Diagnosis and Treatment of Hypertension Due to Occlusive Disease of the Renal Artery *

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Introduction

ALTHOUGH interest in unilateral renal disease as a cause of hypertension followed the experimental production of hypertension by Goldblatt,[7] in 1934, the lack of specific diagnostic methods made the diagnosis uncertain. Nephrectomy in a number of patients with unilateral renal disease of nonspecific type did not give the anticipated fall in blood pressure. A review of the reported experiences by Smith,[19] in 1948, demonstrated that only a minority of patients had relief of hypertension following nephrectomy.

Interest in a more exact diagnosis was aroused by the report of Howard, Berthrong, Gould, and Yendt,[8] in 1954, of eight hypertensive patients with renal artery disease who were improved following nephrectomy, and some of whom were found before operation to have a decreased excretion of water and sodium by the ischemic kidney. Subsequent experiences with this technic recently were summarized by Connor, Thomas, Haddock and Howard.[3] Additional important diagnostic technics appeared with the demonstration of the value of aortography by Poutasse and Dustan,[15] and with the development of the radioactive renogram by Winter.[23] All of these diagnostic methods, however, have been limited by either failure to detect renal disease causing hypertension in some patients or by not determining whether a renal abnormality found to be present was causing hypertension.

Uncertainty has also existed about the manner in which renal artery obstruction causes hypertension. As severe renal ischemia has not been found, it has been suggested that an obstruction causing a change in pulse pressure in the renal artery may cause hypertension without causing a either a decrease in mean arterial pressure distal to the obstruction or a decrease in renal blood flow.[13]

Several surgical procedures have been used for correction of an obstructed renal artery. One of the first successful cases was reported by Freeman [6] in 1954, who removed an atherosclerotic plaque by endarterectomy. DeCamp,[4] Hurwitt [9] and Luke [10] each have reported favorable results with anastomosis of the splenic artery to the left renal artery. An extensive experience with the use of bypass grafts has been reported by Morris, *et al.;* [11, 12] these authors have also described the use of patch graft reconstruction of the arterial wall following a local endarterectomy. Additional surgical experiences have been reported by Brown,[2] Yendt [25] and Trippel.[22] There is at present little to show the advantages or limitations of the various surgical procedures which have been reported.

A urea-inulin test of differential renal function recently developed in the Department of Urology has been found to be of greater diagnostic value than any other

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previously used diagnostic technic. In addition, comparative studies of renal function have shown consistent physiological abnormalities which seem to characterize an ischemic kidney causing hypertension. This report presents our experiences with this and other diagnostic methods in diagnosis and surgical treatment of 27 hypertensive patients with renal artery obstruction.

Clinical Material

Pathological Findings. Data from the 27 patients described in this report are shown in Table 1 grouped according to the disease process obstructing the renal artery and according to the time when operation was performed. The first operation (Case 1) was in June 1958 and the last in February 1961 (Case 12).

In 12 patients (Cases 1–12) the renal artery was obstructed by an atherosclerotic plaque, almost always located at the origin of the renal artery from the aorta. Fibromuscular hyperplasia of the renal artery caused obstruction in 11 other patients (Cases 13–23). In two the obstruction was associated with accessory renal arteries (Cases 24, 25); in one of these (Case 24) an accessory renal artery was stenosed at its origin from the aorta. The other patient had diffuse arterial disease but involving only the intrarenal vessels with thrombosis and recanalization and hence the association with an accessory renal artery may be coincidental. An aneurysm of the main renal artery was present in one patient (Case 26), and in aneurysm of an accessory renal artery was present in the other (Case 27). Obstruction of both renal arteries was found in only two patients (Cases 2, 3), and in each of these the stenosis was caused by an atherosclerotic plaque. These data are summarized in Table 2.

The disease process termed "fibromuscular hyperplasia" is a poorly understood condition which has been found to cause renal artery obstruction in children and young adults. In addition to the histological picture it differs from atherosclerosis in the segment of renal artery involved and the age and sex incidence. Atherosclerosis is usually limited to the immediate area of origin of the renal artery from the aorta. By contrast, in only three of our 11 patients with fibromuscular hyperplasia was the disease limited to a short segment of the renal artery (Cases 13–15). In the others the disease involved the distal renal artery and its segmental branches to such an extent that renal artery reconstruction was possible in only one of these eight patients (Case 20). Table 3 correlates the location and type of renal artery obstruction.

Figure 1 shows the contrast in ages of the patients with fibromuscular hyperplasia and those with atherosclerosis. Our youngest patient in the former group was five years of age, and the oldest was 50; in the atherosclerotic group the youngest was 39 and the oldest 69. Figure 2 contrasts the sex incidence of the two conditions. The atherosclerotic lesions occurred predominantly in men, whereas fibromuscular hyperplasia was found with about equal frequency in the two sexes.

Symptoms and Signs. Headache, often of a severe degree, was the most common complaint (18 of 27 patients). An unusual restlessness or nervousness, which has been found to be an important symptom by DeCamp, was seen in only five patients. In two of these, however, the prompt disappearance of this feature shortly following operation was impressive.

The hypertension was usually severe, with a systolic pressure of 200 mm. Hg or higher and a diastolic pressure above 100 mm. Fluctuations in the blood pressure were common, often with elevation as high as 240/140 mm. Hg. The presence of hypertension had been recognized for less than a year in 11 patients, but some of these had not previously had the blood pressure measured for several years. By contrast nine patients had known severe hypertension for five years or longer. A severe

TABLE 1. *Clinical Findings in 27 Patients with Hypertension and Occlusive Disease of the Renal Arteries*

Case No. Initials	Age Sex	Duration Hypertension	Blood Pressure Range (mm. Hg)	Symptoms	Abdominal Bruit	Disease Present; Renal Artery Involved	Treatment; Date	Operative Findings Systolic Pressure Gradient (mm. Hg) Before	After	Postoperative Blood Pressure Time Since Operation	Comments
1 M.B.	40 F	3 yrs.	250/150	headache, chest pain, dyspnea	no	atherosclerotic stenosis, left main	endarterectomy only 6-58	100	—	149/90—2 mos.; 220/115—24 mos.	possible recurrence of renal artery disease; evaluation incomplete
2 B.H.	57 F	7 mos.	240/120	headaches, dyspnea, uremia	no	atherosclerotic stenosis, left main	splenorenal anastomosis 11-58	160	0	210/90—10 mos. 130/70—19 mos. 152/90—25 mos.	good result; additional BP decrease after 10 mos.; had had right nephrectomy 12–57
3 D.S.	55 M	3 mos.	220/130; 170/110	dyspnea	no	atherosclerotic stenosis both renal arteries	endarterectomy, bilateral; 3-59	faint pulse beyond constriction	—	—	renal artery thrombosis; death
4 M.C.	57 M	2–3 wks.	220/110	headaches, depression	no	atherosclerotic stenosis, right main	Teflon patch; 2-60	120	20	170/100—10 das; 150/80— 9 mos.	good result
5 D.G.	51 F	2 yrs.	290/140; 160/100	headaches, blurred vision	no	atherosclerosis; left main; distal thrombosis	nephrectomy 3-60	artery thrombosed	—	180/100—10 das; moderate hypertension—12 mos. controlled with drugs	operative benefit uncertain
6 C.G.	51 M	5 mos.	200/120; 180/100	headaches, depression	no	atherosclerotic stenosis, left main	splenorenal anastomosis 4-60	90	0	150/90—10 das; normotensive—9 mos.	good result
7 J.K.	45 M	5 yrs.	180/130; 150/90	headaches; extreme nervousness; history of flank pain	no	atherosclerosis and thrombosis, segmental renal artery	nephrectomy; 4-60	artery thrombosed	—	130/80—3 das 150/100—9 mos.	good result; nervousness quickly subsided; mild systolic hypertension
8[1] F.R.	39 M	4 yrs.	240/150; 190/125	headaches, angina	no	atherosclerotic stenosis, left main	Dacron patch; 7-60	100	0	140/90—6 mos.	good result
9[2] F.W.	49 M	5 mos.	260/160; 160/90	headaches	no	atherosclerotic stenosis, left main	Dacron patch; 7-60	100	0	120/70—10 das 100/80— 6 mos.	good result
10 E.Y.	57 M	5–10 yrs.	230/110	angina, claudication	no	atherosclerotic occlusion, right main	by-pass graft 11-60 abd. aneurysm excised	180	0	200/110—2 mos.	benefit uncertain
11 J.W.	43 M	unknown	240/120	dyspnea, 1 yr.	no	atherosclerotic occlusion, left main	splenorenal anastomosis 1-61	180	0	220/120—4 wks.	outcome uncertain; too recent to evaluate
12 R.F.	69 M	3 yrs.	240/140	angina, depression	yes	atherosclerotic stenosis, left main	Dacron patch 2-61	210	0	190/110—2 wks.	too recent to evaluate
13 W.H.	5 M	7 mos.	250/140; 140/80	none	no	fibromuscular, hyperplasia, left main	excision stenosis; anastomosis; 8-58	—	—	155/100—2 wks. 130/70—18 mos.	good result

[1] Operated upon at Walter Reed Army Hospital, Washington, D. C., with Col. Arthur Cohen, M.C., U.S.A.
[2] Operated upon at National Institutes of Health, Bethesda, Md., with Dr. Louis Gillespie.

TABLE 1.—(*Continued*)

Case No. Initials	Age Sex	Duration Hypertension	Blood Pressure Range (mm. Hg)	Symptoms	Abdominal Bruit	Disease Present; Renal Artery Involved	Treatment: Date	Operative Findings Systolic Pressure Gradient (mm. Hg) Before	After	Postoperative Blood Pressure Time Since Operation	Comments
14[1] R.E.	12 M	5 yrs.	230/130; 140/90	headaches	yes	fibromuscular, hyperplasia, left main	Dacron patch 3-60	100	30	140/90—12 mos.	good result; mild systolic hypertension
15 A.R.	18 M	8 mos.	190/110; 160/90	none	no	fibromuscular hyperplasia, left main	excision stenosis; anastomosis; 9-60	120	30	140/70—5 wks. 130/72—6 mos.	good result
16 L.G.	27 F	8 yrs.	200/140; 140/100	headaches, mild	no	fibromuscular hyperplasia; right main and branches	nephrectomy 3-59	—	—	140/90—14 das normotensive—21 mos.	good result
17[2] A.C.	50 M	10 mos.	220/130; 180/110	headaches	no	fibromuscular hyperplasia; left main and branches	splenorenal anastomosis 9-59; nephrectomy 12-59	90	0	recurrent hypertension after 1st operation; 146/96—2 mos. after nephrectomy	splenorenal failed; good result after nephrectomy
18[1] M.C.	28 M	2 yrs.	240/140; 160/110	headaches	yes	fibromuscular hyperplasia; left main and branches	nephrectomy 12–59	45	—	110/80—1 da. normotensive—10 mos.	good result
19 B.L.	25 F	10 yrs.	240/140	headaches, restlessness	yes	fibromuscular hyperplasia, right segmental	nephrectomy 7-60	—	—	prompt blood pressure decrease; 130/105—160/118—7 mos.	good result; mild systolic hypertension
20[2] J.B.	12 F	2 yrs.	220/150	headaches	no	fibromuscular hyperplasia, right main	Dacron patch; 7-60	100	30	120/90—9 das; 110/70—5 mos.	good result
21[2] V.M.	24 F	6 yrs.	210/120;	headaches	no	fibromuscular hyperplasia, left main and branches	nephrectomy 7-60	100	—	120/80—1 da. 120/90—6 mos.	good result
22 L.S.	25 F	8 yrs.	170/110	headaches	yes	fibromuscular hyperplasia, right main and branches	nephrectomy 10-60	70	—	130/90—7 das. 145/105—4 mos.	good result; mild systolic hypertension
23[2] G.S.	29 M	4 mos.	200/105;	history of recent convulsions and flank pain	no	fibromuscular hyperplasia, aneurysm, thrombosis, left main	nephrectomy 12-60	artery thrombosed	—	150/80—2 das. 170/100—2 mos.	good result; residual systolic hypertension
24[3] B.C.	34 M	5 mos.	235/145; 160/110	headaches	yes	3 renal arteries, left kidney; stenosis of one	nephrectomy 11-60	100	—	160/110—2 mos.	good result; mild residual hypertension
25[2] C.P.	63 F	several yrs.	210/110	none	no	accessory renal artery, left; pelvic kidney; atherosclerosis & recanalization of intrarenal arteries	nephrectomy 1-61	—	—	160/90—2 wks. 230/100—4 wks.	uncertain result; systolic hypertension
26 A.M.	35 M	11 mos. intermittent	200/100; 116/70	none; history of flank pain	no	aneurysm, right renal artery; renal infarction	nephrectomy 1-59	—	—	120/80—4 mos.	good result
27 W.G.	19 M	11 yrs.	180/130; 170/110	headaches	no	aneurysm and stenosis in accessory right renal artery	nephrectomy 11-59	—	—	140/90—2 das. 125/85—14 mos.	good result

[3] Operated upon at Walter Reed Army Hospital, Washington, D. C., with Col. Thomas Whelan, M.C., U.S.A.

TABLE 2. *Cause of Renal Artery Obstruction in 27 Patients*

Cause	No. Patients
Atherosclerotic plaque	12
Fibromuscular hyperplasia	11
Accessory renal arteries	2
Aneurysm, renal artery	2

hypertension of recent onset seemed to suggest renal ischemia, but the absence of this finding did not exclude the diagnosis. A similar relationship was observed regarding the response to anti-hypertensive drugs—the failure to respond to drug therapy suggested renal ischemia in some, but in others the response to drugs was not unusual.

The only significant physical finding was the detection of a systolic bruit in the upper abdomen in six patients, usually loudest on one side. It was often missed on initial examination, but could be heard best by pressing the bell of the stethoscope firmly into the abdominal wall. The murmur was not carefully sought in all patients and hence probably was overlooked in some. A systolic bruit, although suggestive, is not diagnostic of renal artery stenosis, however, because it might result from atherosclerotic plaques in the upper abdominal aorta or the celiac or superior mesenteric arteries.

In the 12 patients with renal ischemia from an therosclerotic plaque, additional occlusive disease was present in four, involving the aorta in one, the iliac arteries in two, and the femoral arteries in one. Angina pectoris was present in three patients. Other significant physical findings were not found.

In summary, although the symptoms or physical signs suggested renal ischemia in several patients and led to studies which proved the diagnosis, no single finding was noted which either confirmed or excluded renal ischemia. As reported by Dustan, *et al.*,[5] the features which suggest renal ischemia are: hypertension before 30 years of age (11 patients); hypertension of recent onset and severity, especially when appearing in an older person with other signs of atherosclerosis; or hypertension following an episode of flank pain suggestive of renal infarction (3 patients).

Diagnostic Studies

The diagnostic studies performed upon patients with suspected renal ischemia are shown in Table 4, and the frequency with with each test detected a unilateral renal abnormality is summarized in Table 5.

The *intravenous pyelogram* showed an abnormality in the ischemic kidney in 13 of 26 patients. By far the most common abnormality was the finding that the ischemic kidney was usually small (1.5–2.5 cm.) than the other kidney (8 patients). This small difference in size can be readily overlooked unless each kidney shadow is measured on the roentgenogram. The importance of exact measurement is further emphasized by the fact that normal kidneys seldom differ by more than one centi-

TABLE 3. *Site of Renal Artery Obstruction in 27 Patients*

Arterial Disease Present	Site of Obstruction		
	Main Renal Artery Only	Main Renal Artery and Branches	Branch Renal Artery Only
Atherosclerotic* plaque	11	0	1
Fibromuscular hyperplasia	5	5	1
Aneurysm	0	1	1
Accessory renal arteries	0	0	2

* Lesion bilateral in 2 patients.

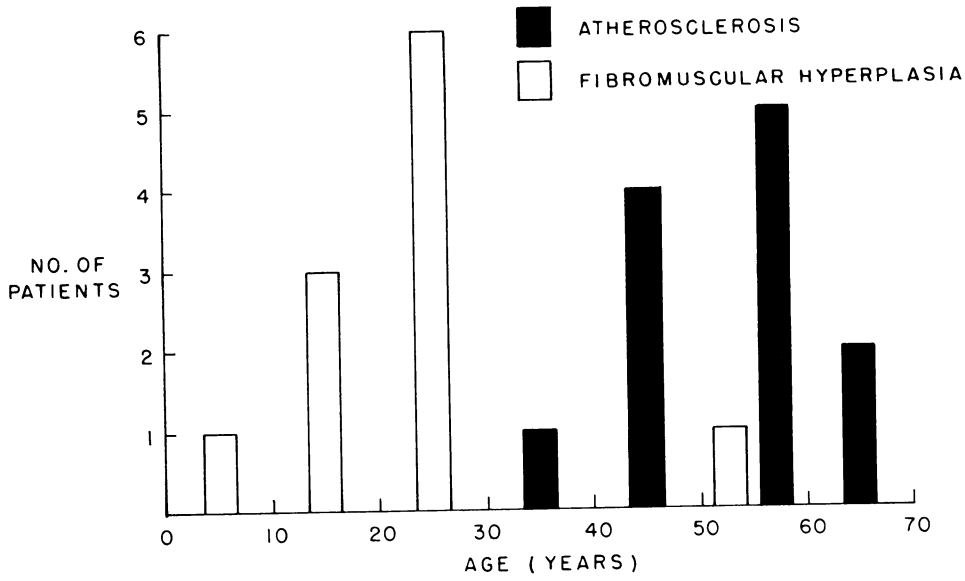


FIG. 1. Difference in age distribution of 12 patients with renal artery obstruction from atherosclerosis and 11 patients with obstruction from other causes.

meter in length. A difference in dye concentration between the two kidneys was observed in three patients. In all of these the dye concentration was *decreased* in the ischemic kidney. It should be remembered, however, that the opposite relationship can also occur, for increased water reabsorption secondary to reduced glomerular filtration can cause an *increased* dye concentration in the ischemic kidney.[21] In four patients the ischemic kidney could not be seen on the pyelogram; on subsequent surgical exploration severe obstruction of the renal artery was found in each of the four.

Elevation of the blood urea nitrogen, indicating severe reduction in renal function, was found in only four patients. Bilateral renal artery obstruction was subsequently found in two of these, and severe unilateral renal artery obstruction in the other two.

Renal blood flow was estimated by performing a radioactive *renogram* in 11 patients, using the technic originally described by Winter.[23] These studies were done by Dr. Francis Chinard in the Department of Medicine at the Baltimore City Hospitals. Although exact measurement of renal blood flow is not possible with this technic, a decrease in renal blood flow was detected in eight of the 11 patients studied.

An *aortogram* was performed in 23 patients and demonstrated the obstruction in the renal artery in 19. The aortography was done either by percutaneous aortic puncture or by the retrograde insertion of a catheter from the femoral artery to the aorta. *Hypaque* was the contrast medium usually employed and did not result in any serious complications. Representative aort-

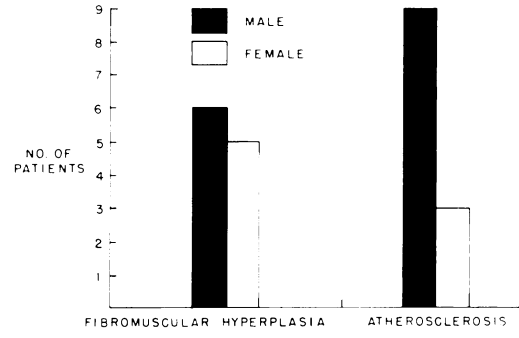


FIG. 2. Bar graph illustration of the difference in sex incidence of patients with renal artery obstruction from atherosclerosis and those with obstruction from other causes.

TABLE 4. *Diagnostic Tests in 27 Patients with Hypertension and Occlusive Disease of the Renal Artery*

No. Initials (Table I)	Location Ischemic Kidney	Intravenous Pyelogram (Ischemic Kidney)	Blood Urea Nitrogen (mg. %)	Renogram (Ischemic Kidney)	Aortogram (Ischemic Kidney)	Howard Test (Na, H_2O Excretion)	Urea Inulin Test
1 M.B.	left	2 cm. smaller	normal	*	stenosis renal artery	pos.	*
2 B.H.	left	nonfilling	65	*	stenosis renal artery	*	*
3 D.S.	bilateral	nonfilling, rt.	40	no function on right	*	no urine excretion	*
4 M.C.	right	normal	normal	decreased blood flow	stenosis, renal artery	*	*
5 D.G.	left	nonfilling; 2 cm. smaller before	38	no blood flow	occlusion of renal artery	no urine excretion	*
6 C.G.	left	normal	normal	decreased blood flow	normal	neg.	*
7 J.K.	right	kidney smaller	normal	*	occlusion of segmental art.	neg.	pos.
8 F.R.	left	normal	normal	normal	stenosis, renal artery	*	
9 F.W.	left	decreased dye concentration	normal	*	stenosis, renal artery	pos.	pos.
10 E.Y.	right	*	normal	*	—	*	*
11 J.W.	left	nonfilling	31	*	occlusion of renal artery	no urine excretion	*
12 R.F.	left	kidney smaller	normal	*	—	pos.	pos.
13 W.H.	left	normal	normal	*	stenosis, renal artery	data uninterpretable	*
14 R.E.	left	normal	normal	*	stenosis, renal artery	*	*
15 A.R.	left	2 cm. smaller	normal	*	stenosis, renal artery	pos.	*
16 L.G.	right	normal	normal	decreased blood flow	stenosis,— segmental renal arteries	pos.	
17 A.C.	left	normal	normal	*	stenosis, bifurcation of renal artery	pos.	pos.
18 M.C.	left	normal	normal	decreased blood flow	stenosis, renal artery	*	*
19 B.L.	right	kidney smaller; decreased dye concentration	normal	decreased blood flow	normal	neg.	pos.
20 J.B.	right	kidney smaller	normal	*	stenosis, renal artery	pos.	pos.
21 V.M.	left	normal	normal	*	stenosis, renal artery and branches	pos.	pos.
22 L.S.	right	2.4 cm. smaller	normal	normal	—	pos.	pos.
23 G.S.	left	decreased dye concentration	normal	*	stenosis, renal artery	neg.	pos.
24 B.C.	left	normal	normal	decreased blood flow	stenosis ? of accessory renal arteries	data uninterpretable	*
25 C.P.	left	normal	normal	*	normal	neg.	pos.
26 A.M.	right	normal	normal	*	aneurysm of renal artery	*	*
27 W.G.	right	normal	normal	normal	normal	neg.	pos.

* Not performed.

ograms of different causes of renal artery obstruction are shown in Figures 3–7.

The location of the renal artery obstruction in the four patients in whom the aortogram did not demonstrate the obstruction is of interest. In one of these (Case 6) a stenosed main renal artery would probably have been seen if the dye concentration on the aortogram had been greater. In the other three patients, however, the stenosis was in a segmental renal artery in two and in small *intrarenal* arteries in one (Case 25). In these three patients it is not surprising that the stenosis was not visualized.

The *Howard test*, ureteral catheterization to obtain comparative rates of urine excretion and sodium concentration from each kidney,[8] was satisfactorily performed in 15 patients. In five other patients a satisfactory study could not be done because of inadequate rates of urine flow. The test indicates renal ischemia if the water excretion from a kidney is reduced 50 per cent or more, and the sodium excretion is reduced at least 15 per cent.[3] A *positive* test, indicating renal ischemia, was found in nine patients. All of these patients except one had stenosis of the main renal artery, and this patient (Case 16) had stenosis of all of the segmental renal arteries. By contrast only one of the six patients with a *negative* test had a stenosis in the main renal artery; a segmental artery was stenosed in four patients, and one had a recent extensive kidney infarction (Case 22).

The only test which detected an ischemic kidney in all of the patients studied was the *urea-inulin* method of evaluating renal function. This technic has only re-

TABLE 5. *Diagnostic Studies for Renal Hypertension*

Study Performed	No. Patients	Abnormalities Found (%)
Intravenous pyelogram	26	50
Howard test (water, Na excretion)	15	60
Renogram	11	73
Aortogram	23	83
Urea-inulin test	11	100

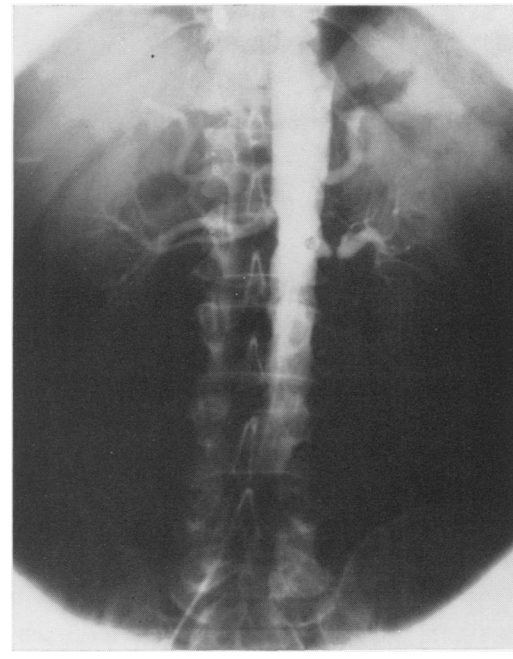


FIG. 3. Aortogram showing atherosclerotic plaque causing marked narrowing of the proximal left renal artery. The plaque was removed by endarterectomy and patch graft reconstruction.

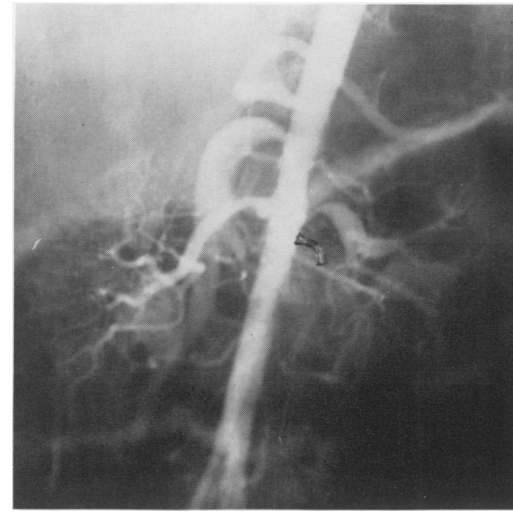


FIG. 4. Aortogram showing narrowing of proximal left renal artery in a five-year-old boy. The excised speciment is superimposed on the aortogram. Arterial reconstruction was done by direct anastomsis.

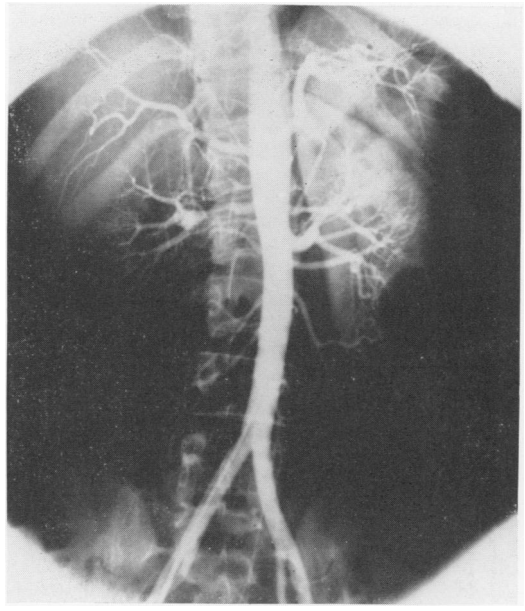


FIG. 5. Aortogram showing diffuse stenosis in the distal right renal artery from fibromuscular hyperplasia in a 12-year-old girl. Reconstruction was done by application of a patch graft.

TABLE 6. *Criteria for Adequate Differential Renal Function Studies by Ureteral Catheterization*

1. No bladder leakage
2. Urine flow rates greater than 2 ml./min. per kidney
3. No uretero-renal reflexes
4. Three Consecutive 10-minute collection periods agreeing within 6 per cent in their ratio of urine flow rates

cently been devolped and is described in detail in the following paragraphs.

Differential Renal Function Measured by the Urea-Inulin Test. During the past four years a method for the study of renal function by ureteral catheterization has been developed in the Department of Urology which avoids some of the limitations of earlier technics.[20, 21] As the details of the method recently have been described, only the essential features will be mentioned here. Under spinal anesthesia ureteral catheters are inserted so that leakage of urine about the catheters does not occur,

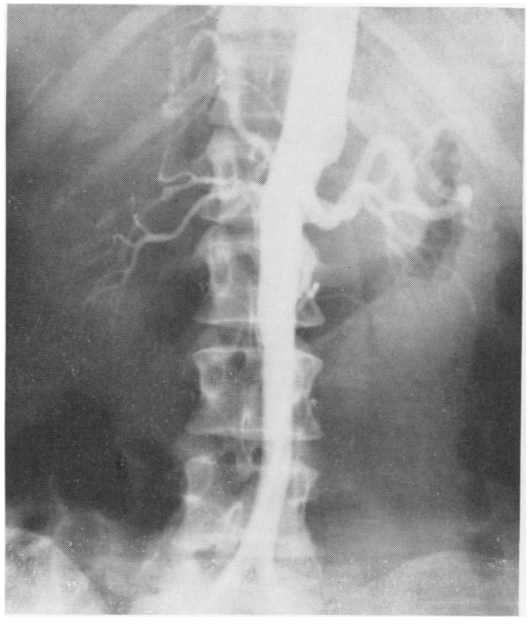


FIG. 6. Aortogram showing diffuse stenosis of the right segmental arteries in a 27-year-old woman. A nephrectomy was required because of the extent of the involvement of the segmental arteries.

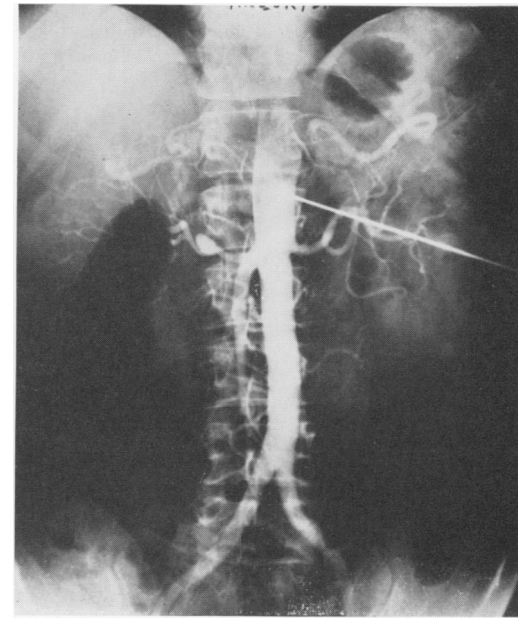


FIG. 7. Aortogram showing aneurysm of the right renal artery involving the bifurcation of the renal artery in a 35-year-old man. A nephrectomy was required.

and uretero-renal reflexes are minimized. The studies are performed using an intravenous infusion of eight per cent urea in saline, which contains inulin, para-aminohippuric acid and Pitressin.

The criteria for an adequate study of renal function by ureterial catheterization are summarized in Table 6. The rate of flow of urine should be greater than 2.0 ml./min. from each kidney, and the ratio

TABLE 7. *Renal Function Data from Studies with Bilateral Ureteral Catheterization*

Case		Urine Flow			Urine Sodium			Urine Creatinine			Urine Inulin			PAH Clearance		
		X	Y	X/Y	X	Y	X/Y	X	Y	X/Y	X	Y	X/Y	X	Y	X/Y
		ml./min.			mEq./L.			mg.%			mg.%			ml./min.		
1. R.F.*		0.07	7.70	.01	30	113	0.26				3,209	382	8.40	41	302	.13
2. C.P.	1.	0.73	3.66	.20	164	160	1.03				563	362	1.56	56	210	.27
	2.*	0.92	9.66	.10	112	103	1.09				437	198	2.21	70	408	.17
3. G.S.	1.	0.47	1.93	.24	41	38	1.08				686	703	0.98	44	214	.21
	2.*	1.00	4.93	.20	80	75	1.07				563	471	1.20	69	380	.18
4. F.W.*		0.71	10.40	.06	58	111	0.51				785	165	4.76	125	518	.24
5. J.B.*		1.22	13.17	.09	34	78	0.44				407	96	4.24	190	434	.45
6. V.M.*		1.63	5.02	.32	40	68	0.60				664	307	2.16	328	532	.63
7. A.C.*		1.56	6.18	.25	84	113	0.74				491	205	2.40	274	367	.74
8. L.S.*		2.29	16.48	.14	41	107	0.39				580	111	5.22	181	236	.77
9. B.L.	1.	3.33	5.73	.58	16	16	0.99				316	272	1.16	126	175	.71
	2.*	2.81	5.86	.48	73	80	0.92				401	312	1.28	135	219	.61
10. J.K.	1.	2.03	3.56	.56	32	32	1.10				427	402	1.06	163	265	.61
	2.*	2.91	5.51	.53	96	100	0.96				285	245	1.16	168	272	.62
11. W.G.*		0.98	3.57	.28	131	139	0.94				510	382	1.34	125	303	.41
12. C.G.		1.69	6.76	.25	42	27	1.56	18	8	2.25						
13. L.G.		2.74	6.43	.43	3.7	18	.21									
14. M.B.		.62	7.64	.08	3.5	27	.13									
15. A.R.		.55	1.09	.50	156	248	.63	114	72	1.58						

X = Affected kidney; Y = Normal or less affected kidney.

* Studies performed with infusion of 8 per cent urea in saline with Pitressin (ADH). All other studies performed with oral water hydration. The data on Cases 1–11 represent the average of 3 or more consecutive 10 min. periods which agree within 6 per cent in their ratio of urine flow rates. The data on Cases 12–15 represent one collection period of approximately 10 minutes in duration selected from two or three reasonably representative periods.

Cases 1–8 = Main renal artery obstructions in ascending order of decreased renal plasma flow. In Case 2, the arterial obstruction was in the arcuate and interlobar arteries, rather than the main renal arteries. Case 3 shows the smallest relative increase in the concentration of inulin. See footnote in text.

Cases 9–11 = Segmental renal artery obstructions. Case 11 was complicated by bladder leakage at the rate of .70 ml./min. This accounts for the increased reduction in urine flow rate and PAH clearance in the affected kidney.

Cases 12–15 = Main renal artery obstructions (studies performed in Dr. J. E. Howard's laboratory). Case 14 was complicated by bladder leakage at the rate of 4.82 ml./min. containing a sodium concentration of 30 meq./L. This was probably from the better kidney, Y.

TABLE 8. *(Case 22) L.S. 25-year-old, White Woman with Right Main Renal Artery Obstruction*

Time (min.)	Urine Flow			PAH Concentration			PAH Clearance			Urine Sodium			Urine Osmolality			Inulin Concentration			Inulin Clearance		
	R	L	R/L	R	L	R/L	R	L	R/L	R	L	R/L	R	L	R/L	R	L	R/L	R	L	R/L
	ml./min.			mg./100 ml.			ml./min.			μEq./ml.			μOsms./Gm. H_2O			mg./100 ml.			ml./min.		
−75	1,000 ml. of water, p.o.																				
−60	Plasma No. 1 drawn.									Plasma = 146.7			Plasma = 255								
−55	17 ml. of 10% inulin and 2.0 ml. of 20% PAH injected I.V.; start infusion of 5% D/W at 1.1 ml./min. to deliver 20 mg./ml. of inulin and 10.9 mg./ml. of PAH.																				
−50	Nupercaine saddle anesthesia.																				
−30	400 ml. of water, p.o.																				
−10	200 ml. of water, p.o.																				
0	No. 8 polyethylene catheter passed easily to the right mid-ureter.																				
2	No. 8 polyethylene catheter passed easily to the left mid-ureter.																				
15	Plasma 2 drawn.									Plasma = 144.7			Plasma = 245								
12–37	.11	.21	.53	2,660	1,530	1.74	105.5	115.8	.91	40.2	68.9	.58	453	655	.69	4,640	4,440	1.05	19.9	36.4	.54
47	Urine flow rates meaningless; infusion changed to 8% urea in saline at 9.2 ml./min. to deliver 2.39 mg./ml. inulin, 1.3 mg./ml. PAH and 5 mu/Kg./hour of ADH.																				
76	5 mU ADH/kg. given I.V.																				
105–115	1.89	14.88	.13	280	42.9	6.53	190.0	230.0	.81	32.3	111.0	.29	600	318	1.89	705	120	5.90	52.0	69.5	.75
115–125	2.22	15.99	.14	242	40.7	5.94	193.0	234.0	.82	43.1	99.5	.43	590	320	1.84	598	114	5.24	52.0	71.3	.72
125–135	2.23	15.59	.14	208	41.6	4.99	166.0	234.0	.71	43.1	105.3	.41	565	330	1.71	550	113	4.82	47.9	69.5	.69
135–145	2.80	19.50	.14	174	34.9	4.99	175.0	244.0	.72	45.9	111.0	.41	550	318	1.73	468	94	5.01	51.2	71.1	.71
146	B.P. 190/120. Plasma 3 drawn. 950 ml. of 8% urea in saline absorbed. No bladder leakage.									Plasma = 144.7			Plasma = 283								

of urine flow rates in consecutive 10-minute collection periods should not vary more than six per cent (Table 7). Reproducible ratios in the rate of urine flow from the two kidneys is the best indication that a steady state of renal function has been measured.

Urea is infused in order to produce the high rate of urine flow required to obtain reproducible data, and to create maximal disparity between the ischemic and non-ischemic kidney in total water reabsorption.[21] Pitressin is infused to stimuate maximal water reabsorption in the distal tubules and thereby to eliminate variations which could result from changes in the rate of production of endogenous antidiuretic hormone. Inulin is given as it is handled only by glomerular filtration; hence, its concentration in the urine is a comparative measure of the amount of total water re-absorption by the kidney. Para-aminohippuric acid (PAH) may be used to measure renal plasma flow. The concentrations of PAH may be used as a simpler method of comparing total water reabsorption.[20]

The data obtained from these studies permit a comparison of the two kidneys in four ways: 1) rate of urine flow; 2) degree of total water reabsorption (inulin concentration); 3) renal plasma flow (PAH clearance); and 4) sodium concentration. Only the first two measurements are required for the diagnosis of renal ischemia.[20]

Table 7 shows the average values for these four determinations in 11 patients, and Table 8 shows the complete data obtained from the studies on one patient (Case 22). Table 9 summarizes the range of the differences found between the ischemic and the opposite kidney in these 11 patients.

The ischemic kidney was found to differ from the opposite kidney in three ways: 1) The rate of flow of urine was 47 to 99 per cent less; 2) The inulin concentration, indicating the degree of water reabsorption, was 16 to 840 per cent greater; and 3) The renal plasma flow was 23 to 87 per cent less.[21] The urine sodium concentration from the ischemic kidney did not show a consistent alteration: it was decreased in eight patients from 1.0 to 74 per cent, and increased in three from 1.0 to 9.0 per cent.

TABLE 9. *Results of Urea-Inulin Differential Function Studies in 11 Patients*

Function Measured	Function of Ischemic Kidney Compared to Opposite Kidney	
	% Incr.	% Decr.
1. Quantitative urine flow rate	0	47–99
2. Inulin concentration	16–840	0
3. Para-aminohippuric acid clearance (renal plasma flow)	0	23–87
4. Na Concentration	1–9 (3 patients)	1–74 (8 patients)

The finding of at least a 50 per cent reduction in rate of urine flow and an increased total water reabsorption has to date invariably characterized an ischemic kidney causing hypertension. The urea-inulin test, therefore, has been found to be the most reliable method of confirming the diagnosis of unilateral renal ischemia.

Surgical Treatment

A midline abdominal incision extending from the xiphoid to the pubis was found to give the best exposure of the renal arteries. A thoraco-abdominal incision was used in several patients but was found to give less adequate exposure of the aorta and the opposite renal artery. A retroperitoneal plane of dissection was used. The duodenum was displaced to the left to expose the right renal artery, and the spleen and pancreas were displaced to the right to expose the left renal artery.

In most instances the arterial obstruction was readily seen or felt after the renal artery had been exposed. The blood pressure proximal and distal to the arterial

TABLE 10. *Systolic Pressure Gradient Across Renal Artery Obstruction Before and After Operation in 19 Patients*

Before Operation		After Operation	
Pressure Gradient (mm. Hg)	No. Patients	Pressure Gradient (mm. Hg)	No. Patients
45	1	0	8
50– 99	3	10	0
100–149	8	20	1
150–200	4	30	3
Artery thrombosed	3	Nephrectomy	7

obstruction was measured in 21 patients with a strain gauge by needle puncture of the artery proximal and distal to the obstruction. The systolic pressure gradient across the obstruction was 100 mm. Hg or more in 15 of the 19 patients; the lowest gradient observed was 45 mm. (Table 10). In two patients no obstruction could be found by palpation or by determining the blood pressure in the renal artery (Cases 19, 25). A nephrectomy was done, however, because the physiological studies had been characteristic of unilateral renal ischemia. Subsequent examination of the excised kidney in these two patients showed that the obstruction was in a segmental artery in one and in the intrarenal arteries in the other.

The renal artery stenosis was corrected in 15 patients and a nephrectomy was performed in 12 (Table 11). Occlusion of the renal artery during reconstruction was limited to 20–30 minutes: hypothermia was seldom used. *Endarterectomy* alone was not a satisfactory procedure, and was only used in two patients. One of these died from renal artery thrombosis following bilateral endarterectomy, and hypertension recurred one year later in the other. The death following endarterectomy was the only death in the group. In only two patients was the stenosis sufficiently localized to permit *excision and direct anastomosis*, which would normally be the operation of choice (Fig. 8). *An endarterectomy with patch graft reconstruction* was satisfactorily used in six patients, four of whom had a localized obstruction of the proximal renal artery from an atherosclerotic plaque, and two of whom had a more diffuse obstruction from fibromuscular hyperplasia (Figs. 8, 9). In the patients with atherosclerosis, the plaque was easily removed after the artery had been incised, following which a small elliptical patch of an arterial prosthesis (Dacron or Teflon) was sewed onto the artery in order to widen the lumen. Subsequent determination of arterial pressure showed that the pressure gradient had been abolished (Table 10).

In the two patients with fibromuscular hyperplasia the narrowed area in the artery was incised longitudinally and the patch sewed onto the artery. Endarterectomy was not done as gross intimal disease was not observed. In both of these patients the extension of the stenotic area to the bifurcation of the renal artery prevented excision and end-end anastomosis. Following arterial reconstruction, it was found that the

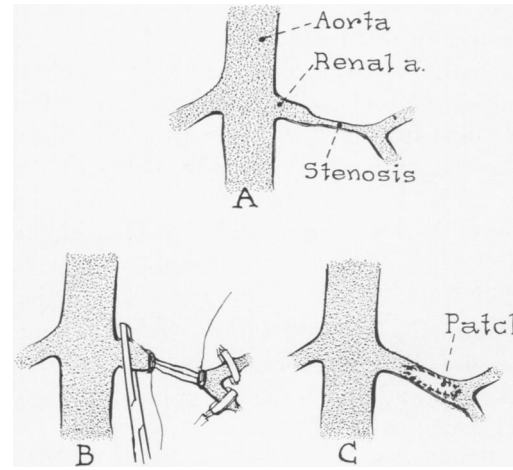


FIG. 8. Illustration of the surgical treatment of diffuse stenosis of the distal renal artery from fibromuscular hyperplasia. Excision and end-to-end anastomosis (B) is preferred but was possible in only two patients. A patch graft may be applied to widen the artery (C) if involvement of the bifurcation prevents direct anastomosis.

systolic pressure gradient had been reduced from 100 mm. Hg to 30 mm. Hg; this small residual gradient did not seem to adversely influence the outcome of the operation, as a good result was obtained in both patients (Cases 14, 20).

It was found that atherosclerotic stenosis was a more favorable lesion for arterial reconstruction than was fibromuscular hyperplasia. Only two of the 12 patients with atherosclerosis had a nephrectomy because the renal artery could not be repaired; in both of these the artery was occluded by a thrombus which could not be removed. Fibromuscular hyperplasia, however, often extended to the bifurcation of the renal artery or into the segmental arteries (Table 3). The involvement of the small arteries prevented arterial reconstruction in several patients in this group; largely for this reason seven of the 11 patients with fibromuscular hyperplasia eventually had a nephrectomy. In four of the seven, attempted arterial reconstruction was unsuccessful (patch graft in three, splenorenal anastomosis in one), and a nephrectomy was performed. The nephrectomy was done at the initial operation in three patients after a patch graft reconstruction failed to correct the obstruction. A nephrectomy was subsequently done in one patient (Case 17) after a splenorenal anastomosis to a segmental renal artery three months before had failed to correct the hypertension, and renal function studies showed that renal ischemia was still present.

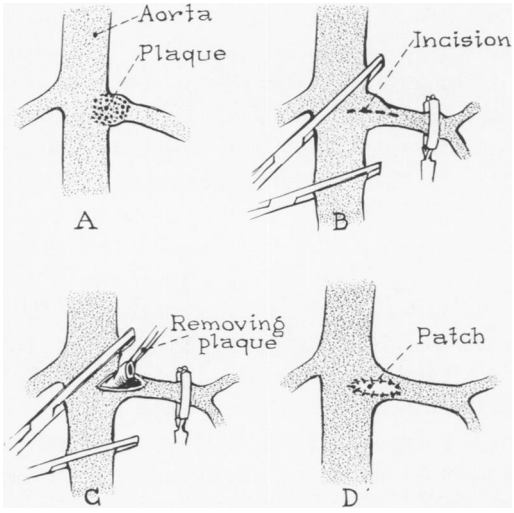


FIG. 9. Illustration of removal of atherosclerotic plaque at the origin of the renal artery from the aorta with reconstruction by widening the renal artery with a patch graft.

TABLE 11. *Operation Performed in 27 Patients with Renal Artery Disease*

Operation	No. Patients
Endarterectomy with patch graft reconstruction	6
Splenorenal anastomosis	4
Excision stenosis and end-to-end anastomosis	2
Endarterectomy	2
Bypass graft	1
Nephrectomy	12

As mentioned above, eight of the 12 *nephrectomies* performed at the initial operation were because of extension of the disease into segmental renal arteries. The other four nephrectomies (Cases 24–27) were done because of an aneurysm of the renal artery in two patients, occlusive disease of the intrarenal arteries in one patient, and obstructive disease of uncertain location in one patient with three small renal arteries to one kidney.

Anastomosis of the splenic artery to the left renal artery was performed in four patients; a splenectomy was also done in three of the four. Two of these patients obtained a good result, and one has only recently been performed. The one failure in the group was described in the preceding paragraphs (Case 17).

A *bypass graft* was used in one patient who was found to have occlusion of the right renal artery during the excision of an abdominal aneurysm. An 8.0 mm. Dacron graft was inserted between the prosthesis in the abdominal aorta and the renal artery distal to the obstruction.

TABLE 12. *Blood Pressure Following Operation in 24 Patients*

Operation	Blood Pressure (No. Patients)		
	Normotensive	Residual Hypertension	Hypertension Unchanged
Nephrectomy	5	7	0
Renal artery reconstruction	7	3	2*

* 1 Normotensive after subsequent nephrectomy; one is 4 mos. postoperative.

Results

The postoperative course was uncomplicated in most cases. Two patients (Cases 11, 12) had an immediate diuresis of several liters of urine in the first 24 hours after operation with urinary sodium concentrations as high as 100 mEq. per liter. At operation one of these patients had complete obstruction of the ostium of the renal artery and the other (Case 1, Table 7) had almost complete obstruction with the lowest renal plasma flow of any of the 11 patients studied (41 ml./min.). Electrolyte imbalance was prevented by intravenous infusion of saline until the diuresis subsided by the fourth postoperative day. This transient urinary loss of water and electrotyte appeared similar to that which is often seen in the diuretic period of recovery from renal shutdown.

The only patient with severe renal insufficiency (Case 2) had a blood urea nitrogen of 65 mg. per cent before operation. The right kidney had previously been removed, and at operation atherosclerotic obstruction of the left renal artery was found. Following a splenorenal anastomosis, the urea nitrogen decreased to normal levels by the twelfth postoperative day and has subsequently remained at 20–25 mg. per cent in the two years since operation.

The single postoperative death was caused by renal artery thrombosis following bilateral renal endarterectomy. This patient is the only one in whom obstruction of both renal arteries was found at operation. After operation the previously narrowed abdominal aorta thrombosed, and the thrombosis extended upward to involve the ostia of the renal arteries.

Many patients showed an immediate decrease in blood pressure following operation, but analysis of their subsequent course showed that this initial response was of little prognostic value, since in some the blood pressure became elevated again after the patient left the hospital. An analysis of the response of the hypertension to operation based upon the most recent blood pressure obtained in 24 patients is shown in Table 12. The blood pressure was normal in 12, a residual systolic hypertension was present in 10, and the blood pressure was unchanged in two. Data was not available from three of the group of 27 patients because one died shortly after operation and two were only recently operated upon. Of particular interest was the finding that residual systolic hypertension was slightly more common following nephrectomy (7 of 12 patients) than following arterial reconstruction (4 of 11 patients). The residual hypertension was mild (range of 140/90 to 160/105 mm. Hg) and asymptomatic in most patients. In two patients a more serious hypertension was still present with systolic levels of 200 mm. Hg unless antihypertensive drugs were used. In neither of these patients, however, has the existing hypertension been proved to be of renal origin. One of these (Case 5) had a nephrectomy when diffuse thrombosis of the renal artery was found at operation. The other (Case 1) was normotensive for almost a year following a renal endarterectomy but in the subsequent year has had a recurrence of her hypertension almost to preoperative levels. As diagnostic studies have not been possible, it is not known whether renal ischemia has again developed, either in the kidney previously operated upon or in the

opposite kidney. This patient is the only one who initially obtained a good result from operation but subsequently had a recurrence of her hypertension.

Two patients had no benefit from renal artery reconstruction. One of these (Case 17) previously discussed in the section on *Surgical Treatment* represented a failure of a splenorenal anastomosis to correct renal ischemia although the pressure gradient measured at operation was eliminated; subsequent nephrectomy resulted in a normal blood pressure. The other (Case 10) was found to have complete occlusion of the ostia of the right renal artery during excision of an abdominal aneurysm. Revascularization of the kidney with a bypass graft has not changed the blood pressure from its preoperative levels in the four months since operation.

Discussion

Fibromuscular Hyperplasia. This descriptive term refers to an obstructive disease of the renal artery, the etiology of which is unknown. Its occurrence predominantly in patients less than 30 years of age (Fig. 1) suggests a congenital origin. Eleven of our 27 patients had this type of arterial obstruction, and a similar frequency has been described in several reports.[4, 5, 24, 25] On the other hand, renal artery stenosis in most of the patients treated by Morris, *et al.*[12] was caused by atherosclerosis.

The histologic changes described by Wylie and Wellington[24] chiefly involved the media of the arterial wall. In our patients involvement of any of the three layers of the arterial wall has been seen. The histological changes were chiefly in the adventitia in two patients; in others the intima was the most diseased. Disruption of the internal elastic membrane was a prominent finding in one patient, but in most of the others it was intact. An external constriction of the artery was such an impressive finding in three patients we initially classified them as "congenital stenosis." The disease in the intima, however, was so similar to findings in patients without an external constriction a separate classification did not seem justified. Much additional information is needed about this unusual disease process.

Diagnostic Considerations. An important decision in the evaluation of patients with hypertension is the selection of those in whom specific studies for renal ischemia should be done. Our experience supports the recommendations of Dustan, Page, and Poutasse[5] and Connor, Thomas, Haddock, and Howard[3] that renal artery disease should be considered especially in hypertension developing before 30 years of age or in severe hypertension of recent origin in older patients. Wider use of studies of renal function may in the future, however, reveal renal ischemia as a much more common cause of hypertension than previous studies have shown. The intravenous pyelogram and the radioactive renogram are useful screening technics for unilateral renal abnormalities, but both fail to demonstrate some lesions and do not reveal whether a detected abnormality is causing hypertension. Both aortography and the Howard test of differential renal function are of much value in detecting obstruction of the main renal artery but often do not show segmental arterial obstruction causing ischemia only of part of the kidney. In addition, a plaque in a renal artery seen on aortography may be partly obstructing the renal artery, but this may not be the cause of hypertension; and in some pyelonephritic kidneys a *false positive* Howard test may be found.[21]

In our experience thus far the urea-inulin studies of differential renal function have been the most reliable diagnostic tests, because neither *false positive* nor *false negative* tests have been found.[20, 21] All 11 hypertensive patients studied with renal artery obstruction have had the diagnostic

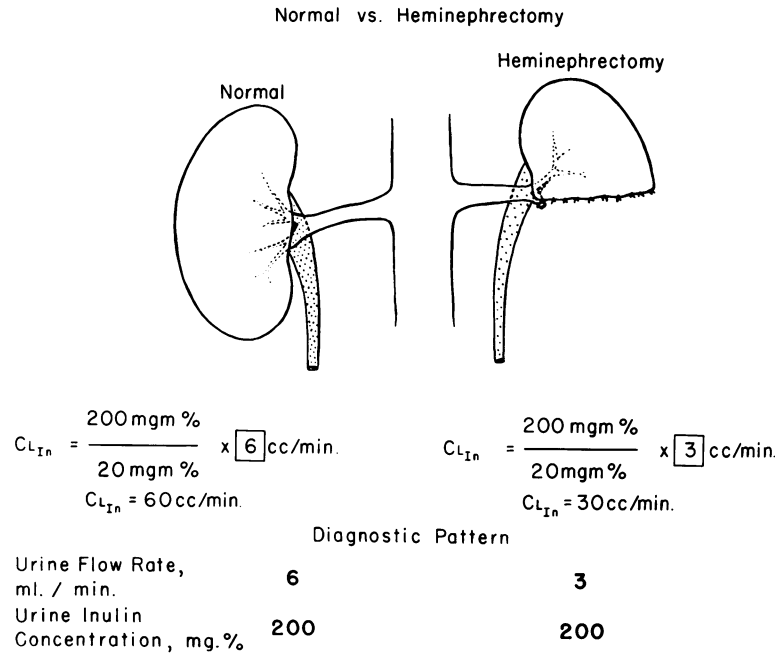


FIG. 10. $Cl_{In} = U \times V/P$ = clearance of inulin = glomerular filtration rate (GFR). The identical inulin concentrations in the urine indicate that water reabsorption is the same in the two kidneys. Urine flow is smaller by 50 per cent. These two features characterize a normal but smaller kidney unrelated to hypertension.

pattern of at least a *50 per cent decrease in the excretion of urine and a 16 to 840 per cent increase in the concentration of inulin* (Table 9). None of the studies in a large number of normotensive patients with unilateral renal disease has shown these findings. In the usual pyelonephritic kidney the concentration of inulin in the urine is *decreased* relative to the contralateral kidney because of the inability of the injured kid-

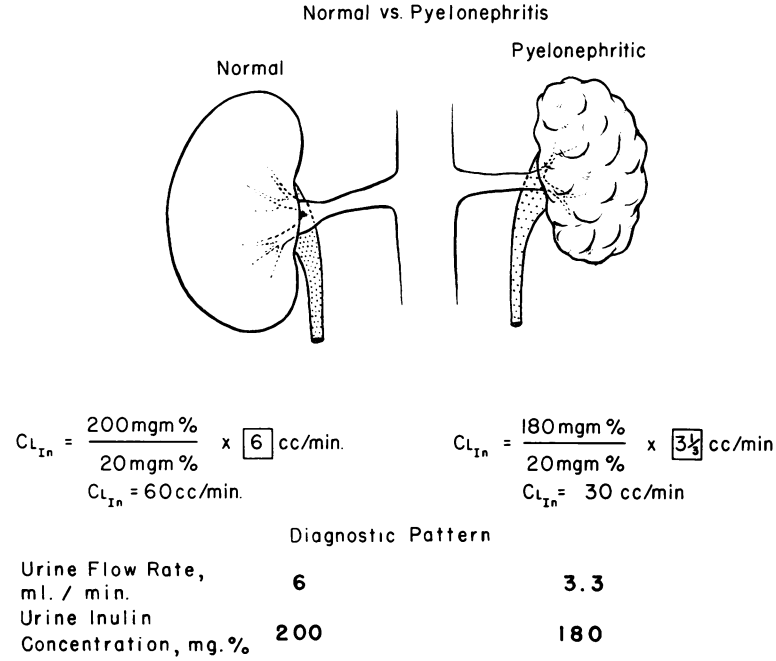
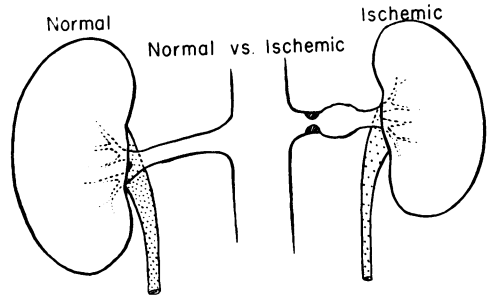


FIG. 11. Urine inulin concentration and urine flow rate are less in diseased kidney. These two features characterize a diseased kidney unrelated to hypertension.

ney to reabsorb water as well as the opposite normal kidney. The urea-inulin study is not much more complicated than other studies performed with ureteral catheterization, and has been simplified in a technic which prevents leakage of urine about the catheters, ureterorenal reflexes, and inadequate urine flow rates.[20] In this technic, para-aminohippuric acid (PAH) may be conveniently substituted for inulin when studies are performed only for diagnosis, since the analytical determination for PAH is simpler than for inulin.

As the urea-inulin study thus far has been surprisingly free from diagnostic errors,[21] and has also not caused any serious complications, some patients with suspected renal disease have been studied only by this method before operation. It was believed surgical exploration of the renal arteries would show whether arterial reconstruction was possible or whether a neprectomy should be done. This approach was first suggested by experiences with two patients with equivocal findings on aortography and also on surgical exploration. A nephrectomy was performed in each instance because of the strongly positive findings with the urea-inulin studies. A good result was obtained in both patients, and histological studies of both removed kidneys showed previously unrecognized occlusive disease of small renal arteries.

Attempts to find simpler diagnostic methods of differential renal function which avoid the necessity of obtaining exact urine flow rates from each kidney have been reported.[1, 16] A major objection to any of these methods is that only by demonstrating reproducible urine flow rates can one be sure that a "steady state" of renal function is being measured.[21] Data obtained from only a single collection period can be completely unreliable. Another objection to methods which do not determine exact urine flow flow rates is that the *wrong* kidney may be considered the ischemic one.[21] This problem is shown in Figures 10–12, which illustrate three common conditions in which glomerular filtration rate (GFR), and hence urine flow rate, is decreased. The first of these (Fig. 10), illustrates a heminephrectomy or a congenitally small but otherwise normal kidney which has a decreased GFR



$$Cl_{In} = \frac{200 mgm\%}{20 mgm\%} \times \boxed{6} \text{ cc/min.}$$

$$Cl_{In} = 60 cc/min.$$

$$Cl_{In} \frac{1200 mgm\%}{20 mgm\%} \times \boxed{.5} \text{ cc/min.}$$

$$Cl_{In} = 30 cc/min.$$

Diagnostic Pattern		
Urine Flow Rate, ml. / min.	6	0.5
Urine Inulin Concentration, mg.%	200	1200

FIG. 12. Urine inulin concentration is markedly increased in ischemic kidney. Urine flow rate is reduced greater than 50 per cent. This pattern has been found only in an ischemic kidney causing hypertension.

because of its small size and accordingly excretes less urine than the opposite kidney. The identical inulin concentration in the urine from the two kidneys shows that water reabsorption is the *same* in the two kidneys. Figure 11 illustrates a pyelonephritic kidney with reduced urine flow. In this instance the inulin concentration is decreased, indicating that water reabsorption is *less* than that in the opposite kidney. If urine flow rates were not measured from these two kidneys, the higher inulin concentration from the normal kidney would suggest that it was the ischemic kidney! Figure 12 shows the typical findings in an ischemic kidney causing hypertension. Again the urine flow is decreased, but in this instance the inulin concentration is greatly increased, showing that water reabsorption is markedly *greater* in the ischemic kidney than in the opposite one. An additional observation shown by these three illustrations is that a diagnosis of renal ischemia causing hypertension cannot be made solely from finding a decrease in renal blood flow.

Conclusions concerning the validity of the urea-inulin method cannot yet be final because only 11 patients have been studied and subsequently operated upon, and none of these has yet been studied following correction of the obstruction of the renal artery. The consistency of the obtained data, however, as well as the absence of similar findings in approximately 25 studies on normotensive patients with unilateral renal disease, and 75 patients with essential hypertension, suggests that similar findings will be found in a larger group of patients with curable renovascular hypertension. Similar findings have been reported recently by Brown, Owen, Peart, Robinson, and Sutton.[2] Patients with obstruction of both renal arteries have not been studied, but it would be unusual to have such an identical degree of renal ischemia that an abnormality would not be found in comparing the urine from the two kidneys.[21]

Physiological Observations. Although not essential for the diagnosis of renal ischemia causing hypertension, renal plasma flow was routinely determined from PAH clearances performed with the urea-inulin test. It was impressive that the plasma flow of the ischemic kidney was always significantly less than that of the opposite kidney,[21] the least difference being a 23 per cent reduction with a segmental arterial occlusion, and the range of differences being 23 to 87 per cent (Table 7). Similarly, at operation the smallest systolic pressure gradient across the renal arterial obstruction was 45 mm. and most gradients were 100 mm. or greater. The finding of a large pressure gradient was expected, because experimental constriction of a renal artery may not cause a reduction in blood flow until large pressure gradients are produced, presumably because a decrease in renal arteriolar resistance can compensate for the reduction in flow which would be produced with an obstruction causing smaller pressure gradients.[17, 18] These observations are of much significance if confirmed by additional experiences because hypertension has been produced in dogs without demonstrating a decrease in blood flow, and in man some hypertension has been thought to occur from renal disease without a reduction in blood flow.[13] It should be emphasized that our findings have showed only that the plasma flow is decreased in comparison to the opposite normal kidney.[21] The plasma flow from the ischemic kidney varied from 41 to 328 ml./min., but was always at least 23 per cent less (range 23 to 87 per cent) than the flow in the opposite kidney. The range of normal values for renal plasma flow in man is a wide one. If the renal plasma flow were measured only in the ischemic kidney, without a flow measurement on the opposite normal kidney, a decreased flow might not be recognized because of this wide normal variation.

Surgical Treatment. In our experience the operation of choice for renal artery

stenosis is excision of the stenotic area and end-to-end anastomosis (Fig. 8). Unfortunately, this procedure is not often possible because either the renal artery is involved at its origin from the aorta or the stenosis extends into the segmental branches. The procedure of incision of the stenotic area, followed by endarterectomy if intimal disease is present, and subsequent insertion of a patch graft to widen the arterial lumen seems to be applicable in most patients (Fig. 8, 9). It should be remembered, however, that the insertion of a patch of arterial prosthetic material into an arterial wall is a procedure which has been used only for a short period of time, and long-term observations are not available. A probable contraindication to endarterectomy is extensive atherosclerosis of the aorta at the point of origin of the renal arteries. Incision and suturing of such an aorta may be technically difficult and hazardous. In such patients a splenorenal anastomosis or a bypass graft is a preferred procedure. Good results have been reported from the use of either technic. An unusually large experience with bypass grafts has been reported by Morris, *et al.*[11, 12]

We are fearful of attempting to perform endarterectomy on atheroslerotic renal arteries and close them by direct suture. It has been successfully done in some patients and was the procedure used by Freeman who reported one of the first successful reconstructions of the renal artery, in 1954.[6] In many patients, however, atherosclerosis in the aorta wall makes suture of the incision in the renal artery and aorta difficult.

Good results have been reported from anastomosis of the splenic to the left renal artery, and such a procedure has the advantage that mobilization of the aorta is unnecessary. We have no information at present to substantiate a choice between a splenorenal anastomosis and a local endarterectomy and patch graft reconstruction. As the splenic artery is not a large vessel, a larger renal artery is probably obtained by patch graft reconstruction. On the other hand, a splenorenal anastomosis has the advantage that only autogenous tissue is used.

A nephrectomy has been done only when the arterial stenosis could not be corrected. It is not known from what degree of renal ischemia recovery of normal renal function may be obtained following revascularization. In two patients complete occlusion of the ostia of the renal artery was found, but collateral blood flow was enough to maintain a mean arterial pressure in the distal renal artery of about 40 mm. Hg. As there was no gross evidence of renal infarction, the renal artery was reconstructed in each patient. The hypertension has not yet subsided in either patient, but both operations were performed less than four months ago, and conclusions cannot be made whether this degree of renal ischemia is associated with irreparable renal injury or not. Complete renal artery occlusion was found in two other patients in whom there was a thrombosis superimposed upon a previous stenosis. The segmental renal arteries were also thrombosed in each of these, and a nephrectomy was done.

Hypertension Following Operation. The finding of some residual hypertension in approximately one-half of the patients following operation was of considerable interest, especially since the hypertension was slightly more frequent after nephrectomy than after revascularization. A similar frequency of mild systolic hypertension following nephrectomy has been reported by others.[2, 3, 14, 25] Fortunately, residual hypertension has been mild and seemingly of limited clinical significance. Longer periods of postoperative observation are needed before further conclusions can be made, especially as many of the reconstructive operations have only recently been performed. Only two patients have been followed for two years or longer since operation. Six have been followed one to two years, nine for six to 12 months, and nine for less than six months.

In this group of cases residual postoperative hypertension could not be correlated with the age of the patient, the disease process causing the renal artery obstruction, the duration of the hypertension before operation, the operative procedure performed, or a small residual systolic gradient (30 mm. Hg or less) remaining following renal artery reconstruction. Residual hypertension was as frequent in patients under 30 years of age as in those over 40. It was as frequent in patients with atherosclerosis as in those with fibromuscular hyperplasia. Patients with known hypertension for less than a year had residual hypertension as often as those with hypertension for four years or longer. Nephrectomy and arterial reconstructive procedures were followed by a similar frequency of residual hypertension. In the four patients who had a small residual pressure gradient, the blood pressure became normal in three and remained slightly elevated in one.

Analysis of the time required for the hypertension to subside following different operations showed that the blood pressure often returned to normal levels within two weeks after a nephrectomy but often did not reach similar levels for four to six weeks after arterial reconstruction. The actual number of patients in each group, however, was too small (5 nephrectomies, 7 reconstructions) to permit definite conclusions. It did seem clear, however, that there was little chance of improvement in the hypertension if it had not occurred within six months after operation. Only one exception to this generalization was seen (Case 2). Ten months following operation the blood pressure was 210/90 mm. Hg; at 19 months it was 130/70 and at 25 months 152/90. It may be significant that in this patient the right kidney had been removed one year before the left kidney was revascularized.

Summary

1. Twenty-seven patients, ranging in age from 5 to 69 years, have been operated upon in the past three years for hypertension caused by obstruction of a renal artery.

2. The obstruction was caused by an atherosclerotic plaque in 12, and by fibromuscular hyperplasia in 11. In two patients it was associated with accessory renal arteries, and in two with an aneurysm of the renal artery. Fibromuscular hyperplasia was usually found in patients less than 30 years of age and commonly involved the distal renal artery and its segmental branches. Atherosclerosis was found in an older age group and usually was limited to the main renal artery near its origin from the aorta.

3. The diagnostic tests used included an intravenous pyelogram, a renogram, an aortogram, differential sodium and water excretion (Howard test), and a urea-inulin test of differential renal function. The urea-inulin test, which has been only recently developed, was performed in 11 patients and was the only test which confirmed the diagnosis in each patient studied. The diagnosis was made by finding that the urine flow rate from the ischemic kidney was at least 50 per cent less than from the opposite kidney, and the urine inulin concentration was at least 16 per cent (range 16–840%) greater. The renal plasma flow in the ischemic kidney was 23 to 87 per cent less than in the opposite kidney.

4. The operations performed were: endarterectomy and patch graft reconstruction—6; splenorenal arterial anastomosis—4; excision of stenosis and end-to-end anastomosis—2; endarterectomy—2; bypass graft—1; nephrectomy—12. The systolic pressure gradients resulting from the renal artery obstruction were measured at operation and were 100 mm. Hg or more in most patients.

5. The blood pressure following operation in 24 patients was normal in 12 and unchanged in two. A systolic hypertension was still present in 10 patients, but was clinically insignificant (systolic pressure of 140–160 mm. Hg) in eight of the 10. Residual systolic hypertension was slightly more common after nephrectomy than after re-

construction of the renal artery. There was one operative death, and one patient unimproved following a splenorenal anastomosis was subsequently cured with a nephrectomy.

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