MEDICAL GRAND ROUNDS

Parkland Memorial Hospital
October 31, 1963

RENOVASCULAR HYPERTENSION

CASE # 1: [redacted]. Unilateral renal artery disease

[redacted]., a 46 year old [redacted]e female, had been normotensive during a pregnancy in 1952 and while receiving urologic therapy for renal stones and psychiatric therapy for extreme nervousness from 1959 to early 1963. On [redacted], 1963, her blood pressure was 140/85. On [redacted], 1963, she came to the EOR with a severe headache and her BP was 180/110. Thereafter, headaches and hypertension persisted. On [redacted]/63, her B.P. was 230/120.

I.V.P. [redacted]/63) - sizes equal, but no excretion on right at 5 minutes
Renal scan [redacted]/63) - decreased function on right
Angiotensin infusion [redacted]/63) - incomplete response to 15 mμg/Kg/min.
Howard test ([redacted]/63) -

		Rt	Lt
Volume (ml.)		7.5	
Na conc(mEq/L)	<	10	18

Retrograde pyelogram [redacted]/63) - right kidney 1 cm. smaller than left
Aortagram [redacted]/63) - stenosis of right main renal artery with post-stenotic dilation.

On [redacted]/63, a right renal thromboendarterectomy was performed. On [redacted]/63, her B.P. was 140/85; on [redacted]/63, 150/180. However, on [redacted]/63, the B.P. was 170/100. This persistent hypertension may reflect the extensive arteriolar nephrosclerosis noted on biopsy of her left kidney. She now has equal and rapid excretion of dye on I.V.P. and responds to 4.5 mμg/Kg/min of angiotensin.

CASE # 2: [redacted] Bilateral renal artery disease

[redacted] a 39 year old [redacted] man was first found to have hypertension in 1961. He sought medical attention after being turned down for work because of hypertension. His B.P. was 190/110 and there was arteriolar narrowing in the fundus.

I.V.P. ([redacted]/63) - right kidney had dilated pelvis and was 1 cm. larger than left; excretion equal at 5 minutes.

[redacted] [redacted]/63)	Rt	Lt	
Volume (ml)	12.0	3.0	(↓75%)
Na conc (mEq per L)	35	27	(↓23%)

[redacted] ([redacted]/63)	Rt	Lt	Rt:Lt
Volume (ml)	13.3	2.0	6.6:1
PAH conc(mg%)	136	320	1:2.3

Angiotensin infusion test ([redacted]/63) - pressor response to 10 mμg/Kg/min
Arteriogram ([redacted]63) - bilateral renal artery narrowing at the take-off

On [redacted]/63, bilateral renal thromboendartectomies were done. On [redacted]/63, B.P. - 130/75, on [redacted]/63 = 190/110, on [redacted]/63 = 190/110. Repeat I.V.P.s on [redacted]/63 showed decreased excretion on the right and on [redacted]/63, no excretion was evident. On [redacted]/63 repeat angiotensin infusion revealed marked insensitivity, with no response to 16 mμg/Kg/min. On [redacted]/63, arteriography revealed virtually complete occlusion of right renal artery. A large thrombus was removed from the right renal artery and he has remained normotensive since then.

CASE # 3: [redacted] Bilateral renal artery disease

[redacted]., a 71 year old [redacted] woman had no medical attention until late 1962, when she came to the EOR because of epistaxis and was found to have a blood pressure of 300/120. She remained asymptomatic thereafter, but was admitted after nose bleed in early October. She had arteriolar narrowing and a few old exudates on fundoscopic. Bruits were heard over all major arteries.

Angiotensin infusion test ([redacted]/63): response to 22 mμg/Kg/min.
Arteriogram ([redacted]/63): extensive bilateral renal arterial disease with multiple plaques.

Surgery was thought to be contraindicated because of the severe and extensive nature of arteriosclerosis. She was begun on Reserpine and sent home.

CASE # 4: [redacted] Renal artery disease without relation to hypertension

[redacted]., a 63 year old [redacted] man, had been hypertensive for 12 years, with only occasional headaches. B.P. = 180/120. Eyegrounds revealed arteriolar narrowing and A/V nicking.

I.V.P.: Delayed excretion on left, sizes equal
Renogram: Slightly decreased function on left
Arteriogram: Small plaque in left renal artery
Angiotensin infusion: Pressor response to 3.4 mμg

A left renal thromboendartectomy was done, but no pressure gradient was observed above and beyond the plaque. The blood pressure has remained around 180/120.

CASE # 5 [redacted] Renal artery disease without relation to hypertension

[redacted], a 50 year old white man, was found to have hypertension in 1960, but has remained virtually asymptomatic other than for occasional headaches. B.P. = 200/110. Eye grounds show arterial narrowing, A/V nicking bilaterally and a few hemorrhages on the right. BUN = 27.

Angiotensin infusion [redacted]/63) pressor response to 3.4 mμg
I.V.P. [redacted]/63): Sizes equal, bilateral but poor excretion by 3 minutes
Renal scan ([redacted]/63): Bilateral poor function

[redacted] ([redacted]/63):	Rt	Lt
Volume (ml)	52	54
PAH conc(mg%)	162	152

Arteriogram ([redacted]/63): Two renal arteries on the left, with partial stenosis at the take-off of the larger one.

Surgery was felt not to be indicated by the vascular surgeons.

Pathogenesis

A. The mechanism by which partial occlusion of a renal artery will cause hypertension is thought to involve the release of renin from the juxtaglomerular cells and, thereby, the activation of angiotensin.

1. Goldblatt, H., J. Lynch, R.F. Hanzal and W.W. Summerville. Studies on experimental hypertension: I. The production of persistent elevation of systolic blood pressure by means of renal ischemia. J. Exper. Med. 59:347, 1934.

   Chronic hypertension in the dog can be induced only by involving both kidneys, e.g. clamping one renal artery and removing the other kidney. In the rabbit and rat, however, as in man, sustained hypertension may follow manipulation of only one renal artery.

2. Goldblatt, H. The renal origin of hypertension. Physiol. Rev. 27:120, 1947.
   A measureable decrease in renal blood flow is not necessary for the development of renal hypertension and a change in pulse pressure may by itself cause the process, by stimulating the release of renin.

3. Kohlstaedt, K.G. and I.H. Page. Liberation of renin by perfusion of kidneys following reduction of pulse pressure. J. Exper. Med. 72:201, 1940.

   Although the measurements of renin and angiotensin are still technically difficult, most agree that they are elevated with renovascular hypertension.

4. Page, I.H. and F.M. Bumpus. Angiotensin. Physiol. Rev. 41:331, April, 1961.

5. Lever, A.F. and W.S. Peart. Renin and angiotensin-like activity in renal lymph. J. Physiol. 160:548, March, 1962.

   Even without measureable increases, the chronic administration of angiotensin will induce hypertension in the rabbit.

6. Dickinson, C.J. and J.R. Lawrence. A slowly developing pressor response to small concentrations of angiotensin. Lancet 1:1354, June 22, 1963.

   The interesting concept of relative and not actual renal ischemia has been proposed.

7. Schlegel, J.U. and S. Okamoto. Some studies in experimental renal hypertension. J. Urol. 86:27, July, 1961.

   Of particular interest is the study in rats with hypertension caused by unilateral renal artery clamping, in which the clamped kidney had no significant damage, but the "normal" kidney was often severely damaged. After removal of the clamp, hypertension persisted in those with significant damage.

8. Wilson, C. and F.B. Byrom. The vicious cycle in chronic Bright's disease. Quart. J. Med. 10:65, 1941.

   A clinical counterpart has been reported.

9. Thal, H.P., T.B. Grage and R.L. Vernier. Function of contralateral kidney in renal hypertension due to renal artery stenosis. Circulation 27:36, January, 1963.

The possible importance of the normal kidney in maintaining normotension was proposed by Grollman and supported by the reduction of renovascular hypertension by grafting a normal kidney into the circulation.

10. Grollman, A., E.E. Muirhead and J. Vanatta. Role of the kidney in pathogenesis of hypertension as determined by a study of the effects of bilateral nephrectomy and other experimental procedures on the blood pressure of the dog. Am. J. Physiol. 157:21, 1949.

11. Blaques, P., A. Gomez and S.W. Hoobler. Role of the intact kidney in experimental hypertension. Fed. Proc. 17:16, 1958 (abstract)

The importance of renoprival hypertension in man was questioned by the failure of 4 nephrectomized patients to develop hypertension.

12. Merrill, J.P., C. Giordana and D.R. Heetderks. The role of the kidney in human hypertension. Am. J. Med. 31:931, Dec. 1961.

B. Evidence in the human

Some direct and a great deal of indirect evidence supports the concept of renal ischemia, stimulation of the J-G apparatus and increased levels of renin-angiotensin.

13. Stamey, T.A., I.J. Nudelman, P.H. Good, F.N. Schwentker and F. Hendricks. Functional characteristics of renovascular hypertension. Medicine 40:347, December 1961.

14. Crocker, D.W., R.A. Newton, E.M. Mahoney and J.H. Harrison. Hypertension due to primary renal ischemia. New England J. Med. 267:794, October 18, 1962.

15. Morris, R.E. Jr., P.A. Ransom and J.E. Howard. Studies on the relationship of angiotensin to hypertension of renal origin. J. Clin. Invest. 41:1386, 1962. (abstract)

II. Pathology

The pathological demonstration of renal arterial occlusion is difficult, but evidences of "ischemic" tubular atrophy may be seen.

16. Yuile, C.L. Obstructive lesions of the main renal artery in relation to hypertension. Am. J. Med. Sci. 207:394, 1944.

17. Connor, T.B., W.C. Thomas, Jr., L. Haddock and J.E. Howard. Unilateral renal disease as a cause of hypertension. Ann. Int. Med. 52:544, March 1960.

The types of renal occlusive lesions are many; but atherosclerotic plaques are most common in the older patients and fibromuscular hyperplasia in younger women.

18. Morris, G.C. Jr., M.E. DeBakey, D.A. Cooley and E.S. Crawford. Experience with 200 renal artery reconstructive procedures for hypertension or renal failure. Circulation 27:346, March 1963.

The causal relationship of hypoplasia without selective lesions of the renal arteries is unknown but appears likely (Reference 14).

19. Dustan, H.P. and I.H. Page, Unilateral renal disease and hypertension. Disease-a-Month, December, 1962.

III. Clinical Features

A. Incidence

The papers by Smith in 1948 and 1956 emphasized the need for critical evaluation of the results of nephrectomy for relief of hypertension. He urged extreme caution in view of a 26% cure rate, and suggested that fewer than 2% of hypertensive patients would benefit from renal surgery. However, most of these collected cases were of renal parenchymal disease and his findings should not be taken as evidence for the frequency of renal vascular disease.

20. Smith, H.W. Unilateral nephrectomy in hypertensive diseases. J. Urol. 76:685, December 1956.
There are few series of unselected hypertensives in whom the incidence of renovascular hypertension was determined. An incidence of 5 to 10% has been noted.

21. Sutton, D., F.J. Brunton and F. Starer. Renal artery stenosis. Clin. Radiology 12:80, 1961.

22. Maxwell, M.H. and G.B. Prozan. Renovascular hypertension. Prog. Cardiovasc. Dis. 5:81, July 1962. (An excellent review of the entire subject.)
The incidence among Negro hypertensives is lower than among white.

23. Stewart, B.H., M.S. DeWeese, J. Conway and R.J. Correa, Jr. Renal hypertension. Arch. Surgery 85:617, October 1962.

B. Clinical Features:

Here again, earlier papers give a deceptive view of the clinical features. Whereas, renal vascular hypertension was considered to be of short duration and rapid acceleration, recent reviews have stressed the more typical features.

24. Perera, G.A. and Haelig, A.W. Clinical characteristics of hypertension associated with unilateral renal disease. Circulation 6:549, Oct. 1952.

References 18, 19, 21 and 22.

The frequency will probably be highest in patients with these criteria:

(1) onset of hypertension before age 30 or over age 50.
(2) recent acceleration of benign hypertension.
(3) malignant hypertension.
(4) history of renal trauma, peripheral emboli or unexplained flank pain.
(5) prominent bruit over renal area.
(6) evidence of atherosclerosis

The presence of hypokalemic alkalosis and hypertension may closely mimic primary aldosteronism and increased secretion of aldosteronism may occur with renovascular hypertension.

25. Itskovitz, H.D., E.A. Hildreth, A.M. Sellers, W.S. Blakemore. The granularity of the juxtaglomerular cells in human hypertension. Ann. Int. Med. 59:8, July, 1963.

26. Slaton, P.E., Jr., and E.G. Biglieri. Hypertension and hyperaldosteronism of renal and adrenal origin. Circulation 28:806, October 1963 (abstract)

On the basis of the proposed hypothesis of the renin-angiotensin system in renovascular hypertension, excess aldosterone secretion is to be expected. However, it usually does not occur clinically or experimentally.

27. Sambhi, M.P., B.A. Levitan, J.C. Beck and E.H. Venning. The rate of aldosterone secretion in hypertensive patients with demonstrable renal artery stenosis. Metabolism 12:498, June 1963.

28. McCaa, C.S., T.Q. Richardson, R.B. McCaa, L.L. Sulya, A.C. Guyton. Decreased aldosterone secretion in Goldblatt hypertension. Circulation 28:765, October, 1963 (abstract).

IV. Diagnostic procedures

A number of procedures (I.V.P., renogram, split function, renal biopsy and aortography) will reveal differences in renal blood flow or function which could reflect renal vascular stenosis. However, only assays of renin - angiotensin, and, hopefully, the angiotensin infusion test, will prove the functional significance of these lesions.

A. Intravenous pyelography

Difference in renal size of 1.0 cm or more may in itself be helpful. Reference 14 and 19.

The clearance of these contrast media is predominantly by glomerular filtration. Various modifications have been proposed to better demonstrate renal ischemia.

29. Maxwell, M.H. Reversible renal hypertension. Am. J. Cardiol. 6:126, January, 1962. Rapid injection with films every minute X 5.

30. Rathe, J.C. Differential "nephropacification", a screening procedure for unilateral renal artery occlusion. Radiology 76:629, April, 1961. Even more rapid injection of 50 ml 50% Hypaque and film taken 15 seconds later may show delay in diffuse opacification with renal ischemia.

31. Amplatz, K. Two radiographic tests for assessment of renovascular hypertension. Radiology 79:807, November, 1962. Rapid injection of 50 ml. of 75% Hypaque, with 1/2, 1,3, 5 minute films. Then obtain a diuresis by rapidly infusing 500 ml. normal saline with 40 Gm. urea and take films every 5 minutes. Washout should occur more rapidly from the normal kidney.

The positive findings by I.V. P. are varied:

(1) differences in renal size, with the abnormal side being smaller
(2) delayed and decreased excretion on the abnormal side
(3) excretion may be delayed and prolonged with hyperconcentration on the abnormal side
(4) failure of visualization with a renal outline demonstrated by retrograde pyelography.

The usefulness of pyelography as a screening test has been variable. The overall results are about 75% positive in patients with renovascular hypertension, and about 25% false positive in patients without.

32. Howard, J.E. and T.B. Conner. Hypertension produced by unilateral renal disease. Arch. Int. Med. 109:62, January, 1962.

References 14, 18, 21, 23 and 29.

Intravenous pyelography will seldom be useful if significant renal insufficiency exists (serum creatinine above 3.0 mg%)

33. Schwartz, W.B., A. Hurwit and A. Ettinger. Intravenous urography in the patient with renal insufficiency. New England J. Med. 269:277. Aug. 8, 1963.

B. Radio-renogram

Two techniques with variations have been used. Although relatively simple to perform and interpret, the techniques require expensive equipment and meticulous attention to positioning and may introduce a significant radiation hazard to the patient.

Results with I^{131} - Hippuran have revealed an overall incidence of positive results in about 75% of patients with renovascular hypertension and about 25% false positives.

34. Brown, F.A., R.H. Gelver, L.H. Youkeles and L.R. Bennet. Quantitative approach to the I^{131} renogram. J.A.M.A. 186:211, October 19, 1963.

35. Stewart, B.H. and T.P. Haynie. Critical appraisal of the renogram in vascular disease. J.A.M.A. 180:454, May 12, 1962.
The use of Hg^{203}-Neohydrin has recently been advocated to overcome the variations encountered with I^{131}-Hippuran caused by changing rates of urinary flow.

36. Reba, R.C., J.G. McAfee and H.N. Wagner, Jr., Radiomercury - labelled chlormerodrin for in vivo uptake studies and scintillation scanning of unilateral renal lesions associated with hypertension. Medicine 42:269, July, 1963.

C. Split function tests

All attempts at using renal functional disparity as evidence for renovascular hypertension must be suspect, on the basis of this study, showing functional disparity exceeding that in normotensives in 40/50 patients with essential hypertension. Only 2 had positive Howard Tests, however.

37. Baldwin, D.S., W.H. Hulet, A.W. Biggs, E.A. Gombos and H. Chasis. Renal function in the separate kidneys of man. J. Clin. Invest. 39:395, 1960.

Howard Test:

The procedure is based upon experiments in dogs wherein unilateral partial renal artery occlusion caused an increased reabsorption of sodium and water proportionately greater than the concomitant decrease in G.F.R. Presumably, the decreased G.F.R. results in the delivery of less fluid to the distal tubule and a proportionately greater amount of sodium and water is reabsorbed, leading to a decrease in the urine volume and sodium concentration on the affected side. A reduced renal medullary blood flow may also be a factor.

38. Mueller, C.B., A. Surtshin, M.R. Curlin and H.L. White. Glomerular and tubular influences on sodium and water excretion. Am. J. Physiol. 165:411, 1951.

Technique: Reference 17

(1) Patients on normal sodium intake, without diuretics and with no infusions of saline, inulin, PAH, mannitol etc.
(2) Drink 800 ml. water during hour before cytoscopy
(3) Insert ureteral catheters 1-2 cm. above ureteropelvic junction.
(4) Obtain adequate urine flow (1-3 ml/min)
(5) Insert third catheter into bladder to check for leakage
(6) Obtain simultaneous collections X 3, with 30 ml. or more urine from one kidney during each
(7) Empty bladder at end of each collection period
(8) Measure volume and sodium concentration of each
(9) Discard results and repeat test if:

(a) urine flow stops during a collection period
(b) excessive leakage occurs around ureteral catheter
(c) urine sodium concentration less than 10 mEq/L from each kidney
(d) urine volume less than 1 to 2 ml. from one kidney
(e) results not consistent in all periods
(f) excessive blood in small volumes of urine (5 to 10 ml) (20 to 50% noninterpretable)

Interpretation (Values for abnormal side)

	Volume	Sodium conc.
Curable main artery obstruction:	↓ 50% (or 38%)	↓ 15%
Curable segmental obstruction	↓ 50%	equal or ↑ (creatinine ↑)
Non-curable segmental disease or pyelonephritis	↓ 50%	equal or ↑ (creatinine ↓)

Results:

Reference	Positives	False -	Negatives	False +
Conner, Ann. Int. Med.52:544, 1960	9/9	4	9/9	
Scott, J. Urol.86:31, 1961	12/14	2/14		
Crocker, N.E.J.M.267:794,1962	22/22			
Baker, N.E.J.M.267:1325,1962	11/14	3/14	4/6	2/6
Yendt, Am. J. Med. 28:169, 1960	17/20	3/20		
Brown, Brit. Med. J. 2:327, 1960	12/14	2/14	9/11	2/11
Maxwell, Am. J. Card. 9:126, 1962	7/14	7/14	1/2	1/2
Perloff, Circ. 24:1286,1961	14/35	21/35	25/26	1/26
Stamey, Postgrad. Med. 29:496, 1961	9/14	5/14		

Evaluation:

Advantages: Relatively easy to perform and usually predicts "curable" lesions.

Disadvantages: Danger, cost, often technically unsatisfactory, not specific for renal arterial stenosis, may miss bilateral or segmental "curable" lesions, may be falsely positive with unilateral pyelonephritis.

Stamey Test:

This test is based upon experiments in dogs wherein clamping of the renal artery was used to decrease GFR to variable degrees. With 10-30% decrease, urine concentration in the clamped kidney was increased. With greater than 30% decrease and low solute flow rate, urine concentration was decreased, but with a urea-induced osmotic diuresis, urine concentration increased, even when GFR was decreased more than 60%.

39. Levinsky, N.G., D.G. Davidson and R.W. Berliner. Effects of reduced glomerular filtration on urine concentration in the presence of antidiuretic hormone. J. Clin. Invest. 38:730, 1959.

Technique:

40. Stamey, T.A. The diagnosis of curable unilateral renal hypertension by ureteral catheterization. Postgrad. Med. 29:496, 1961, and Reference 13.

(1) During 2 hours before study, patient drinks 1,000 ml. water.
(2) After drawing a serum blank, a priming dose of PAH and inulin is given and an infusion of PAH and inulin in 5% D/W started at a slow rate to maintain desired plasma concentration. These concentrations are calculated from an estimate of the patient's GFR and RPF.
(3) Saddle block anesthesia is obtained with spinal puncture done with the patient sitting.
(4) Patient drinks another 500 ml. water.
(5) Fifteen minutes after anesthesia, cystoscope introduced and largest possible polyethylene catheters passed 10 to 15 cm. up the ureters. In males, only one ureter need be catherized and bladder urine used as the other specimen.
(6) One hour after priming dose given, and at least 15 minutes after ureteral catherization, begin consecutive 10-minute ureteral collections and record flow rates. (Reliable studies not possible in significant number of patients.)
(7) After initial collections under oral water diuresis obtained, change infusion to 8% urea in 1000 ml. saline containing inulin, PAH and Pitressin at a rate of 10 ml/min. Give loading dose of pitressin (5mμ/Kg) I.V. and infuse 5 mμ/Kg/hour.
(8) Obtain 3 additional consecutive 10-minute collections with flow rate at least 2 ml/min/Kidney, and agreeing within 6% of each other in the ratio of respective urine flow rates, without bladder leakage.
(9) Obtain serum before and at end of ureteral collections.
(10) Determine flow rates, urine osmolality, serum and urine inulin and PAH concentrations.

Interpretation (values for abnormal side)	Vol.	Inulin or PAH Conc.
Curable main renal art. stenosis (24)	↓ 66%	↑ 100% (1 with 16%)
Bilateral renal artery disease (2)	↓ 90%	↑ 400%
Curable segmental stenosis (4)	↓ 50%	↑ 16% or more
Normotensive unilateral renal disease(35)	↓	↑ less than 6%
Essential hypertension (theoretical)	↓ 40%	↑ 30%

Results:

Reference 23: 8/9 positive in unilateral renal hypertension, 3/4 positive in bilateral, 0/42 positive in essential hypertension.

Evaluation:

Advantages: Probably will uncover curable segmental renal artery disease which Howard test will not; probably easier to interpret.
Disadvantages: Morbidity higher than any other procedure, including aortography; overlap between essential hypertension and segmental renovascular.

D. Aortography

This is being used increasingly as the main diagnostic procedure and should be performed in every patient before surgery.

41. Morris, G.C., E.S. Crawford, D.A. Cooley, H.M. Selzman and M.E. DeBakey. Renovascular hypertension. Am. J. Cardiology 9:141, Jan., 1962.
" Almost 20% of severely hypertensive patients may have demonstrable renovascular abnormality," and "after age 60, arteriography will demonstrate the process in nearly one-half of hypertensive persons."

However, caution is advised in accepting the demonstration of a lesion as evidence of significant renal arterial occlusion.

42. Eyler, W.R., M.D. Clark, J.E. Garman, R.L. Rian and D.E. Meininger. Angiography of the renal areas including a comparative study of renal arterial stenosis in patients with and without hypertension. Radiology 78:879, June, 1962.
In this study, 32% of 304 normotensive patients had renal arterial disease, with all types of vascular lesions seen, including significant narrowing with post-stenotic dilation and fibromuscular hyperplasia.

	Normotensive		Hypertensive	
Age	Normal	Abnormal	Normal	Abnormal
31-40	7	3	6	10
41-50	26	8	14	22
51-60	99	35	28	50
Over 60	69	56	15	48

With proper techniques of aortography, mortality and morbidity have been decreased but still occur. The translumbar route is preferred by most.

43. Leadbetter, G.W. and C. Markland. Evaluation of technics and complications of renal angiography. New England J. Med. 266:10, 1962.
Suggest use of general anesthesia, lowering of blood pressure to below 150/90 with Arfonad, compression of lower aorta, initial injection to insure proper positioning, use of 10 - 15 ml. of 50% Hypaque per injection and no more than 35 ml. total.

44. Edholm, P. and S.I. Seldinger. Percutaneous catheterization of the renal artery. Acta Radiol. 45:15, 1956.

45. Kottle, B.A., J.F. Fairboirn, II, and G.D. Davis. Complications of aortography. Circulation 28:752, October, 1963 (abstract)

Multiple renal arteries are not in themselves significant and are found in 25% of normotensive and hypertensive patients.

46. Geyer, J.R. and E.F. Poutasse. Incidence of multiple renal arteries or aortography. J.A.M.A. 182:120, October 13, 1962.

Renal venography may be a simpler and safer procedure but has not been adquately evaluated.

47. Abrams, H.L., S. Baum and T. Stamey. Renal cinevenography in renovascular hypertension. Circulation 28:683, October, 1963 (abstract)

E. Renal Biopsy

The presence of impressive J-G cell hyperplasia in the involved kidney may be evidence for functionally significant renovascular disease.
(See References 14 and 25)

If marked nephrosclerosis is present in the "normal" kidney, hypertension may not be alleviated and surgery may be contra-indicated.

48. Vertes, V. and J.A. Grauel. Observations on renal hypertension. Circulation 28:536, October, 1963.

49. Baker, G.P., L.B. Page and G.W. Leadbetter. Hypertension and renovascular disease. New England J. Med. 267:1325, Dec. 27, 1962.

F. Pressure Gradients

A significant pressure gradient should be found at surgery (or perhaps with catherization) in patients with functionally significant renovascular disease. Stewart, et al. (Reference 23) have had poor results with patients having gradients less than 25 mm/Hg, whereas the Houston group (References 18 and 41) have found no correlation between the pressure gradient and the response to revascularization and accept a 5 mm. gradient as significant. It may be possible to measure gradients by catheterization at the time of selective renal arteriography. Reference 31.

G. Renin-Angiotensin Assays

Though they remain technically difficult, simpler technics using peripheral blood may soon become available.

50. Fitz, A.E. and M.L. Armstrong. Plasma vasoconstrictor activity in patients with renal, malignant and primary hypertension. Clin. Res. 10:288, 1962 (abstract)

51. McPhaul, J.J. and D.A. McIntosh. Evaluation of diagnosis and treatment of renovascular hypertension. Clin. Res. 11:171, 1963 (abstract)

H. Angiotensin Infusion Test

The pressor response to the intravenous infusion of angiotensin has been found to differentiate renovascular hypertension from other types of non-malignant hypertension.

52. Kaplan, N.M. and J. Silah. The clinical application of the angiotensin infusion test. J. Lab. and Clin. Med. (In press) (abstract)

Patient	No.	Mean Dose mμg/Kg/min	Range mμg/Kg/min
Essential H.T.	46	3.1	1.1 -- 5.0
Renovasc. H.T.	12	9.5	6.0 --22.0

The response to a single five-minute infusion of 4 mμg/Kg/min may serve as a screening test.

Treatment

The obvious therapy is surgical revascularization. Nephrectomy should rarely, if ever, be performed, particularly since the kidney with stenosis may be "protected."

The blood pressure becomes normal in 50 - 80% of patients. This frequently occurs in the immediate post-operative period but may take as long as a year (Reference 18).

53. Dustan, H.P., I.H. Page, E.F. Poutasse and L. Wilson. An evaluation of treatment of hypertension associated with occlusive renal arterial disease. Circulation 27:1018, June, 1963.
Ten of 99 patients died in the immediate post-operative period. Thrombosis of the renal artery occurred in 6. Re-stenosis occurred or new lesions appeared in 11.

Objective evidence of improvement in renal function after revascularization has been shown.

54. Simon, N.M. and F. del Greco. Kidney function after renal revascularization for hypertension. Circulation 28:805, October, 1963 (abstract)

Particularly impressive and significant are the results of surgical revascularization in patients with renal failure.

55. Morris, G.C., Jr., M.E. DeBakey and D.A. Cooley. Surgical treatment of renal failure of renovascular origin. J.A.M.A. 182:609, Nov., 10, 1962. Reference 53.

Some patients are not candidates for surgery and medical therapy may be successful in controlling their hypertension. The following types of patients are considered to be best treated medically (Reference 53):

(1) Patients with symptomatic coronary or cerebral arterial disease.
(2) Patients with mild hypertension and severe bilateral nephrosclerosis.
(3) Patients with unilateral lesions but no disparity in function of the kidneys.
(4) Patients without diastolic hypertension.