is related to the glomerular change. The portion of the afferent vessel close to the hypertensive glomerulus is usually normal. The subendothelial hyaline deposit with its resultant narrowing of the lumen is some distance from the glomerulus.

There are all transitions from normal to hypertensive hyaline glomeruli.

Bell [23] has described a diffuse thickening of the basement membrane in all the glomeruli in three cases of lipoid nephrosis. There was no hypertension, no tubular atrophy and no arteriosclerosis. Evidently a glomerular basement membrane thickening need not be secondary to vascular disease. The glomeruli in such a type of lipoid nephrosis are normal in size and lobulation, in contrast to the glomeruli of hypertension which are small with a decreased number of loops. Also, in these three cases of lipoid nephrosis the basement membrane of *all* the glomeruli is involved while in hypertension the percentage varies.

The glomerular tuft may be thought of as a filter with the glomerular basement membrane as the gel lying between endothelium and epithelium. The greatly increased thickness of the gel in hypertensive glomeruli must alter its permeability. This change may explain the urinary albumin in such cases.

Inflammatory glomeruli (Fig. 5) may occur in all types of essential hypertension and it is not justifiable to separate benign (without renal insufficiency) and malignant (with renal insufficiency) on such lesions. However, the greatest number of inflammatory glomeruli is found in the renal group (Table III) and a high percentage is usually indicative of a uremic death. All cases in the uremic group of this series show glomeruli with inflammatory lesions. The changes in these glomeruli are considered inflammatory rather than vascular in origin because they are generally identical with the intracapillary lesions of glomerulonephritis.

It has been suggested by others that the younger patients dying of essential hypertension have a greater number of inflammatory glomeruli. My series does not support such a view, for Cases 47 and 48, aged 60 and 69 years respectively, have the greatest inflammatory change. Neither is the highest percentage of hypertensive contracted glomeruli found in younger cases. Cases 21 and 49 who were 55 and 71 years of age have the greatest number of such glomeruli. There are not sufficient data available to determine the correlation between duration of symptoms and percentage of hypertensive glomeruli.

The renal group of essential hypertension has much in common clinically and microscopically with those cases of chronic glomerulonephritis which have severe vascular disease. Death is from uremia in both conditions and microscopically both show arteriolosclerosis and inflammatory glomeruli. However, in the kidney of chronic glomerulonephritis almost all the glomeruli are diffusely inflamed, while there are rare hypertensive and practically no normal glomeruli. On the other hand, the renal hypertensive kidney has a small number of diffusely inflamed glomeruli, a larger number with focal lesions, a high percentage of hypertensive glomeruli and a definite proportion of normal glomeruli. An anilin blue stain shows that glomerulonephritis is an intracapillary obstruction of the tufts while essential hypertension is a change in the glomerular basement membrane.

Conclusions

1. The glomerular lesion of essential hypertension is as typical as the arteriolar lesion. It consists of a decrease in size and a simplification of the glomerulus with a marked thickening and wrinkling of the glomerular basement membrane.

In this series of fifty-one cases, the average percentage of such glomeruli is 47 in the renal group (death from uremia), 33 in the cardiac group (death from myocardial insufficiency or coronary disease), and 24 in the cerebral group (death from apoplexy).

2. The arteriolosclerosis precedes and is related to the change in the glomerular basement membrane.

3. Kidneys from individuals dying in the fifth, sixth, seventh and eighth decades with a history of normal blood pressure show 96.2 per cent normal glomeruli. A rare hypertensive contracted glomerulus may be found.

4. There are inflammatory glomeruli in any type of essential hypertension but they are most numerous in the renal group. The lesions are usually focal and as many as 15 per cent of the glomeruli may be involved.

5. Anilin blue (Mallory-Heidenhain azan carmine) is recommended as a routine stain for kidney tissue. It is particularly helpful to differentiate the renal group of essential hypertension from those cases of chronic glomerulonephritis which have extensive vascular disease.

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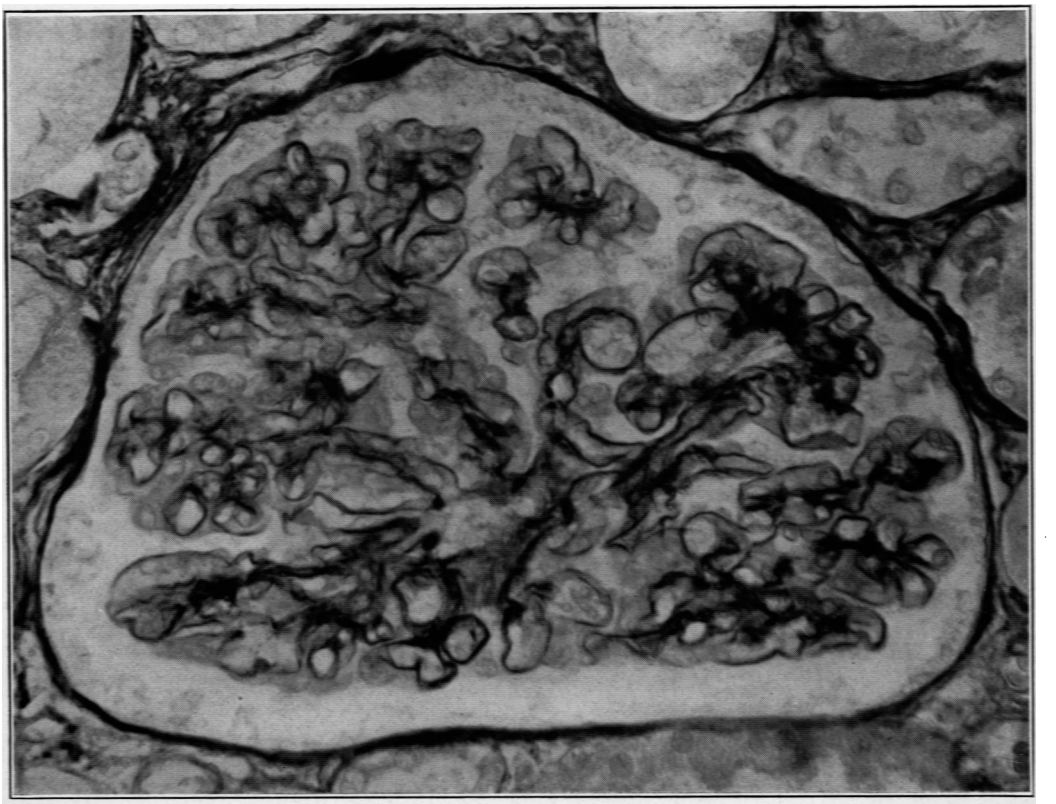
DESCRIPTION OF PLATES

PLATE 75

FIG. 1. A normal glomerulus from Case 49. Essential hypertension with death from uremia in a man of 71 years. Only 20 per cent of his glomeruli were normal. The photomicrograph shows (1) the normal thinness and continuity of the glomerular basement membrane which forms the middle layer of the wall of the tuft, (2) the continuous layer of glomerular epithelium lying external and adjacent to the membrane, and (3) a few endothelial cells lining the internal surface of the membrane. Stain, Mallory-Heidenhain azan carmine. × 500.

FIG. 2. A hypertensive contracted glomerulus from Case 37. Essential hypertension with death from uremia in a woman 37 years of age. Seventy-one per cent of her glomeruli were of this type. The photomicrograph shows (1) a small simplified glomerulus with many less loops than normal, and (2) a marked thickening and wrinkling of the glomerular basement membrane. Stain, Mallory-Heidenhain azan carmine. × 500.



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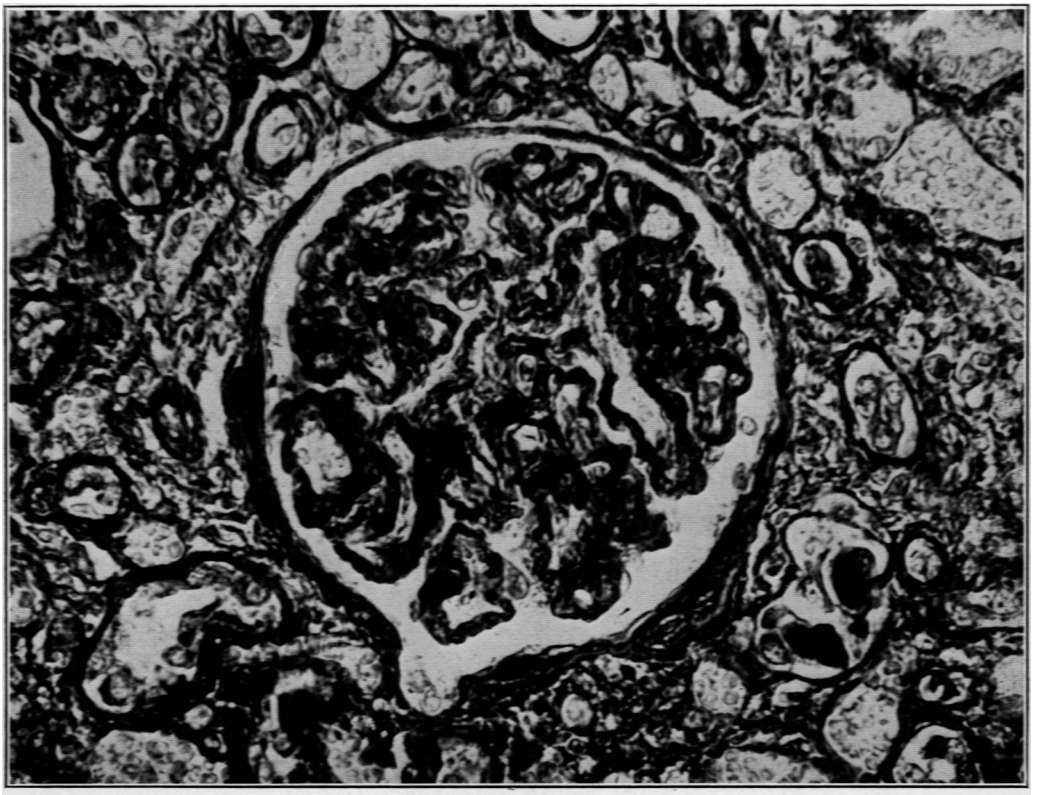

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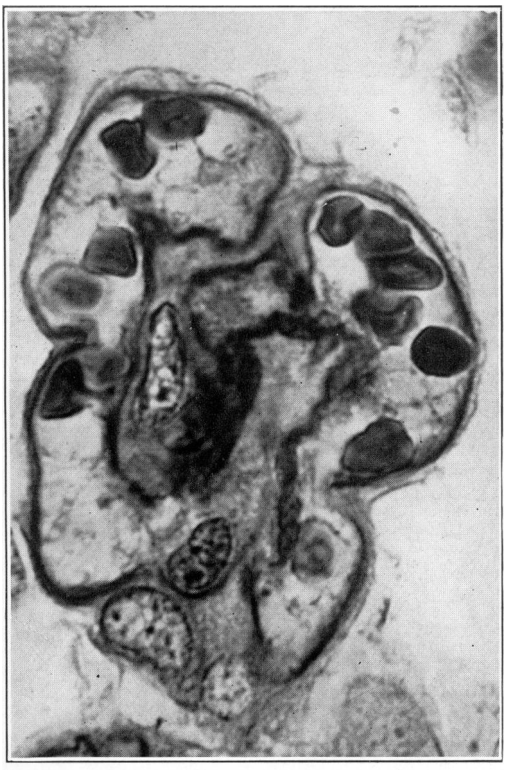
PLATE 76

FIG. 3. Two normal loops from a normal glomerulus. Case 50. Essential hypertension with death from rupture of the aorta in a man 47 years of age. Only 18 per cent of his glomeruli were normal. The photomicrograph shows (1) the thinness of the normal glomerular basement membrane, and (2) the continuous covering layer of glomerular epithelial cytoplasm. There are four nuclei in the field of which the upper one and the lower two are external to the basement membrane and are epithelial. The fourth nucleus which lies in the center of the group is internal to the basement membrane and is endothelial. Stain, Masson's rapid method with iron hematoxylin substituted for the azo carmine in the Mallory-Heidenhain azan carmine technique. × 1500.

FIG. 4. Two loops from a hypertensive contracted glomerulus. Case 50 (same as Fig. 3). Essential hypertension with death from rupture of the aorta in a man 47 years of age. Seventy-one per cent of his glomeruli were of the type in this illustration. The photomicrograph shows (1) a marked thickening and wrinkling of the glomerular basement membrane (contrast with Fig. 3), (2) normal glomerular epithelium external to the membrane, and (3) normal glomerular endothelium internal to the membrane. Stain, the same as in Fig. 3. × 1500.

FIG. 5. A glomerulus showing diffuse acute inflammation. Case 21. Essential hypertension with death from cardiac decompensation in a man 55 years of age. Only 2 per cent of such glomeruli were found. The photomicrograph shows (1) an enlarged glomerulus, (2) glomerular epithelium which is swollen and undergoing hyaline granular degeneration, (3) a glomerular basement membrane of normal thinness, and (4) obstruction to the circulation by intracapillary fibers and proliferated endothelium. The loops on the right contain mononuclear cells filled with fat. (5) In the upper left portion of the field, an arteriole with an irregular subendothelial deposit of hyalin is seen. Stain, the same as in Fig. 3. × 500.



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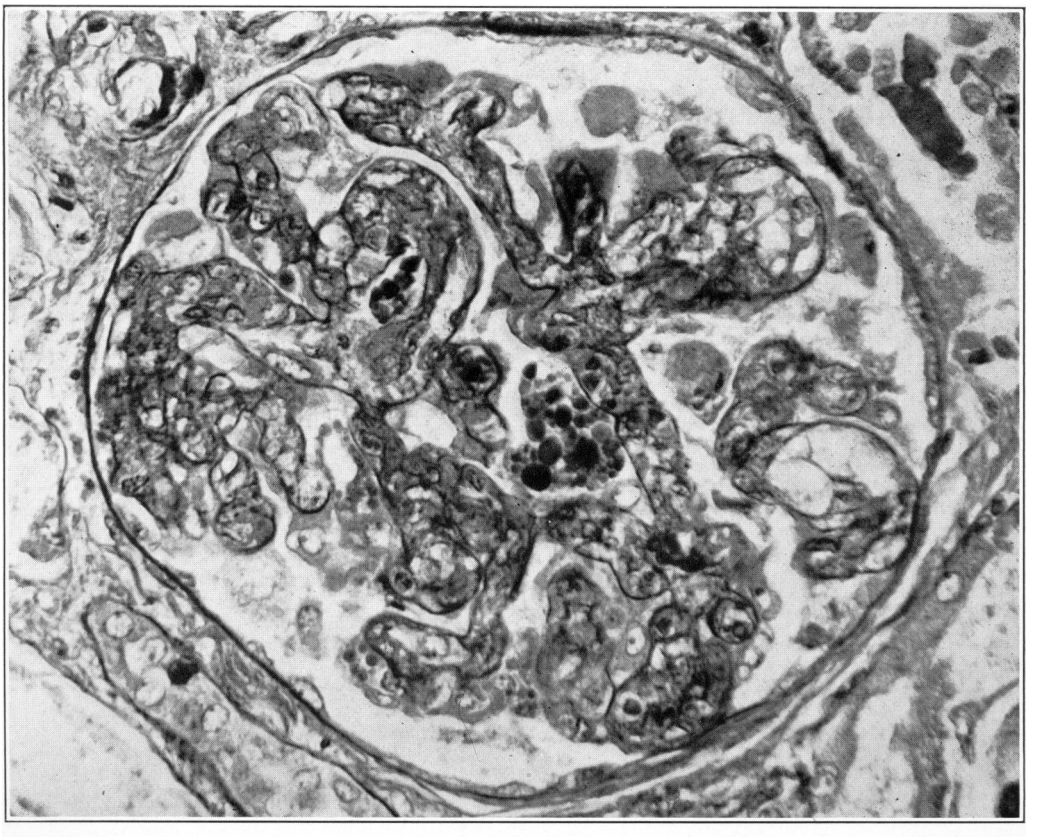

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