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HYPERTENSION DUE TO UNILATERAL RENAL ISCHEMIA

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INTRODUCTION

Renal hypertension, which has long been a controversial subject has now been given sufficient study experimentally and invivo to be accepted as fact. In this paper there will be given information for different views, beginning with early experimental renal hypertension and continuing through more recent studies. Included will be research data and recent case histories.

Richard Bright has been credited with the idea of renal origin of renal hypertension before blood pressure in man was determined but he never proved that hypertension actually exsisted. He recognized that a large heavy heart was associated with abnormality of kidneys. His idea of increased action of the heart and increased peripheral vascular resistance is the basic mechanism of elevated blood pressure.

There are those who deny that the kidneys ever play a primary part in the pathogenisis of hypertension. It is now generally recognized that primary renal disease may be associated with human hypertension.

Arguments against renal origin of essential hypertension include occasional failure to find any significant intrarenal vascular disease or any other abnormal

condition of renal tissue. After exsistance of elevated blood pressure had been established, the fact that hypertension was the cause of the heavy heart observed by Bright was fully realized.

Experimental production of renal hypertension was done for the most part before 1928. The methods used were; unilateral and bilateral disturbance of renal excretory function, unilateral and bilateral nephrectomy, reduction of amount of functioning renal tissue by resection, effect of nephrotoxic substances, irradication with roentgenrays, occlusion of one or both ureters, acute compression of kidneys, embolism, passive hypermis due to constriction of main renal vein, permanent occlusion of main renal artery, vein and ureter of both kidneys, arteriovenous anastomosis and occlusion of main renal arteries. Few of these methods were followed by some elevation of blood pressure but in most of them the hypertension did not persist. Other investigators using the same methods produced contradictory results tho none actually reproduced anatomic or even physiologic state of the kidney in benign essential hypertension.

Since the main effects of intrarenal arterial and arteriolar disease of the kidneys are probably reduc-

tion of intraglomerular capillary pressure and alteration, passive reduction of blood flow to functioning components of the kidneys, it was thought that these two effects and other physiologic disturbabces that may occur might be produced by permanent constriction (not occlusion) of the main renal artery by clamp. The method used was a compromise and does not infer that stenosing arteriosclerosis of main renal artery was a frequent finding in human essential hypertension.

In experiments, constriction of one main renal artery proved sufficant to induce rise of blood pressure within twenty-four to seventy-two hours. Because of the effects on a variety of experimental animals it was considered that even human hypertension may be a unilateral renal condition and also that removal of one diseased kidney results in blood pressure returning to normal.

If both renal arteries are constricted at the same time or at intervals, the results are permanent elevation of blood pressure. Others have also shown that this is true in hypertension with both systolic and diastolic pressures becoming elevated.

Responsibility for elevated blood pressure in experimental renal hypertension by humoral mechanism was indicated first by the effect of tying of renal veins in dogs with the main renal artery adequately constricted to cause hypertension. The animals died within two to seven days but did not show any elevation of blood pressure. Most recent contributions to this subject have dealt with the humoral mechanism about which there are now two views, (1) that a kidney with constricted main renal artery or any other pathologic condition which brings on a disturbance of renal circulation may be the source of a chemical substance which raises the blood pressure. (2) the normal kidney is ordinarily the source of a substance which has the ability to prevent hypertension and that in its absence, neutralization or destruction, elevated blood pressure will occur. More evidence favors the first view but unequivacal proof is still lacking.

Various names have been suggested for different constituents of humoral mechanism, but the tendancy at present is the acceptance of the original terms; Renin; an enzyme from the kidney which enters the blood stream through renal vein and interacts with

hypertensinogen. Hypertensin(polypetide formed by the action of renin). Hypertensinogen(a globulin in blood plasma upon which renin acts to form hypertensin). Hypertensinase (enzyme in blood and in extracts of some organs capable of inactivating hypertensin.

Limited information is given on exact mechanism and site of formation or release of renin. Most in vito experiments on the origin of renin.have indicated that it originates in the cortex of the kidney and especially in the lining of the epithelium of the convoluted tubules. Renin can be detected in the kidneys of the dolphin. It cannot be extracted from kidneys in which the proximal tubules have been destroyed by sodium tartrate poisoning. These facts indicate that the convoluted tubules are the most probable site of origin(production and storage) of renin at least of prorenin, if this exists. The exact nature of the stimulus which brings about the release of renin or prorenin has not yet been determined. Some investigators have suggested that reduction of intrarenal pulse pressure rather than decreased blood flow to kidneys is what determines release of renin and formation of vasoconstrictor substances depends upon demonstration of a pressor substance. This method is not accepted as a

specific test for renin or angiotonin as it is questionable just what significance should be attached to these experiments.

Even the assumption of a presumable change from intermittent to continuous pressure beyond the site of the efferent glomerular arterioles is not justified for the very reason that a pulse pressure has never been proven in the glomerulus. The reduction of the blood flow through the functioning components of the kidneys is another possible stimulus for formation and release of these substances.

Although it has been demonstrated that renin does appear in the blood in the state of hypotension due to excessive bleeding, the amount of renin present is not sufficient to account for the pronounced and sustained pressor action of the hypertension produced by the renin in the amount of plasma used in the experiments. More work is required before the exact nature of the mechanism involved in the acute and chronic phases of experimental renal hypertension can be considered established.

Investigators have found that in the serum of rabbits, dogs and guinea pigs injected subcutaneously or intramuscularly with renin from various species (not

with homologous renin) a substance develops in the blood which is capable of neutralizing in vitro the acute pressor effect of an intravenous injection of renin. They regard this principle as analogous to an antibody, antienzyme or antihormone, hence the name antirenin. It has been found that repeated injection of hetrologous renin subcutaneously or intramuscularly into hypertensive animals for several months will prevent the development of renal hypertension when the renal arteries are constricted. It is not considered that the evidence on which the significance of antirenin was repudiated was conclusive. This phase of the problem requires more investigation.

The possible application of the results obtained in animals to the treatment of human hypertension is beset by the difficulty that homologous renin does not induce the development of antirenin and the fact that human beings respond with a pressor effect to the intravenous injection of only homologous (human) renin.

The view that human essential hypertension in both the benign and malignant phases is primarily of renal origin has been adopted by many. The existance of many similarities between any two processes or substances does not necessarily prove their identity,

experimental renal hypertension does, howerver faithfully reproduce human essential hypertension in many respects and therefore we may have the view that essential hypertension in man may be of renal origin.

The thought that essential hypertension may be of renal origin is a controversial subject and not yet settled. There has been relief of essential hypertension by sympathectomy . One study by Smithwich[33] of 2600 hypertensive patients who had through renal studies, exploration of kidneys and renal arteries at the time of operation and biopsies from each revealed only two cases of hypertension due to unilateral kidney disease. Studies by other men have shown no apparent renal involvement with most cases of essential hypertension.

Ferris[9] in his study of hypertension and the effects of the injection of a ganglionie blocking agent demonstrated that the person with stenosis of the renal artery had the same response as did the person with acute glomeruli nephritis in which there was only slight fall of blood pressure during active process of kisease and marked fall of blood pressure after active process was resolved. Marked fall in blood pressure was noted in parxnchymal renal lesion.

The entity of hypertension caused by unilateral kidney disease is but a small portion of the causes of hypertension ranging from 1 to 5% of cases according to different authors. The condition can be cured if the diagnosis is made early and adequate therapy follows. There are varied causes of unilateral kidney disease ranging from congenital defects to arteriosclerosis of the renal artery. The symptom may be sudden or gradual in onset.

The condition should be thought of when there is hypertension which occurs:

1. in a young person with no family history of hypertension.

2. sudden onset of hypertension with high diastolic pressure.

3. essential hypertension with recent malignant hypertension.

Other findings which follow the majority of cases are albuminuria, leukocytosis, polyuria, polydipsia,[5] headaches and loss of visual acuity.

In a series of cases by E.G. Margolin[16] et all where hypertension was caused by unilateral renal artery occlusion proved by surgery or autopsy, the following symptoms were obtained.

90% albuminuria

60% polyuria and polydipsia

50% leukocytosis 10-30,000

50% impaired renal concetrating ability

In a series of cases of G.A. Perera and A.W. Haelig[20] , 70% had grade IV retinepathy and headaches.

The age range varies from author to author but is predominently the third and fourth decades with cases at birth and with aged individuals. The male sex predominates in 60-70-% of the cases.

The diagnosis can be made by kidney function tests and aortography. The kidney function study usually reveals normal retrograde pyelograms and occasional decreased function of one kidney with intravenous pyelograms. There is usually unequal size of kidneys. The split studies of the kidney with uretral catheters reveals decreased dye excretion and decreased urine and electrolytes from one side.[13]

The intravenous pyelogram will occasionally show a decreased function on one side and may show a difference in size of kidney. This test is an important aid to reveal good function one one side so that affected kidney may be removed. Split function studies can follow the retrograde pyelogram which should be-

normal unless the difficultly is within the ureter such as hydronephrosis due to blockage of the ureter. The split studies should show decreased amount of urine from affected side with decrease of sodium and chloride concentration and protein because of the effect of renin which is the proposed cause of the hypertension. Renin causes inhibition of water, sodium and chloride reabsorption probably by supression of tubular reabsorption.[14]

There has been recent work done by C.C. Winter[38] using radioactive diodrast as a screening test for hypertensive persons to determine defective renal function. The method is a simple nontraumatic, screening test which appears applicable. His series of 44 persons revealed significant difference between normal, unilateral abnormal and bilateral abnormal kidney function. The test is comprised of injection of one micro curie/5kg of diodrast I^{131} intravenous and measuring radioactivity over each kidney area for 10-30 minutes. The test has apparent value but the problem is availability of necessary equipment.

Aortography is of great value in diagnosis, although the procedure is not without danger. The chief

danger is from injection of a large amount of concentrated solution into one renal artery, mesenteric artery or coeliac axis. In a report by Poutasse and Dustan[25] using aortography on 104 patients with history of either of the following;

1. hypertension; difference in kidney size and function

2. hypertension in a young person without family history of hypertension

3. sudden onset of hypertension

4. essential hypertension with recent onset of malignant hypertension.

They found 30 cases or 29% with abnormal renal blood flow and 23 cases due to arteriosclerosis. Another group of cases reported by Perera and Haelig[21] showed 14 of 20 caused by infection. This procedure is of value where there is a defect in the blood flow to the kidney which is not the major cause of unilateral kidney disease. A large number of reports were reviewed by Smith[31] in 1956. Of 575 collected cases a successful report as result of nephrectomy was obtained in 26%. In these cases the blood pressure remained below 140mmHg systolic and 90mm diastolic for a year. The number of patients apparently cured but followed about

a year would bring the percentage to 35. Marked symptomatic improvement with substantial lowering of the blood pressure may be highly satisfactory clinically, even if the pressure does not fall to strictly normal figures.

In patients giving a favorable response, the fall in blood pressure may vary from almost immediate to as much as a few weeks. Instability of the pressure rises in response to stress may be observed. Usually any relapses occur within a few weeks or months, but some have been observed after more than a year.

Thompson and Smithwich[33] in a review of 2600 patients, only two cases of unilateral disease were found who were cured at least a year after nephrectomy. They also reported 26 out of 57 hypertensives who had unilateral involvement of the kidneys. Smith[31] reports 47 out of 242 cases. This is a total of 73 out of 299 or 24.4%. The pathologic involvement of the kidneys revealed 50% were due to infection mainly pyelonephritis. The remainder was divided between congenital defects and arterial lesions.

In a report by C.L. Yuile[39] in relation to obstructive lesions of the renal artery the primary cause of intrinsic narrowing is due to arteriosclerotic plaques.

Secondary causes were thrombi, emboli and congenital narrowing. Extrinic causes were due to kinking, torsion, aneurysm, extrinsic pressure(tumor, hydatid cyst and syphilis), and trauma.

W. J. Engel, in his report, found that arteriosclerotic plaques and stenosis due to fibrous intimal proliferation were the major causes of hypertension of kidney origin.[8]

The condition may be caused by accidental[12] or surgical trauma to the renal region. Embolism or thrombosis of the renal artery is often mistaken for appendicitis because of an acute attack of pain in the flank or lower abdomen.[26] This sometimes leads to unnecessary surgery. Such a history is very important as is a known source of emboli. When a person is known to have a normal blood pressure at the time of such an attack, hypertension has developed within a few days or even a few hours after trauma. This condition can become severe with encephalopathy and retinopathy within three weeks and in some after a much longer interval of time.

In reading over the cases reported in the literature, there was one case where a sample of blood was drawn and checked for hypertensive activity and found to be positive.

There has been considerable experimental work done in the past twenty years in relation to the hypertension agents produced by the kidney.

Renin was isolated and found to be a protein chiefly a pseudoglobin and partial euglobin. It is non dialysable and is destroyed by heat (60° C), strong alkali and acid precipitated by half saturated solution of ammonium sulfate.[22]

The pressor agent produced by action of renin with plasma (angiotonin or hypertensin) has been isolated and synthesized as an octapeptide which is heat and acid stable and destroyed by oxidizing agents and forms a crystalline salt with oxalic and picric acids. These substances have been used in both human and animal experiments and various results have been reported.[20-29-36]

It has been shown that renin is formed and stored in the epithelium of the proximal convoluted tubules[10] and also that the metabolism of the ischemic kidney is reduced.[26] This lowers enzymatic activity and oxidizing powers of amines and amino acids which could be a factor in increased renin production or decreases production of antirenin substances since the inhibitors of both renin or angiotonin appear to originate in the kidney.

Page[18] has shown that there is increased renin and decreased renin activator, decreased angiotonin activator and increased angiotonin inhibitor in the renal vein after clamping the renal artery or producing silk or cellophane perinephritis, but decreased renin, increased renin activator, increased angiotonin activator and decreased angiotonin inhibitor would give a higher effective level of angiotonin. Page[17] has developed a sclematic for the development of hypertension due to unilateral kidney disease.

Reduced pulse pressure in kidney

↓

Efferent arteriolar constrition

↓

Relative tubular ischemic

↓

Increased permeability of tubular wall

↓

Renin activator + Renin inhibitor + Renin → inert-substance

Alpha globulin

↓

angiotonin inhibitor + angiotonin + angiotonin activator from serum RBC → pressor substance

→ inert substance

BP activators and inhibitors are from the kidney. Taehyphylaxis develops when any step of the the above scheme is broken.

The effect of hypertension produced by renal ischemia is unchanged by kidney deneration, severance of spinal cord in thorasic region, severance of vagus nerves, adrenalectomy, splenectomy[4], pithing[6] or excision of corotid sinuses.[11]

There have been several noted effects of physiologic changes due to renal hypertension. These were carried on by injection of renin or angiotonin into animals. Hypertension can be maintained by repeated injections of either substance until tachyphyalaxis develops.[33-36] The method of injection caused different responses: intravenous caused hypertension and proteinuria; intraperitoneal caused no hypertension and massive proteinurea,; intravenous with adrenalectomy caused hypertension but no proteinuria.[28]

Renin and angiotonin injections also caused increased glomular filtration rate, increased urine flow, increased urea chloride[3] and sodium excretion, increased sodium, chloride and potassium decreased in the extracellular fluid,[7] no change in inulin excretion but decreased diodane and PAH clearance.[12-14-23] These injections also cause strong muscle contractions of smooth muscle of the intestine.[19]

Plente and Page[24] developed a method of analysis

of angiotonin-renin pressor system which is moderately accurate by a time ratio incubation of extracted plasma from patient with normal plasma and then injecting into animals and measurement of the hypertensive response if they are present.

Skeggs, et all[30] have developed a method for the isolation and assay of angiotonin. The method involves drawing of arterial blood into an ethanol solution which stopped the action of the enzymes renin and hyperteninase and precipitates the proteins of the blood. The hypertensin or angiotonin in the filtrate was then concentrated and purified sufficiently for final assay in anesthetized rats.

With this method they were able to isolate angiotonin to a level of 0.01 Goldblatt units.

In other studies by Wakerlund et all, they showed no effect on renal hypertension from extracts of liver pancrease, pituitary, adrenal and gonadotropins.[35] The hypertension was reduced by administration of renal extracts.[36]

The following are some case histories which show a variety of methods of diagnosis of unilateral kidney disease with hypertension.

W.W.

This patient is a four week old white male with an abdominal mass in the right upper quadrant. The only other finding was that the child did not void for the first thirty-six hours of life. Since then there has been no difficulty with urination, however, there was a trace of albumin.

Examination: Temperature was 98.60. Heart rate 140; respirations 56. Head circumference 40cm.; chest circumference 41 cm.; abdominal circumference 49 cm. The patient was a well developed, well nourished white male infant in no acute or chronic distress. Blood pressure in the arms was 146/80 and in the legs 154/40. Remainder of the physical examination was within normal limits, except for the abdomen which was obviously enlarged. A mass was palpable, which occupied most of the right side of the abdomen. The margins were fairly well defined and the mass seemed globular. It was thought to be a fairly firm mass in consistancy. Peripheral pulses were normally palpable.

Laboratory data; Hemoglobin, on admission was 15 grams, WBC 12,800. Urinalysis was essentially normal, with a specific gravity of 1.013 and reaction of6. NPN, on admission was 32 mg.%. Repeat NPN's postoperatively, have been 34 mg.% and 30 mg. %.

IVP revealed no function of right side. The right kidney was removed surgically and was a multicystic kidney weighing 525 gm. The cysts were thin walled and contained yellow fluid. There was a small amount of kidney tissue present which contained numerous glomuli some were fetal and others hyalinized. The proximal tubules were normal and distal tubules were dialated.

The postoperative course was uneventful except that his blood pressure was 160/50. Three months after operation his blood pressure was 106/30 and after five months it was 90/60.

This case represents unilateral renal disease causing hypertension which developed in less than four weeks of post partum life. It also shows an interesting finding in that the blood pressure did not fall immediately after surgery but fell gradually over a period of three months. This may represent the inability of the youthful system to respond immediately.

HB

This is a 61 year old white female who seven months ago had a blood pressure of 160/94. She developed severe headache three weeks ago and also left abdominal pain. There were no other complaints except nausea and frequency.

Examination revealed grade II retinopathy and blood pressure of 230/140 to 250/150 and urine output of 12-1300cc daily.

Urinalysis revealed a 3 plus albumin and 2 plus white blood cells and 1 plus granular and cellular casts. Complete blood count revealed white count of 21500/cu mm. Serum electrolytes were as follows: sodium, 134meg/l; chloride, 75.2meg/l; potassium, 3.8meg/l; carbon dioxide 28mM/l and blood urea nitrogen 13.2meg %.

PSP excretion revealed 60% excretion in the first hour and urea clearance of 83% in one hour. Intravenous pyelogram revealed no function on the left side and showed that the left kidney was small and the right kidney was enlarged.

Retrograde pyelogram revealed bifid renal architecture and small left kidney with right kidney enlarged. Aortagrams revealed complete occlusion of left renal artery.

The left kidney was removed and at operation there was no plusation of the left renal artery. There was considerable calcification of the abdominal aorta. Pathologic examination revealed a small kidney(70gm) with a capsule which stripped easily with smooth surface. The glomerli were normal with a few hyalinized. The arteries were thickened with bloth medial and intimal thickening.

The post operative course was uneventful with the blood pressure ranging between 160/80 and 190/100 which is approximately the level seven months before.

This case represents a case of essential hypertension with sudden onset of malignant hypertension probably due to occlusion caused by arteriosclerous and thrombosis. The findings are all compatable except for the finding of low serum chlorides which could be due to a loss through the kidney.

EF

This thirty-nine year old white female eighteen months ago had an abortion at five months gestation and had associated nausea and hypertension. This condition was controlled by medication and low sodium diet until four weeks ago when she developed convulsions of Jacksonion type. She was semi comotose for nine days.

Since then she has had some syncope and diplopia. She has had albuminuria and recently developed frequency and hypertension of severe degree. Intravenous pyelograms of eighteen months ago revealed good bilateral function.

Examination revealed lateral nystagmus with grade II retinopathy and an old hemorrhage in left fundus. The blood pressure was as follows; right arm-170/110 left arm-240/108, right leg 248/110 and left leg-258/110 the liver was down 4cm. below right costal margin. The daily urine volume varied from 22-4100cc. The urine revealed 4 plus albuminuria with 1.9 gm albumin for twenty-four hours.

PSP showed		R	L
	15 min.	1.3cc	7cc
	30 "	.1cc	4cc
	45 "	.2cc	4.8cc

The twenty-four hour excretion of:

sodium	1240mg	122mg
potassium	112mg	48mg

Complete blood count revealed white count of 1170/cu, mm and electrolytes of sodium, 130.0mg/l; potassium, 3.0mg/l; chloride, 82.0mg/l and carbon dioxide, 25mM.

Intravenous pyelogram revealed decreased function on right and retrograde pyelogram showed normal architecture except for small right kidney. The right kidney was removed and it was noted that the right renal artery was small but pulsating. Pathologic report showed a small kidney(76gm) with easily stripping capsule and ecchymosis of kidney surface. The afferent and efferent arteries had thickened walls and narrowed lumen and some occluded and numerous organizing thrombi in the vessels. Many glomeruli were fibrosed. The tubules were compressed with degenerated epithelium.

The level of blood pressure dropped immediatly to hypertensive levels and gradually rose to 130/70-140/85. A recheck four months later revealed pressure at same level.

This case represents an eighteen month history of hypertension and urinary findings with development of nephroclerosis and of findings of decreased urine excretion and increased sodium and potassium excretion which according to Howard et al would be a poor prognosis. She may revert and develop hypertension later. She has responded well during the four month followup.

Howard et all[13] made a through urinary study of patients with benign essential hypertension, hypertension with bilateral renal disease, hypertension alleviated by nephrectomy and hypertension unrelieved by nephrectomy. He found a difference in the split renal studies which demonstrated equal levels of urine and electrolytes from each kidney in essential hypertension and hypertension with bilateral renal disease. In patients with hypertension alleviated by surgery he found decreased urine formation and decreased sodium and chloride excretion of involved kidney as compared with the other side. With the patients unrelieved by surgery he demonstrated decreased urine formation on the involved side but increased sodium and chloride excretion from kidney as compared to the other kidney. He speculated from these findings that he can predict the results of nephrectomy before surgery.

In this study and an earlier one[14] he reported the pathologic findings of the surgically removed kidneys. He found that in most cases there was significant tubular atrophy present. The presence of dilated thyroid-like tubules in the kidney denoted no improvement of the hypertension following nephrectomy.

Renal hypertension is a proven entity and involvement of one kidney has been shown on several occasions.

The diagnosis of unilateral kidney disease should be thought of when hypertension occurs in a young person with no family history of hypertension, sudden onset of hypertension with high diastolic pressure, or essential hypertension with recent malignant hypertension. Other findings which are found in a majority of cases are frequency, nocturia, headaches and loss of visual acuity. There should be leukocytosis in mild form and varing degrees of albuminuria.

The diagnosis can be determined by decreased size of one kidney, decreased function of one side and the size on IVP with a normal retro grade pyelogram. The IVP may show normal function but split studies of the kidney show a decreased excretion of dye, sodium and chloride on involved side. Aortagrams are diagnostic in cases of blockage of arterial blood flow to the kidney.

The renogram is fundtional in screening individuals with hypertension.

There have been recent advances as to the cause of renal hypertension. Angiotonin which is produced by

action of renin with alpha globulin portion of blood to form angiotonin. Angiotonin is the pressor substance and acts by vaso constriction apparently on smooth muscle without any nervous component.

There has been recent isolation of angioyonin from blood of hypertensive animals which is diagnostic of level of angiotonin in the blood sample.

BIBLIOGRAPHY

1. Addis, T. and others, Renin Proteinuria in the Rat J. Exp. Med. 89:131-4 1949

2. Brandt, I.L. and Grahm, J.G., Effect of Renin of Proteinuria and PAH Clearance at Low Plasma Levels, Am. J. Physiol. 153:458-64 1948

3. Cororan, A.C. and Page I.H., The Effect of Angiotonin on Renal Blood and Glomerular Filtration, Am. J. Physiol. 130:335 1940

4. Cullins, D.A. and Hamilton, A.S., Pressor Responses Following Renal Ischemia, Am. J. Physiol. 130:90 1940

5. Deming, Q.B., Association of Polyuria and Albuminuria with Hypertension of Unilateral Renal Origin, Arch. Int. Med., Vol. 93 (Feb.)1954

6. Dock, B., Vasoconstriction in Renal Hypertension Abolished by Pithing, Am. J. Physiol. ppl30-1 (June 1) 1940

7. Eichelburger, L., The Distribution of Water and Electrolytes Between Blood and Skeletal Muscle in Experimental Hypertension, J. Exp. Med. 77:205 1943

8. Engel, W.J., Hypertension of Urology Importance, West. J. Surg., Ob. & Gyn., 66:210-4

9. Ferris, E.B. and Brust, A.A., The Diagnostic Approach to Hypertension Due to Unilateral Kidney Disease, Ann. Int. Med. 47:1049-1065 1957

10. Friedman, M. and Kaplan, A., Studies Concerning the Site of Renin Formation in the Kidney, J. Exp. Med. 77:65 (Jan. 1) 1943

11. Goldblatt, H. et all, The Effect of Exeision of the Caroted Sinuses on Experimental Hypertension Produced by Renal Ischemia, J. Exp. Med. 71:175 1940

12. Haller, J.A. and others, Hypertension Due to Segmented Infarction of the Kidney, J. Med. Vol. XXII pp303-5 (Feb.) 1957

13. Howard, J.E. and others, Hypertension Due to Unilateral Renal Disease with a Report of a Functional test Helpful in Diagnosis, Bull. Johns Hopkins Hosp. 100:241-276 1957

14. Howard, J.E. and others, Hypertension Resulting from Unilateral Renal Vascular Disease and its Relief by Nephrectomy, Bull. John Hopkins Hosp. 94:51-75 1953

15. Hughes, N.C., et all, The Nature of the Action of Renin and Hypertension on Renal Function of the Rabbit, J. Physiol. 109:288 1949

16. Margolin, E.G. and others, Diagnosis of Hypertension Due to Occlusions of the Renal Artery New England J. Med. Vol. 256 #13 pp581-7 (March 28) 1957

17. Page, I.H. and Helman, O.M., Angiotonin Activator Renin and Angiotonin Inhibitor and the Mechanism of Angiotonin Tachyphylaxis in Normal Hypertension and Nephrectomized Animals, J. Physiol. 71:490 1940

18. Page I.H., Liberation of Renin in Experimental Hypertension, Am. J. Physiol. 130:22-28 (June) 1940

19. Page I.H., Effects of Hypertension and Normal Plasma on Intestinal Segments Treated with Renin, J. Physiol. 130:29-33 (July 1) 1940

20. Page, I. H. and Helman, O.M., A Crystalline Pressor Substance Resulting from Reaction Between Renin and Renin Activator, J. Exp. Med. 78:477 1943

21. Perera, G.A. and Haelig, A.W., Clinical Characteristics of Hypertension Associated with Unilateral Renal Disease, Circulation (Oct.) Vol. 6 #4 1952

22. Pickering, G.W. and Punzmetal, M., Some Observations on Renin, Am. J. Physiol. 3:211 1937

23. _____, The Effect of Renin on Urine Formation Am. J. Physiol 98:314-35 pp40

24. Plente, A.A. and Page, I.H., Kinetic Analysis of the Renin Angiotonin Pressor System and the Standardization of the Enzymes Renin and Angiotonin, J. Exp. Med. 78:367 (Nov.) 1943

25. Poutasse, E.F. and Dustan, H.P., Arteriosclerosis and Renal Hypertension, J.A.M.A. Vol 165 #12 (Nov) 1957

26. Poutasse, E.F., Occlusion of the Renal Artery as a Cause of Hypertension, Circulation, 13:1-37 (Jan.) 1956

27. Raska, S.B., Metabolism of the Ischemic Kidney, J. Exp. Med., 78:75 1943

28. Sellers, A.L. and others, Experimentsl Proteinuria J. Exp. Med. 96:643-54 1952

29. Schwartz, H. and others, Synthesis and Pharmacology of the Octapeptide Angiotonin, Science 125:886 1957

30. Skeggs, L.T. and others, The Assay of Hypertensin from the Arterial Blood of Normotensive and Hypertensive Human Beings, J. Exp. Med. 95:717-731 1958

31. Smith, H.W., Unilateral Nephrectomy in Hypertensive Disease, J. Urol. 76:685-701 1956

32. Swann, H. G. and others, The Intrarenal Pressure During Experimental Renal Hypertension. J. Exp. Med. 96:281 1952

33. Taggart, J. and Drury, D.R., Action of Renin on Rabbits with Renal Hypertension, J. Exp. Med. 71:887 1940

34. Thompson, J.E. and Smithwich, Human Hypertension Due to Unilateral Renal Disease with Special Reference to Renal Artery Lesions, Angiology 3:493 1952

35. Wakerlind, G.E. and Gaines, W., Effects of Various Agents on Renal Hypertension, Am. J. Physiol. 130:568-573 (August) 1940

36. Williams, J.R. and others, Reduction of Blood Pressure of Hypertensive Dogs by the Administration of Renal Extracts, Am. J. Physiol. 130:496-502 (August) 1940

37. Witson, C. and Pickering, G.W., Acute Artereal Lesions in Rabbits with Experimental Renal Hypertension, Am. J. Physiol. 3:343 1937

38. Winter, C.C., Unilateral Renal Disease and Hypertension. Use of the Radioactive Diodrast Renogram as a screening Test, J. Urol. 78:107 1957

39. Yuile, C. L., Obstructive Lesions of the Msin Renal Artery in Relation to Hypertension Am. J. Med. Science 207:394 1944