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Evaluation of renal function using the radioisotope renogram

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THE EVALUATION OF RENAL FUNCTION USING THE RADIOISOTOPE RENOGRAM

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INTRODUCTION

The renogram was developed through animal studies by Taplin, Meredith, and Kade in 1955 and first used clinically by Winter in 1956. Since its introduction, potential usefulness has been evident, originally being suggested for its value as a screening test for unilateral renal disease in hypertensive patients.[3,20] The test was an almost self-apparent analogy to the radioactive Rose-Bengal test of liver function and biliary tract patency.[21]

Though the clinical use of renography is gaining prominence in larger hospitals, its useage is still largely experimental. In practice, the problem of obtaining accurate, reproducible tracings has been difficult. In 1960, Dollery concluded that the test is "unsuitable as a screening test." He suggested that it "is quite possible that the use of other chemical compounds or alteration in technique may surmount some of the difficulties . . ."[13] Such changes have since been applied to renography, greatly simplifying its use.

RATIONALE

When a physician in practice or in the hospital undertakes to test kidney function on the basis of the literature, he must ask whether the method applied at present still suffices, whether a part of it is unreliable and surpassed, and whether a new procedure has been introduced which will advance his work with the progress of science.[4]

It has become evident that hypertension in the presence of unilateral renal disease does not always improve following nephrectomy, and a more accurate recognition of the type of hypertension resulting from renal ischemia was desirable.

Adams and Perea and Haelig in analyzing cases benefitted by nephrectomy noted the following factors which apparently accounted for success: (1) There was a short history of hypertension, usually of less than 2 years duration; (2) there was a rapid progression of the disease process; (3) severe headaches were present; (4) the diastolic pressure was above 120 mm. Hg.; and (5) minimal retinal changes were noted. These factors, however, were general in nature and have not permitted a definitive selection of those patients who would be ideal candidates for nephrectomy.[8]

The more accurate evaluation of the hypertension in relation to unilateral renal ischemic disease has been made possible by the development in recent years of newer methods of study. These consist of roentgenographic procedures employing contrast media; comparative physiopathologic study of renal excretion; and, more recently, the use of an isotope labeled substance to evaluate the vascular state and tubular function of the kidneys.

Unilateral renal disease is an infrequent cause of hypertension, occurring in less than 2 percent of unselected patients. Such a small proportion of patients with unilateral kidney disease

respond to removal of the affected kidney that hypertension per se is not an indication for nephrectomy.[1,8,16,18,22]

Hypertensive patients with unilateral renal arterial stenosis form an even smaller group, but their response is good to surgery performed before the development of extensive vascular disease involving the contralateral kidney. Ureteral catheterization or aortography may lead to earlier diagnosis and better surgical results in this condition, but associated technical difficulties, inconvenience, significant morbidity and mortality, and other complications of these procedures have limited their use in screening hypertensive patients in the incipient stages of the disease.[1]

For 25 years, it has been a foremost theory that these lesions cause an ischemia of part or all of the kidney, stimulating the production of a substance that reacts with a liver substrate to become a peripheral vasopressor causing hypertension. True to this theory, removal of an affected kidney or correction of an arterial lesion has resulted in many instances of reduction of blood pressure to normal levels. This has not occurred in the majority of cases. In efforts to detect these renal-arterial lesions, many tests of individual kidney function and renal arterial flow have been employed. In addition, some investigators have suggested that through the interpretation of appropriate tests, an accurate prediction could be made as to which

individuals would be cured by surgery.[22]

However, in considering nephrectomy, it is imperative to be certain that the remaining kidney be capable of sufficient function to maintain life.

METHOD

Apparatus

Two matched scintillation probes, each attached to a rate-meter and rectilinear recorder, are used. The scintillation crystal should be properly collimated. Each probe is calibrated using an I^{131} standard source, to assure identical recorded responses from each counting-recording unit. Physical testing of the equipment is necessary to determine the operating voltage (plateau curves) and the individual response of each detector, rate meter, recorder, and system. The voltage may not be identical for each detector. The electronic component must be allowed a satisfactory warm-up period to allow stabilization to occur. It is essential to determine whether the rates of travel of the recording paper and recording stylus are uniform so that the detectors sense and signal equal responses to the same stimuli.[7,18]

Chart speed is a matter of personal preference, economy, and the desirability of including the tracing in the patient's chart.[18] A speed of 12 inches per hour seems to be convenient.

Standard equipment is now available and much of the matching

of the scintillation probes is taken care of prior to purchase. The price range for equipment is between $5,000 and $10,000.

Radioactive Testing Material

A most fundamental change that has taken place since the introduction of renography has been the radioactive test material. The first substance applied to radioisotopic kidney function testing was I^{131} labeled iodopyracet (diodrast). In practice, it was quickly found that diodrast is in part taken up by the liver; therefore, when detecting probes are placed directly over the kidneys, the right curve is skewed. In order to prevent liver uptake of the radioactivity, two approaches were taken. One was to block the hepatic uptake of diodrast by adding an intravenous load of diodrast (nonradioactive). The desired result was obtained, but simplicity was sacrificed.[13] The second was to use a material which is excreted rapidly by the kidneys only. I^{131} labeled urokon, mokon, renografin, and hypaque were not appreciably taken up by the liver, but their rate of extraction from the blood was slow, thus dulling the differences in kidney uptake and excretion. Only 10 to 15 percent of the injected dose of urokon I^{131} could be recovered in the patient's urine after 30 minutes, whereas in rabbits over 90 percent is recovered in 30-minute urine samples. With this demonstration that the rate of urokon excretion in man is many times slower than in rabbits, clinical trials with urokon were temporarily

discontinued, and similar studies were instituted using radioactive diodrast. When the first normal patient was tested with diodrast, it was obvious that the uptake-secretion curve was nearly identical to those found in normal rabbits. However, for application in general medicine and for research, I^{131} urokon, in doses used in urography, could be used to estimate glomerular function, and diodrast to indicate renal tubular secretory function.[21]

Approximately 10 percent of administered dose of diodrast is excreted by the liver. Approximately 20-30 percent is protein-bound and not available for glomerular filtration.[20]

Using diodrast to minimize liver background radiation, the scintillation probes were placed angling downward from above the kidneys to avoid the liver. Because of this angulation, counters cannot always be accurately placed. If counters do not detect all the radiation in the renal areas, tracings are in error. In addition, the necessity for the angulation of the counters results in greater soft tissue filtration and in a reduced amount of radiation detected because of the increased distance (inverse square law). For these reasons, the use of I^{131} diodrast requires technique that is exacting.

Hypaque^{131} was abandoned because the resulting curves were too flat and difficult to interpret.[3]

Finally a test material was reported which circumvented

these difficulties and which has proved in subsequent trials to be an ideal test agent. This is I^{131} labelled iodohippurate (Hippuran) which is rapidly removed from the blood by the kidneys and has essentially no hepatic uptake. The use of Hippuran allows the external probes to be aimed directly at the kidneys without elaborate techniques to circumvent or block the liver, while at the same time retaining a high level of sensitivity.[13]

With Hippuran, the kidneys remove 98 percent, and it is rapidly excreted, making more accurate placement of probes possible. As compared with diodrast, the peak is higher and occurs earlier. Diodrast is excreted 47 percent by glomerular filtration and 53 percent by tubular filtration. Hippuran is secreted almost entirely by the tubules. Since the tubular function of the kidneys is usually first to be involved in renal impairment, the use of Hippuran results in a renogram that provides a more sensitive and earlier evaluation of renal impairment, and less time is required for the examination.[3]

The initial stock may be diluted with sterile saline to facilitate handling of small quantities.

Radio-Hippuran I^{131} is supplied by Abbott Laboratories in a sterile solution, each milliliter containing approximately 250 uc I^{131}, and has a specific activity of approximately 500 uc/mg Hippuran. The concentration of Hippuran is approximately 0.5 mg/ml. The solution also contains 0.9% benzyl alcohol as a pre-

servative and sodium cytrate, 2 mg/ml as a stabilizing agent.[7]

Another change in renography is in instrumentation and derives from having a test agent which is not taken up by the liver. Early monitoring probes used for obtaining the renogram had small apertures, with the detecting crystal placed close to the skin over the kidneys. Positioning was accomplished by preliminary abdominal roentgenograms. This had the advantage of using less radioactivity, but it had the marked disadvantage that small differences in kidney position make considerable differences in the obtained curves. Theoretically, the farther the detector from the source of radioactivity, the less difference position changes of the source make. A satisfactory compromise in practice is to withdraw the detecting crystal 6 inches from the skin surface and provide a wide crystal view while maintaining interkidney shielding. The application of this simple principle has greatly improved comparability of kidney function and excretion, as well as reproducibility of results.[13] Commercial apparatus now available.

Positioning

A third change in the technique for renography concerns the position of the patient. Originally the test was done in the sitting position, mainly because of its convenience. However, when the patient is upright, the right kidney usually drops a varying distance, and in some individuals it may be displaced into the pelvis. Many testers now place the patient in the

supine position. In this position, the kidneys have little tendency to relocate. Most of the previous geometric problems have thus been eliminated.[13]

PROS AND CONS OF RENOGRAM

Although side effects have been associated with intravenous administration of large amounts of Hippuran, such reactions are not encountered with the small amount of I^{131} Hippuran employed. The amount of Hippuran which is necessary for performance of a radio-renogram is considerably less than 1 mg.[7]

The radiation dose to the kidney, at the recommended dosage, should be negligible, since the peak concentration of Hippuran occurs in the normal kidney at 2 to 5 minutes after injection. Approximately 71 percent of the injected dose was found in urine collected 30 minutes after injection. The radiation dose to the bladder wall is also low, although precise calculation of the dosage is not possible due to the number of variables involved.[7]

Little Hippuran is taken up by either the liver or thyroid; bile from T-tube drainage in one patient contained only 0.04 percent of the injected dose 20 minutes after injection. The thyroid uptake of I^{131} was measured in two patients at 24 hours. Both had I^{131} uptakes of less than 1 percent.[7] Winter hascalculated that the exposure using diodrast is approximately .001 that of a KUB film.[23]

Nordyke reports that 50 uc gives approximately 0.02 rads to

the bladder wall and much less to the total body and rapid clearance, 65 to 85 percent being excreted in 30 minutes in the normal individual, suggests usefulness in pregnant women and in children.[13]

The dose of Hippuran should be calculated on the basis of body weight. The dosage tends to vary somewhat with the sensitivity of the detecting apparatus, but 0.4 microcurie per kilogram is a convenient dose used by many.[7]

The renogram is a split function test based upon external gamma ray detection of radioactive substances undergoing renal clearance. Other standard split function tests, such as indigo carmine, Howard, phenolsulfonphthalein (PSP), and creatinine clearance, require cystoscopy.

Experimental findings have suggested that reduced urine flow and sodium concentration may be the initial functional abnormalities of a kidney with partial constriction of a main renal artery, and that this may occur without changes in inulin or para-amino hippurate clearances.[1]

Although normal I^{131} renography may rule out unilateral renal disease, an abnormal result with I^{131} may be seen with any lesion resulting in urine flow differences between kidneys.[1]

In over 1,300 renograms reported by Winter, no untoward reaction to the minute amount of contrast medium or radiation effect from the tracer amount of isotope has been encountered.[22] However, one should keep adrenalin and antihistamine nearby in

the event of a sensitivity reaction. Sensitivity testing may also be carried out.

This tracer test provides clinical data of a functional nature which is otherwise obtainable only by excretory urography, or bilateral ureteral catheterization, as well as being a research tool in further investigation in renal physiology on a dynamic basis.

It should not be performed, however, after intravenous urography or tubular cell blocking medications, since these agents would be in competition with the isotope for tubular cell secretion.[22]

Other considerations favoring the use of renography are: The immediate availability of results; it can be used to replace excretory urography in cases where the BUN is elevated; the results are not invalidated by altered metabolic conditions, state of hydration, abdominal opacities, or recent use of radioisotopes for other diagnostic purposes; and the complications of anesthesia or introduction of urinary infections are not encountered.[23] Also, the renogram may be done on an outpatient basis in the hospital.

Disadvantages include the high initial cost of equipment, special training of technician and interpreter, and Atomic Energy Commission approval for the use of isotopes.[22] In reference to the latter disadvantage, it is doubtful that this test

would ever find clinical application in a hospital in which an isotope department does not already exist.

The renogram gives information which is qualitative, not quantitative. Most observers have been unsuccessful in attempts to quantitate results by direct measurement of average amplitude, mathematical determination of the area beneath each curve, and complex calculations of the average slant of various segments of curves.

Much of the difficulty in quantitating the renogram has been due to variables, as (1) the possible inequality of the distance between each kidney and skin surfaces; (2) aberrations in the present complex, sensitive, and as yet crude electronic equipment; (3) reliance upon roentgenographic shadows for the location of kidney positions; and (4) occasional faulty vena puncture technique.[22] A new quantitative approach will be discussed later.

At the present time, reproducibility of a tracing in the same patient is only similar. This may be due to fluctuations in blood volume, isotope dosage (dosage schedule and decay factor), and slight variations in positioning and standardization of equipment from one test to the next.[22]

Most investigators agree that the radioisotope renogram is a safe method of measuring simultaneous separate renal function, but disagree upon its simplicity, since specially trained

personnel, special equipment, and care in interpretation are required. [18, 19]

INTERPRETATION

Qualitative

In the normal renogram after intravenous administration of labeled Hippuran, there is a rapid increase in activity beneath the detecting probe, followed by a slower increase which reaches a peak and then declines. The rapid upstroke represents filling of the vascular space. Its height depends on many variables, including the amount of radioactivity given, the blood volume, the distance and substance between kidney and crystal, and the amount of blood in both the kidney and extrarenal areas detected by the crystal. Little emphasis is placed on its height.[13]

The slower increase phase represents uptake of activity by the kidney and is a result of both tubular function and renal blood flow. Inasmuch as Hippuran in trace amounts is extracted from the blood almost completely with each pass through the kidney, the slope of the curve would seem to depend mainly on kidney arterial flow.[13]

The declining curve represents excretion from the kidney area, which includes the kidney and the pelvis.[13]

The neophyte investigator will have difficulty interpreting his results until he acquires experience. In most studies, a single interpreter has been used to maintain uniformity in inter-

pretation; even then, a significant number of errors have been made, usually reporting of false-positives generally thought to be due to over-interpretation of borderline curves.

The following are some typical patterns which will be found.

BILATERALLY DECREASED KIDNEY FUNCTION

Kidney dysfunction such as is present in moderately severe hypertension or in chronic glomerulonephritis is reflected as a decrease in the second phase; that is, a slower rate of rise after the initial filling; also, decreased "function," with a correspondingly decreased excretion rate.[13]

UNILATERALLY DECREASED KIDNEY FUNCTION

Decreased function on one side.

UNILATERALLY ABSENT KIDNEY OR NON-FUNCTIONING KIDNEY

Very little radioactivity on that side. Some activity will be reflected by the vasculature in that area remaining and some due to incompleteness of the interkidney shielding. There will be a low initial vascular segment, an absent secretory segment, and a slowly falling excretory segment.

URETERAL OBSTRUCTION

Obstruction of the urinary outflow tract above the bladder level usually results in a rising curve on the obstructed side which is approximately equal to the blood disappearance curve. Prolonged obstruction, or obstruction which occurs in a kidney with decreased function, may produce a relatively flat curve.[13]

ACUTE PYELONEPHRITIS

Diagnostic features of the curve obtained in acute pyelonephritis include a flattened prolongation of the secretory segment and a decrease in the slope of the excretory segment for the involved kidney.[21] Improvement usually is followed by a return to a normal renogram.

NEPHROSCLEROSIS

In nephrosclerosis, the renogram quite consistently shows a diminished initial vascular spike, a decrease or absence of the secretory segment, and an abnormal excretory segment.[18]

Analysis of renograms from patients with various forms of nephritis show that the steepness of the excretory lag depends primarily on adequate renal tubular cell function and is modified secondarily by obstructive processes which decrease the rates at which the test substance leaves the kidney areas.[21]

In interpretation, one must be especially careful in respect to the excretory segment and its relation to the secretory segment. Unless there is a distinct secretory lag in the renogram indicating active tubular cell function, a slowly falling excretory lag does not necessarily indicate partial obstruction in the upper urinary passages. However, if there is no neurogenic uropathy and the patient has good tubular function, a diagnosis of upper urinary tract obstruction or stasis may be made. Conversely, a renogram with all three segments in the normal range

strongly indicates the absence of upper urinary tract obstruction or stasis, and also confirms the presence of normal renal vascularity and tubular cell function.[21]

NEPHROTIC SYNDROME

In the nephrotic syndrome, a decrease in the amplitude of the vascular segment, a prolonged secretory segment, and shallow slopes in the excretory segment which parallel the rate of blood clearance are usually seen. These findings suggest diminished renal blood supply and impairment of tubular cell secretion.[21]

CHRONIC GLOMERULONEPHRITIS

The pattern shows decreased amplitude of the initial vascular segment. The tubular secretion segments are prolonged, and the slopes in the excretory segment are decreased.[21]

HYDRONEPHROSIS

The initial vascular segment is usually definitely low, probably caused by a reduction in the amount of renal parenchyma and by an associated impairment of renal vascularity. The secretory segment is prolonged due to impairment of tubular cell function and delayed outflow of urine from the pelvis. The downward slope which is usually present appears to indicate the degree of ureteral patency.[21]

ACUTE URETERAL OBSTRUCTION (CALCULUS)

The initial vascular segment is usually somewhat low, probably due to associated circulatory depression. The secretory segment

of the curve continues to rise as the radioactive material accumulates in the renal tubules and pelvis and finally reaches a plateau. The excretory segment is absent. If the obstruction is only partial, the excretory segment will be prolonged, indicating the degree of ureteral patency.[21]

The excretion segment of the renal curve is similar to (but not as rapid as) the decline in the blood level. As the rate of urinary excretion exceeds that of renal uptake from the blood, the process of clearance from the kidney areas becomes manifest.

QUANTITATIVE ANALYSIS

Stewart and Haynie in their study found great difficulty with interpretation of renograms on a qualitative basis, especially in readings of equivocal or suggestion of unilateral renal disease, and thus reported a 45 percent false-positive rate in patients subsequently shown to have normal renal arteries by arteriographic and ureteral catheterization studies. An overall false-negative rate of 25 percent was also found in patients proven at operation to have correctible renal ischemia. The following is a summary of their attempt to better quantitate the renogram by accurate measurement of the various parameters in each tracing.[19]

They found that the height and angle of the initial rise in count rate (vascular spike) did not correlate well with the degree of renal arterial occlusion found at operation. Patients

with obstructive lesions of the left renal artery often had high vascular spikes on the left, possibly due to the close proximity of the splenic artery to the left renal pedicle. There was, likewise, great variability in the height and angle of the initial rise in count rate in patients subsequently found not to have occlusive renal vascular disease. The height of maximum count rate was also evaluated and also did not correlate well with the presence or absence of renal ischemic lesions.

Any disease that decreases renal function can decrease the height of maximum uptake, and measurement of this parameter does not effectively differentiate patients with renal arterial occlusion from those with chronic pyelonephritis, nephrosclerosis, or other non-ischemic conditions. There was wide variation in height of maximum uptake in patients without evidence of unilateral disease.

They report that maximum diagnostic accuracy can be obtained by measuring only two parameters: The time from point of injection to the point of maximum count rate (T max), and the time from the point of maximum count rate to the point where the count rate has fallen to one-half the maximum count rate (T 1/2).

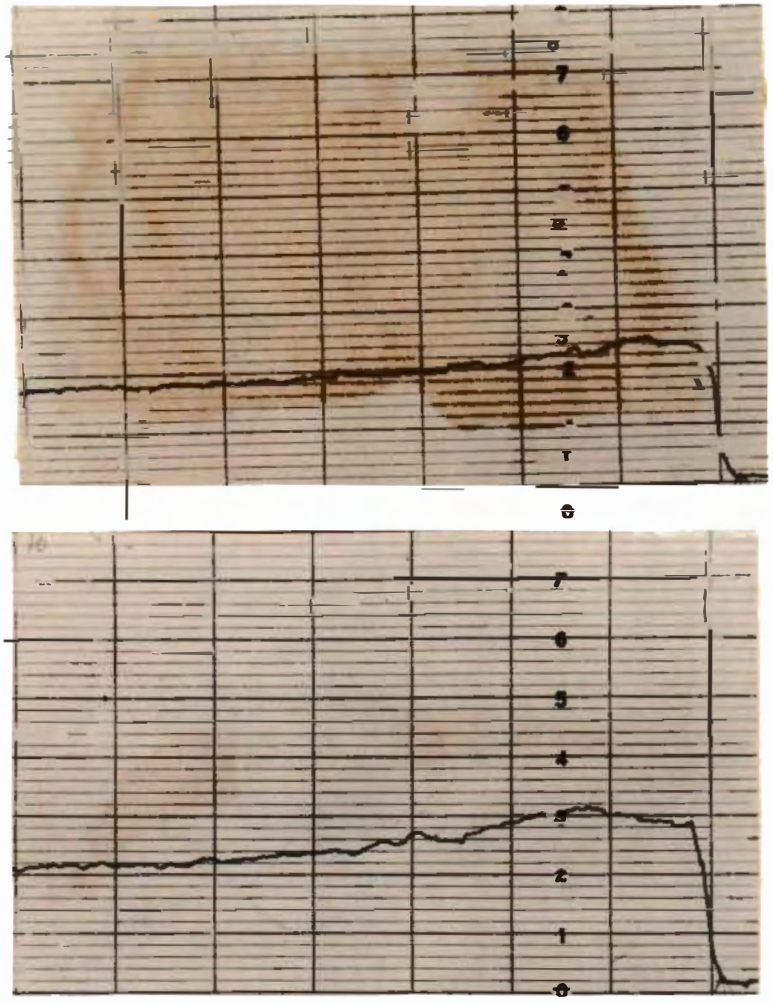
After using this method, the number of false-negative readings remained about the same (25%), while the number of false-positive interpretations was reduced materially (from 45% to 27%) when this quantitative method was used.

The addition of other parameters, such as height and angle, of initial rise in count rate, height of maximum count rate, and count rate at 15 minutes after injection did not increase the percentage of diagnostic tracings, and actually resulted in a higher percentage of false-positive renograms.

Figure 1, below, shows the normal values used in interpretation on a quantitative basis. These values were arrived at after a study of nine patients without hypertension or renal disease.

	RIGHT	LEFT
T max	2.5- 7.2 min.	2.7- 8.7 min.
T 1/2	4.4-21.3 min.	3.2-15.9 min.

Fig. 1. Normal values for parameters in quantitative Hippuran renogram interpretation.



Left

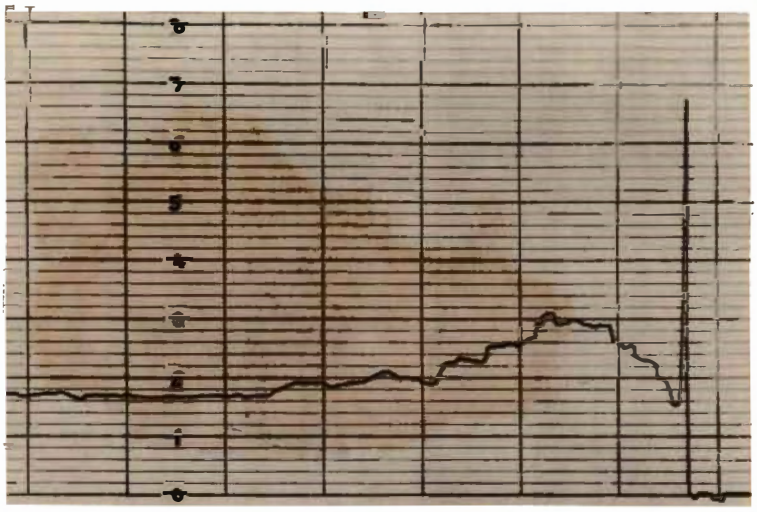
Dose: 9.5 uc I^{131} Hippuran
cpm Range: 10 K
Time Constant: 10
Rate: 1/2" = 3.75 min.

Right

Fig. 2. Forty year old, white, diabetic, hypertensive (B.P. 184/120), female. IVP revealed no anatomical abnormality, but showed poor function bilaterally. Patient has had BUN up to 54 mg % and serum uric acids to 9.95 mg %.

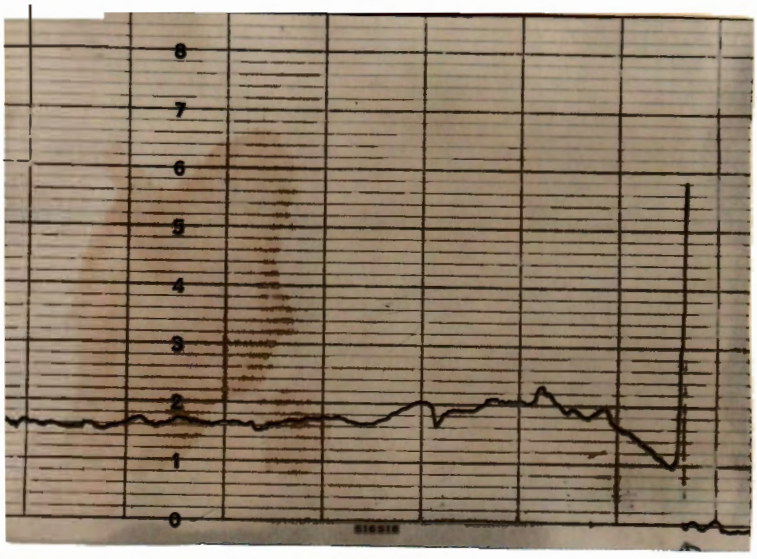
Renogram shows low initial vascular phase, decreased secretory phase, and a prolonged excretory phase, interpreted as decreased function bilaterally, and consistent with chronic glomerulonephritis, moderately severe hypertension, or nephrosclerotic syndrome.

Quantitative interpretation reveals normal T max (left 3.75 min. and right 5 min.), but a prolonged T 1/2, test not carried out to point of T 1/2.



Left

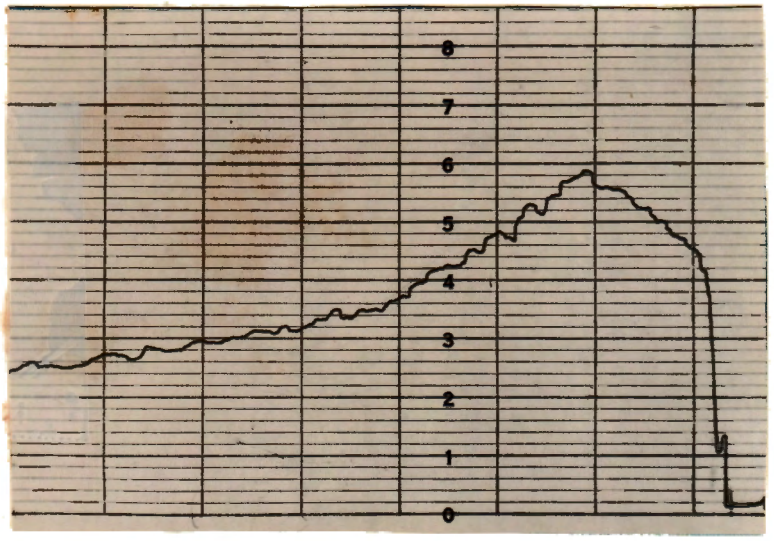
Dose: 5.1 uc I^{131} Hippuran
cpm Range: 30 to 10 K
Time Constant: 10
Rate: 1/2" = 3.75 min.



Right

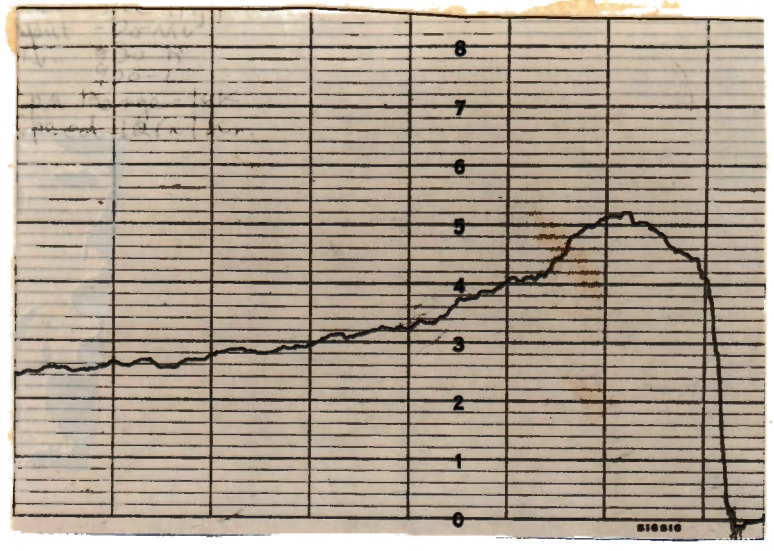
Fig. 3. Fifty-seven year old, white, male, with chief complaint of difficulty in voiding. Retrograde urography revealed 3-4 mm smoothly outlined mass in the upper portion of the left kidney and showing compression of the superior calices, interpreted as a possible cyst or tumor. Cystoscopic examination was negative. At operation a benign cyst of the left kidney was drained and incised.

Renogram shows only borderline diminution in the secretory phase on the right.



Left

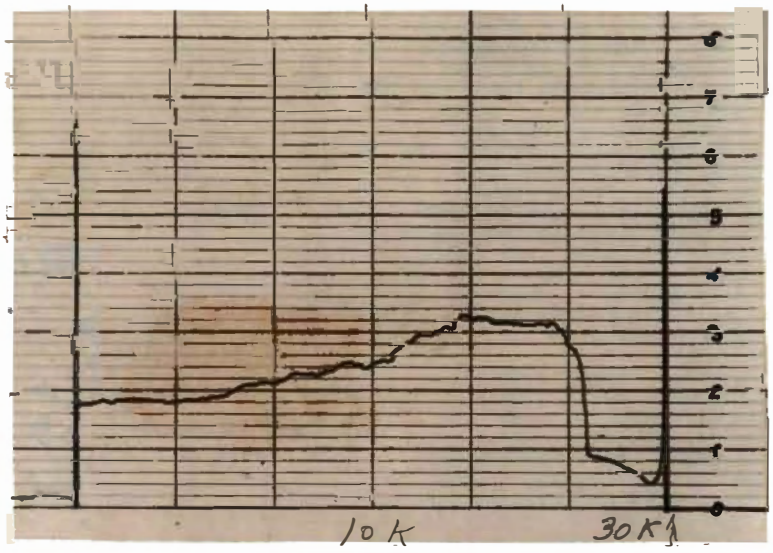
Dose: 10.1 uc I^{131} Hippuran
cpm Range: 10 K
Time Constant: 10
Rate: 1/2" = 3.75 min.



Right

Fig. 4. Fifty-nine year old, white, female, hypertensive. IVP interpreted as being within normal limits for kidneys and ureters but with a questionable filling defect in the right bladder base possibly representing a tumor mass. Cystoscopic exam was negative.

Renogram shows good function of vascular, secretory, and excretory segments. Quantitative analysis (T max rt. 3.75 min., left 5.6 min., and T 1/2 rt. 20, left 18.7 min.) shows slowness in excretion bilaterally.



Left

Dose: 7.1 uc I^{131} Hippuran
cpm Range: 30 to 10 K
Time Constant: 10
Rate: 1/2" = 3.75 min.

Right

Fig. 5. Sixty year old, white, female, with acromegaly for 30 years and hypertensive for 15-20 years. IVP showed a 15 x 11 mm. opacity in the region of the lower pole of the right kidney and another 8 x 9 mm. opacity in the true pelvis. There was prompt excretion of the dye, with good delineation of the collecting systems bilaterally. The collecting systems were somewhat irregular, with blunting of the calices, particularly on the right. The ureters were not well visualized, and the bladder was normal in appearance.

The renogram shows a low and slow responding vascular phase bilaterally. The secretory phase is somewhat decreased on the left. Excretory phases show good excretion.

Quantitative analysis is within normal limits.

RENAL SPLIT FUNCTION TESTS

The advent of aortography and renal angiography led to the recognition of occlusive lesions of renal arteries as causes of onset or exacerbation of hypertension. The proportion of patients having such lesions is not known and may be between 1 and 5 percent. The condition is, therefore, much more common than pheochromocytoma (which issso diligently sought for by the internists), and is usually at least as remediable.[7]

Lesions may affect main or branch (segmental) arteries and may be unilateral or bilateral; they range from atheromatous plaques or emboli to fibrous hyperplasia. One more-or-less characteristic syndrome has been defined; this is hypertension in early youth, with bilateral orificial stenosis by fibrous cushions of both main renal arteries and, usually, some degree of coarctation of the abdominal aorta. Much more common are patients, often with pre-existing hypertension, who suddenly develop hypertension or an exacerbation thereof, as the result of atheromatous occlusion, sometimes with a history of recent flank pain, and occasionally presenting murmurs or thrills over the loins. Changes in intravenous urograms may not be recognizable; the radioisotope renogram has, perhaps, its best usefulness in screening such patients for subsequent anatomical diagnosis by aortography.[17]

Description of the Howard test suggested the possibility of

a simple diagnostic and prognostic procedure. In principle, this consists in demonstrating that ureteral urine from one side has a considerably lower volume and sodium content (and higher osmolality) than urine from the other. For reasons outlined above, such a change occurs when there is partial occlusion of one main renal artery; hypertension due to this cause can be cured by appropriate surgical means. However, Corcoran reports that lesions of main arteries are often bilateral, in which case the more affected side gives the positive test. Again, the lesion may be in a branch artery; depending on the mass of kidney affected, there results some depression of functions such as plasma flow and filtration rate, but without noteworthy differences in sodium concentrations or osmolality, so that the functional pattern resembles that found in many patients with chronic pyelonephritis and is not diagnostic.[17]

In experimental work with the Howard test, decrease in urine volume and sodium excretion occurred before inulin or hippurate clearances were measurably altered. Connor and his co-workers demonstrated a good postoperative result in a series of cases in which both a lowered urine volume and sodium excretion were found unilaterally. Criticism of the test has centered primarily on possible disturbance of function attendant to catheterization of the ureters; i.e., reflex influence on filtration mechanisms. The possible loss of urine around the catheters is

an additional objection to this procedure.[8]

Aortography, developed in recent years, is useful in demonstrating occlusions of the major renal arteries and ischemic areas in the kidney parenchyma. It enables the recognition of hypertension due to unilateral renal ischemia which was not demonstrable by pyelographic or renal function studies in some instances. The rather high incidence of morbidity and a significant rate of mortality associated with aortographs precludes its use as a routine procedure in the evaluation of hypertension. Campbell has collected at least 100 cases from the world literature in which death was directly attributable to the procedure of aortography.[8]

In a report by Cobb, a study of 214 renograms on 172 patients was carried out. Positive correlation with clinical impression and other renal function tests in 150 (87%) of the 172 patients was found. The negative correlation for 22 (13%) was largely the result of improper placement of scintillation probes and he thought that much of this error could be eliminated by good x-ray localization in the upright position.[3]

Included in this group of negative correlation were 2 cases of miscalculated dosage; 2 cases of marked renal ptosis; 1 case with a back brace; 2 cases in which the patient's cooperation was lacking; and 2 possible cases of error in interpretation of borderline curves.[3]

In most of the cases with negative correlation, the renogram demonstrated apparent abnormality which could not be confirmed by other available function studies. His appraisal of these differences was the question of possible over-interpretation of borderline curves.[3]

In a series of 214 patients studied by Winter, who were divided into three groups according to the results, he found: (1) Unilateral abnormal renograms in 56; (2) bilateral abnormal renograms in 96; and (3) bilateral normal renograms in 62. Abnormalities were described as decreased vascularity, decreased function, or delayed drainage.[22]

A comparison of the renogram with the resultant renal evaluation from all individual kidney tests showed the former to be in agreement among 85 percent of group 1. Five false-negative right renograms and two false-positive left renograms occurred with diodrast. One of the latter was also duplicated with hypaque. This compared favorably with the individual renal clearance test results (creatinine, 83%; inulin, 88%; PAH, 80%) and dye excretion tests (PSP 90% and indigo carmine, 83%).[22]

In a study reported by Poker, Becker, and Evans of 234 renograms in 190 patients, the findings agreed with conventional tests in 79.7 percent of cases.[15]

They suggested that in only a small minority of cases, the renogram may reveal important abnormalities now shown by intra-

venous pyelography, 12 percent of cases falling into this category in their study. In 18 of the patients in the 25 instances of discrepancy restudied by the same methods, and in only 3 of these (2.4% of the 123) did it appear likely that the exam with radiodiodrast revealed an abnormality not found by intravenous pyelography.[15]

In 9 percent of cases, it appeared that renography failed to reveal an abnormality which the method could reasonably be expected to demonstrate and which intravenous pyelography did reveal. Intravenous pyelography also disclosed several abnormalities that radiorenography cannot be expected to show; i.e., calculi, vesical neoplasm, tuberculosis, or malrotation of the kidney.[15]

They felt that from the practical point of view, the equipment for the radiodiodrast studies was relatively expensive and demanded considerable technical proficiency and time, each test requiring 20 to 30 minutes, approximately the same amount of time required for intravenous pyelography.[15]

One of the reports having the largest percentage of negative correlation is the following study by Stewart and Haynie in which renography was performed on 64 patients with suspected renal hypertension. They reported 45 percent false-positive and 25 percent false-negative results, which they attributed to an inadequacy of the presently-used method of interpretation. Their

results were brought into range of other investigators after applying a quantitative method to interpretation.[19]

Renography at its present stage finds, perhaps, its greatest value in following patients on whom renal revascularization procedures have been performed. It has been suggested that routine postoperative renal arteriography and ureteral catheterization studies be done in these patients. However, it is difficult to justify these potentially dangerous procedures in patients who are normotensive and asymptomatic after operation. Postoperative renograms can be obtained at frequent intervals in these cases without risk of toxicity or undue radiation exposure. Experience at present indicates that renal circulation is adequate in the patient who remains normotensive and continues to have normal radioisotope renograms after a revascularization procedure. If the renograms show a persistent or progressive abnormality after revascularization, then the patient should be watched more closely, and further studies should be seriously considered.

SUMMARY

The radioisotope renogram is a split-function kidney test which has had a limited clinical use for the past six years. It depends upon external gamma ray detection after intravenously administered I^{131} tagged substances, as they are incorporated into the vascular system, are cleared by the kidneys and excreted.

Originally it was proposed for the detection of unilateral kidney disease in hypertensive patients and the selection of these patients for surgery.[19]

Many difficulties have been encountered in its clinical application, some being eliminated or improved, such as the choice of test material and positioning of the patient, but many remain, including difficulty in the interpretation of borderline curves and the lack of accurate reproducibility.

While results of studies have been encouraging, it would seem premature to compare the radioisotope renogram with other techniques for determining individual kidney function until the intrinsic reproducibility and sensitivity of the renogram have reached a satisfactory level. Nor is it suggested that the renogram will replace standard renal function tests, split-function studies, pyelography, or aortography. Rather, it is suggested that the renogram is helpful in the confirmation of results of other function studies, in screening patients who might need more complex evaluation, and in following the clinical course of patients with known renal disease with respect to progression or improvement in renal function.

CONCLUSION

(1) The radioisotope renogram is a simple, safe, relatively atraumatic test to perform.

(2) The renogram can give useful information on a sufficient

number of patients to warrant its use.

(3) The cost of equipment and the training of technicians is not prohibitive for general hospital use.

(4) Because of the lack of reproducibility in tracings and some difficulty in interpretation, it is not suitable as a screening test when used alone at the present time.

(5) The renogram now finds its best application when used in conjunction with other split-function tests and in the post-operative follow-up of patients after revascularization procedures.

(6) Further improvements in technique and interpretation may widen the scope of usefulness of the renogram in the future.

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