CLINICAL APPLICATIONS OF COMPUTER-ASSISTED RENOGRAPHY

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Radioisotopes were first used to assess kidney function by external scintillation counting in 1955. After preliminary observations in rabbits which looked promising, Taplin and his colleagues tried ^{131}I-Urokon in man (*1*). They were initially disheartened by the "monotonous, noncharacteristic records regardless of renal status" that they obtained (*2*). Iodopyracet (Diodrast) was much more successful, but it was another 5 years before Tubis and Nordyke introduced radioactive orthoiodohippurate or ^{131}I-Hippuran in 1960 (*3*).

Since then ^{131}I-Hippuran has become the tracer of choice for renography. It is handled much like para-amino hippuric acid and is almost exclusively and very rapidly excreted by the kidneys so that 92% of unbound ^{131}I-Hippuran is cleared from the plasma in a single passage through the normal kidney (*4,5*).

After intravenous injection ^{131}I-Hippuran, which is partially protein bound (*6*), spreads throughout the vascular space, starts to exchange with the extravascular space, and is removed from the circulation, partly by glomerular filtration but mostly by tubular secretion. After traversing the renal tubules, collecting ducts, and renal pelvis, the ^{131}I-Hippuran passes down the ureters to the bladder. The renogram is a composite trace of the changing quantity of radioactivity in the nephrons, in the renal pelvis, in the blood within the kidney, and also in the tissues around the kidney that are viewed by the external detector. The activity in the blood and tissues around the kidney makes up a considerable part of a renogram and as the function of a kidney becomes impaired, this blood and tissue background activity accounts for an even larger proportion of the tracing so that interpretation becomes increasingly difficult.

If blood clearance is monitored by a third detector placed over the upper mediastinum, an indication of overall renal function is obtained and furthermore the shape of the mediastinal clearance curve can be compared to the renogram tracings to give an indication of what is happening to Hippuran in a poorly functioning kidney. For instance, if the renogram curve falls less rapidly than the mediastinal clearance curve, Hippuran is accumulating in the kidney.

Several investigators have used ^{131}I-iodinated human serum albumin (^{131}I-IHSA) to measure renal and extra-renal vascular background activity (*7,8*) and in 1966 Hall and Monks described a method of correcting renogram tracings for this blood background activity by giving ^{131}I-IHSA before the ^{131}I-Hippuran (*9*). Britton and Brown adapted this method by using a digital computer to subtract the blood background activity—a technique called Computer-Assisted Blood Background Subtraction Renography (CABBS Renography) (*10*). The technique employed at University College Hospital is based on the method developed by Britton and Brown. This paper describes our experience with computer-assisted renography in more than 100 patients, indicates its relation to other tests of renal function, and outlines areas in which it is clinically useful.

METHODS

The majority of patients in this study were referred for radioisotopic assessment of individual kidney function during the investigation of either hypertension, chronic pyelonephritis, or an obstructive uropathy. With the exception of a few patients with a history of allergy to contrast media, each patient had an intravenous pyelogram. Arteriograms and

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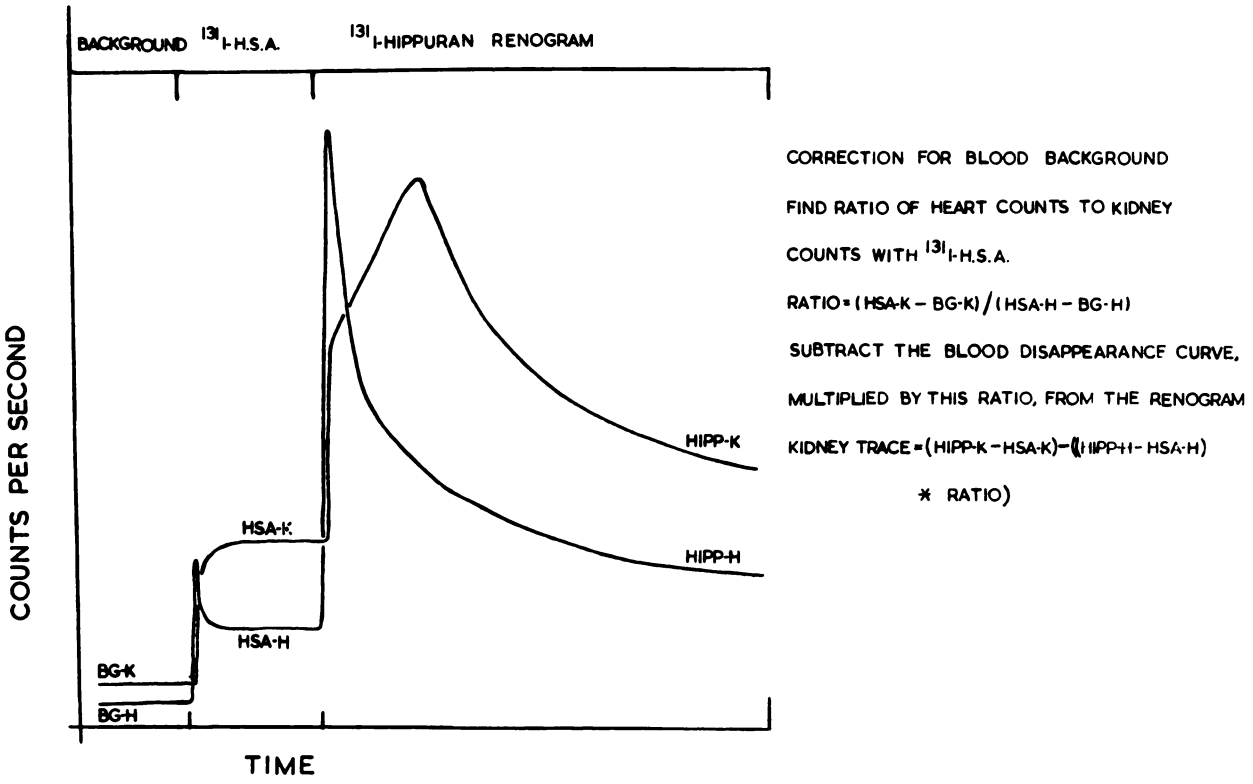


FIG. 1. Method of correcting for "blood background." Tracings from mediastinal detector and one kidney detector are shown. BG-H and BG-K represent background counts; HSA-H and HSA-K represent counts due to radioactive human serum albumin; and HIPP-H and HIPP-K represent counts due to ^{131}I-Hippuran over mediastinum (-H) and kidney (-K), respectively.

retrograde pyelograms were performed when clinically indicated.

Radioisotope renography and kidney scanning were undertaken on the same day, or within 48 hr of each other in all but one patient, and were always performed within 6 hr in the patients with acute obstruction to the outflow of urine, if they had both studies.

The patient lies supine on a couch with a perspex window beneath the renal areas. Matched detectors [Nuclear Enterprises 1¾-in. Na(Tl) crystals with wide-angled collimators] viewed each kidney from beneath the perspex window and a third detector is placed anteriorly over the upper mediastinum.

The kidneys are located from an injection of 2–4 μCi of ^{197}Hg-chlormerodrin given 45 min or more beforehand.

The pulses from the detectors after suitable amplification and pulse-height analysis are fed into ratemeters and scalers (Harwell 2000 series). The ratemeters drive a Honeywell chart recorder, while the scalers are read every 10 sec and reset to zero by a Data Dynamics high-speed punch producing paper tape.

For the renogram, background counts are recorded for at least 100 sec. The patient is then given 5 μCi ^{131}I-IHSA intravenously and the counts from each detector recorded for 6 min; this is followed by ^{131}I-Hippuran (1 μCi/7 kg) and the renogram recorded for 16–20 min. This whole procedure takes up to 30 min. The data tape is then processed on the University of London Atlas Computer.

In addition to renography, most of the patients studied (90/109) had kidney scans following ^{197}Hg-chlormerodrin (1 μCi/kg body weight) as described previously (*11*). The scans were made on either a 3-in. or 5-in. Picker Magnascanner. With the scans performed on the 3-in. scanner, the relative amount of radioactivity within each kidney was determined either by counting the dots on the color scans or else using a slit collimator, and expressing the counts in one kidney as a percentage of the total counts in both kidneys. Fifteen patients also had renograms repeated while seated in front of a gamma camera (Nuclear Enterprises, Mark III). The kidneys were located from the ^{197}Hg-chlormerodrin given for scanning, and then each patient was given up to 150 μCi ^{131}I-Hippuran and pictures were taken every 2½ min for 15–20 min.

Estimations of blood urea and 24-hr creatinine clearance were carried out by Technicon Autoanalyzers in the hospital's biochemistry laboratory.

Outline of computer program. The data tape consists of background counts, ^{131}I-IHSA counts and ^{131}I-Hippuran plus ^{131}I-IHSA counts from the three channels (right kidney, left kidney, and mediastinum) accumulated at 10-sec intervals. After reading in the data and storing the ^{131}I-IHSA counts and ^{131}I-Hippuran plus ^{131}I-IHSA counts from each channel in separate arrays, the mean background counts per 10 sec are determined for each channel and subtracted from the corresponding ^{131}I-IHSA and ^{131}I-Hippuran plus ^{131}I-IHSA arrays. Smoothing of the counts is carried out by a running average over 30-sec intervals, preserving the peak of the mediastinal clearance curve.

The last 2 min of the ^{131}I-IHSA counts in each channel are used to determine the ratio of the counts over the mediastinum to those over each kidney so that for any given level of activity within the blood stream in the mediastinum, the level of activity in the blood stream within the field of view of each kidney detector can be determined.

The mean ^{131}I-IHSA counts per 10 sec in each channel over this same 2 min are subtracted from the corresponding ^{131}I-Hippuran plus ^{131}I-IHSA array to give the activity-time curve of ^{131}I-Hippuran alone as seen by each detector.

For the blood and tissue background correction each point of the mediastinal clearance curve is multiplied by the ratio for each kidney and subtracted from the corresponding point of the renogram to give the computer-corrected renogram or kidney trace (Fig. 1). Although ^{131}I-Hippuran is almost exclusively and rapidly excreted by the kidneys, the blood clearance curve represents both the removal of Hippuran by the kidneys and in addition its spread into the extravascular space. In contrast the clearance curve recorded by the mediastinal detector represents the blood clearance curve modified by the extravascular spread of ^{131}I-Hippuran that takes place into the tissues in the field of view of this detector. We have assumed that this "mediastinal clearance" curve more accurately reflects the rate at which Hippuran enters the kidneys than the blood clearance curve.

In order to determine the outflow of ^{131}I-Hippuran from each kidney the integral of the mediastinal

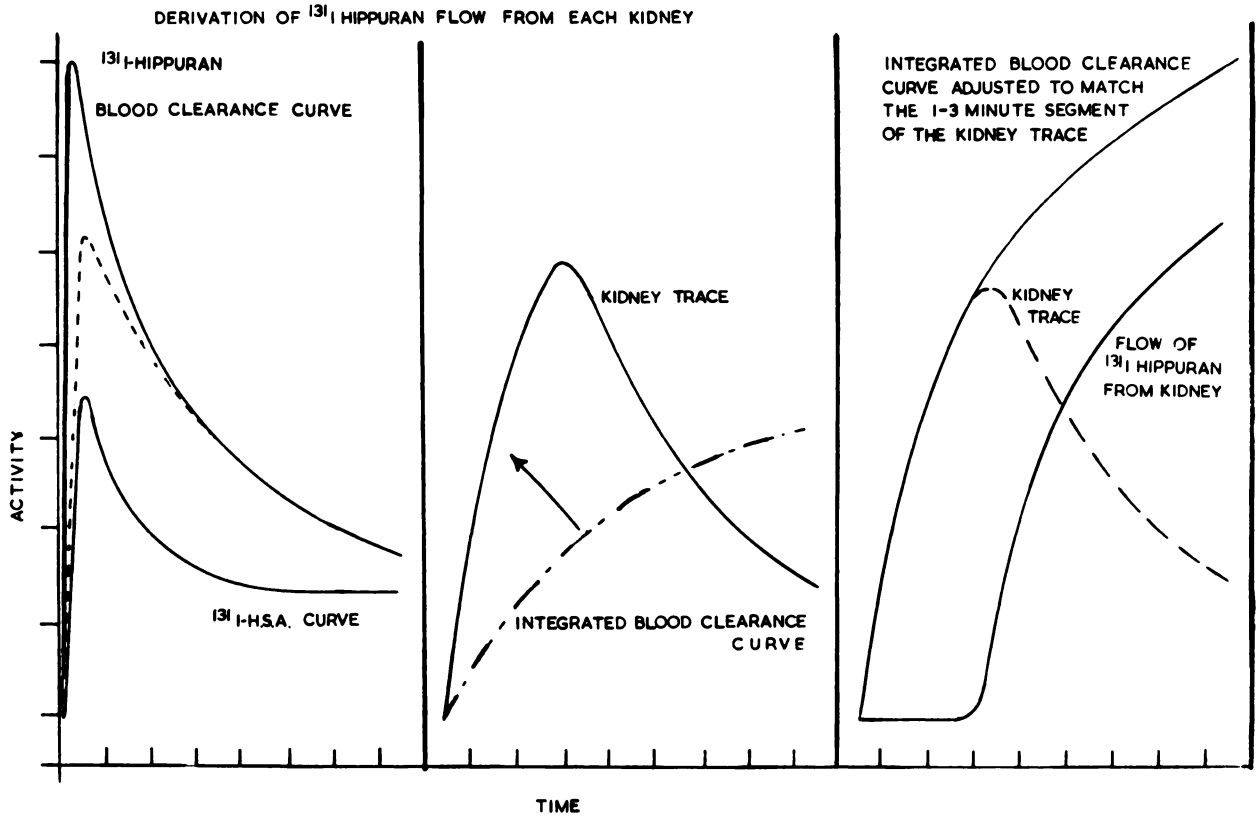


FIG. 2. Method of correcting for initial dilution of ^{131}I-Hippuran throughout vascular compartment and calculating outflow of ^{131}I-Hippuran. In left panel ^{131}I-Hippuran mediastinal clearance curve has been superimposed over the ^{131}I-IHSA curve for first 6 min after injection. ^{131}I-Hippuran curve is adjusted by ratios by which 0–4-min ^{131}I-IHSA curve differs from 4–6-min portion. Corrected clearance curve is dashed lines. Center panel shows integrated mediastinal clearance curve and kidney trace. Integrated clearance curve is adjusted to match 1–3-min segment of kidney trace by multiplying this part of curve by factor which gives best fit determined by least squares. Right shows outflow of ^{131}I-Hippuran obtained by subtracting kidney from matched integrated clearance curve.

clearance curve is matched to the initial portion of each kidney trace from 1 min and 20 sec to 3 min (or the peak of the curve if this is sooner) using the method of least squares to obtain the best fit. The initial peak on the mediastinal clearance curve has to be adjusted to allow for the dilution of Hippuran throughout the vascular compartment and also for its early extravascular spread. The factors used for this adjustment are determined in part from the way in which the ^{131}I-IHSA spreads throughout the vascular compartment during the first 4 min after injection as recorded by the mediastinal detector. Each kidney trace is then subtracted from the corresponding integrated curve to give the outflow of ^{131}I-Hippuran from each kidney (Fig. 2).

The kidney traces are then compared in several ways to determine the relative contribution of each kidney to overall renal function. The area under each curve to the first peak (or to 3 min if the peak is delayed) is determined and the figures for each kidney expressed as a percentage of the total. The relative outflow of ^{131}I-Hippuran is determined by comparing the areas under the ^{131}I-Hippuran outflow curves up to 15 min after the injection.

The "efficiency" with which each kidney transports ^{131}I-Hippuran through its tubules and renal pelvis is determined by comparing the amount of ^{131}I-Hippuran that leaves each kidney for 10 min after flow starts with that which enters during the first 10 min after injection.

The program also determines the time to peak height, the difference between the peak heights of the kidney traces, as well as the percentage fall in the mediastinal clearance curve between 2 and 15 min after the injection of ^{131}I-Hippuran.

RESULTS

Computer-assisted renography has been carried out on 109 patients. These have been divided into several broad groups on the basis of their clinical and radiological findings as shown in Table 1. A normal renogram, kidney trace, integrated clearance curve, and outflow of ^{131}I-Hippuran are shown in Fig. 3.

Estimations of relative function. The relative function of each kidney determined from the areas under the kidney traces to the first peak (or to 3 min after injection if there was delay in reaching the peak) has been compared to the relative function derived from the rectilinear scans. Scans from patients with acute ureteric obstruction and also scans which showed excess hepatic activity have been excluded from this comparison. There is a highly significant correlation between these two methods of estimating the relative contributions of each kidney, $r = 0.96$, $p < 0.001$ (Fig. 4).

In acute obstruction the kidney trace gives a higher figure for relative function than is obtained from the scan, but when the obstruction is chronic the two estimates agree more closely (Table 2).

In the patients with no radiological evidence of back pressure atrophy or obstruction to the outflow of urine or polycystic disease of the kidneys, the relative function determined from the kidney trace has been compared to the relative outflow of ^{131}I-Hippuran derived by the program. There is a highly significant correlation between these methods of estimating relative function, $r = 0.976$, $p < 0.001$ (Fig. 5).

Reproducibility of the estimates of relative renal function. Ten patients, eight of whom had some form of chronic partial obstruction to the outflow of

TABLE 1. COMPUTER-ASSISTED RENOGRAPHY DIAGNOSTIC GROUPS

Diagnostic group	Clinical findings	Computer-assisted renograms		Scans
Normal	Kidneys less than 1 cm difference in length with smooth outline and normal pelvicalycine pattern. Creatinine clearance > 90 ml/min. Diastolic blood pressure < 95 mmHg.		14	10
Hypertension	Kidneys with smooth outline and normal pelvicalycine pattern. Diastolic blood pressure > 95 mmHg.		21	20
Chronic pyelonephritis	Clubbed calcyes with overlying scarred cortex.		9	9
Ureteric calculi	Partially or completely obstructing ureter.		8	7
Backpressure atrophy	Pelvi-ureteric junction obstruction.	17		
	Ureteric strictures (benign and malignant) and postobstructive atrophy.	12	29	23
Polycystic kidneys			7	7
Renal failure	Blood urea greater than 150 mg%. Creatinine clearance less than 20 ml/min.		8	2
Others			13	12
	TOTAL		109	90

urine, were studied on a second occasion. In two, repair of the pelviureteric junction was carried out between the studies. The difference between these paired estimations of the relative renal function of the clinically affected kidney ranged from 0.8 to 8.1%, with a mean of 3.36% (±0.79 s.e. mean). In the two patients who underwent surgery the differences were 0.8% and 3.3% indicating that surgery had not improved the function of the affected kidney.

Transport efficiency. The efficiency with which the kidneys transport ^{131}I-Hippuran through the tubules, collecting ducts, and renal pelvis is shown in Tables 3 and 4.

The mean efficiency of the normal group is significantly greater than that of the hypertensive group, which in turn is significantly greater than that of the polycystic group. The mean blood urea of each of these groups is also significantly different and is inversely related to their mean efficiency.

In the patients with radiological evidence of chronic pyelonephritis the mean efficiency of the radiologically affected kidneys is significantly less than the unaffected ones. The unaffected kidneys are also significantly different from the normal group but not the hypertensive group. Seven of these nine patients had hypertension, and the mean blood urea

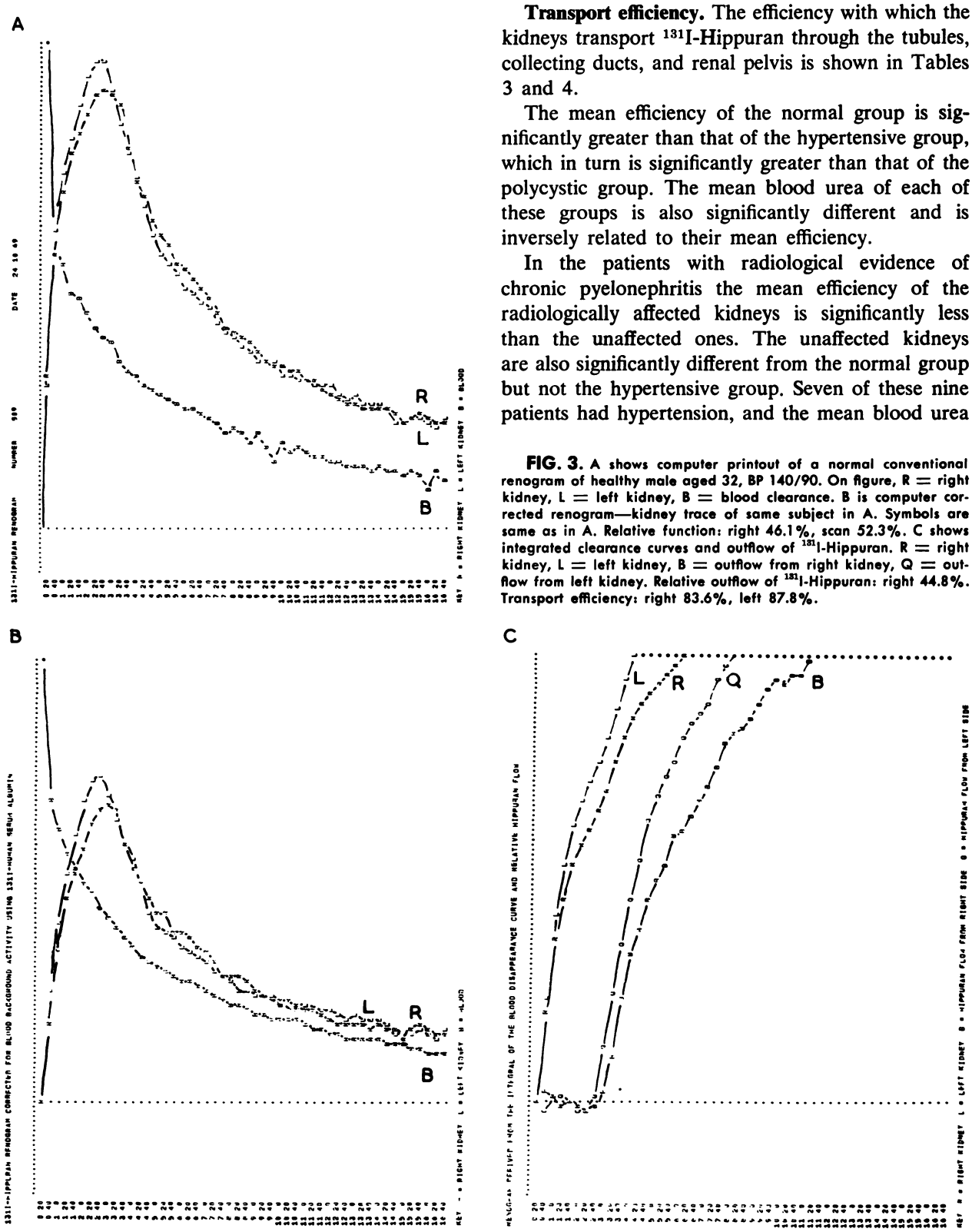


FIG. 3. A shows computer printout of a normal conventional renogram of healthy male aged 32, BP 140/90. On figure, R = right kidney, L = left kidney, B = blood clearance. B is computer corrected renogram—kidney trace of same subject in A. Symbols are same as in A. Relative function: right 46.1%, scan 52.3%. C shows integrated clearance curves and outflow of ^{131}I-Hippuran. R = right kidney, L = left kidney, B = outflow from right kidney, Q = outflow from left kidney. Relative outflow of ^{131}I-Hippuran: right 44.8%. Transport efficiency: right 83.6%, left 87.8%.

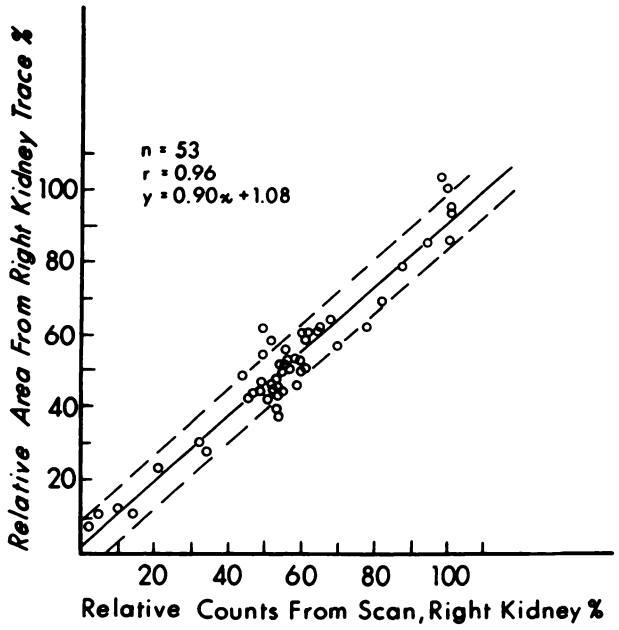


FIG. 4. Relative function of right kidney derived from kidney traces compared to that derived from rectilinear scans in 53 patients.

TABLE 2. RELATIVE FUNCTION OF AFFECTED KIDNEY, %

		Kidney trace	Scan	Difference
Acute obstruction	Cal	38.0	28.0	−10.0
	Cal	31.8	15.8	−16.0
	Cal	33.0	23.9	− 9.1
	PUJ	31.3	0.0	−31.3
Mean		33.5	16.9	−16.6
Chronic obstruction	Cal	19.0	24.3	+ 5.3
	Cal	20.9	17.5	− 3.4
	PUJ	23.7	20.4	− 3.3
	PUJ	39.5	40.0	+ 0.5
	US	30.0	32.7	+ 2.7
	PUJ	39.5	37.8	− 1.7
Mean		28.76	28.78	+ 0.02

Cal = Ureteric calculus, PUJ = Pelvi-ureteric junction obstruction, US = Ureteric stricture.

of this group is not significantly different from that of the other hypertensive patients.

As would be expected in the patients with back pressure atrophy from all causes, the mean efficiency of the kidneys giving rise to symptoms is markedly reduced and significantly less than the contralateral kidney. However, these contralateral kidneys also have a reduced efficiency, which is significantly less than the efficiency of either the normal or hypertensive groups, and one third of these kidneys also had radiological evidence of minor degrees of obstruction to the outflow of urine. The mean blood urea of this group was significantly higher than the normal group but not the hypertensive group.

Among the patients without evidence of back pressure atrophy or obstruction to the outflow of urine, there were 34 in whom the efficiency of each kidney differed by less than 10%. The average efficiency of these pairs of kidneys shows a modest but significant negative correlation with the blood urea, $r = -0.608$, $p < 0.01$. Eight of these patients also had a creatinine clearance, and the correlation between average efficiency and creatinine clearance is highly significant, $r = 0.94$, $p < 0.001$.

"The peak factor" or the correction for dilution throughout the vascular compartment and extravascular spread. In 70% of the renograms a good fit between the integrated mediastinal clearance curve and the 1-min-and-20-sec to 3-min portion of each

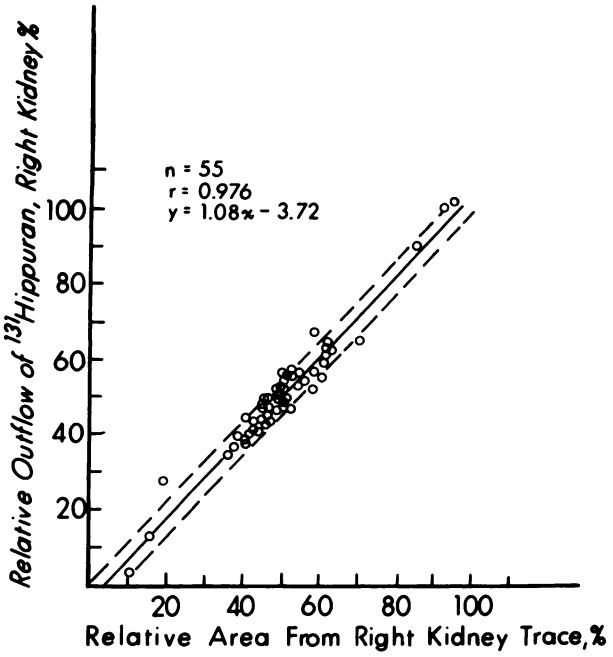


FIG. 5. Relative function of right kidney derived from kidney traces compared to that derived from computed outflow of ^{131}I-Hippuran in 55 patients.

TABLE 3. TRANSPORT EFFICIENCY AND BLOOD UREA IN NORMAL PATIENTS AND PATIENTS WITH HYPERTENSION AND POLYCYSTIC KIDNEYS

Diagnostic group	Mean efficiency (% ± s.e. mean)	Blood urea (mg% ± s.e. mean)
Normals	81.9 ± 1.32 (n = 28)	26.6 ± 1.67 (n = 14)
Hypertensives	71.2 ± 1.75 (n = 42)	33.5 ± 2.03 (n = 17)
Polycystic kidneys	23.0 ± 4.9 (n = 14)	49.0 ± 8.67 (n = 7)

Using Student's t-test the difference between the mean of each of these groups is significant, $p < 0.001$.

TABLE 4. TRANSPORT EFFICIENCY AND BLOOD UREA IN PATIENTS WITH CHRONIC PYELONEPHRITIS, BACK PRESSURE ATROPHY AND ACUTE URETERIC OBSTRUCTION

Diagnostic group	Clinical findings	Mean efficiency (% ± s.e. mean)	Student's t-test	Mean blood urea (mg% ± s.e. mean)
Chronic pyelonephritis (n = 9)	Radiologically affected kidney (n = 11)	51.5 ± 7.03	$p < 0.001$	35.2 ± 3.37
	Radiologically unaffected kidney (n = 7)	71.7 ± 3.34		
Back pressure atrophy	Symptomatic kidney* (n = 27)	21.4 ± 3.54	$p < 0.001$	39.8 ± 3.35
	Opposite kidney (n = 27)	56.7 ± 3.39		
Acute ureteric obstruction	Side of obstruction (n = 6)	5.5 ± 3.70	$p < 0.001$	30.3 ± 3.63
	Opposite side (n = 6)	62.9 ± 5.62		

* Symptomatic kidney here refers to the kidney which gave rise to the patient's symptoms.

kidney trace was obtained as shown by an almost zero baseline trace from 1 min and 20 sec until ^{131}I-Hippuran outflow started. The fit was fair in 27% of renograms and poor in the remaining 3%. After allowing for the initial dilution of ^{131}I-Hippuran throughout the vascular compartment, the peak of the mediastinal clearance curve had to be reduced on average by another 10.4% ± 13.7 s.d. to obtain the best fit between the integrated curve and the 1-min-and-20-sec to 3-min portion of each kidney trace.

The plasma clearance curve of ^{131}I-Hippuran gives an indication of overall renal function, and if continued for 40–60 min can be used to calculate effective renal plasma flow. Because of the extravascular spread of ^{131}I-Hippuran, calculations based on a shorter time interval are inaccurate (*13,14*) but still provide a useful indication of overall renal function. There is a highly significant correlation between the percentage fall in counts over the mediastinum between 2 and 15 min and creatinine clearance, $r = 0.916$, $p < 0.001$ (Fig 6).

Further observations on the kidney traces and ^{131}I-Hippuran outflow curves. In normal kidneys the shape of the renogram is little altered by the correction for blood and tissue background activity although the peak height is lowered. There is, however, no "first phase" in the kidney traces and activity rises in a smooth curve from approximately 30 sec onwards. The time to the peak is lengthened a little, while the shape of the third phase is virtually unchanged. The ^{131}I-Hippuran outflow curves are similar in shape to the matched integrated clearance curves but a little reduced in amplitude and delayed in time (Fig. 3).

In conventional renography a steadily rising tracing indicates obstruction to the outflow of urine but gives no indication as to how complete this is. When

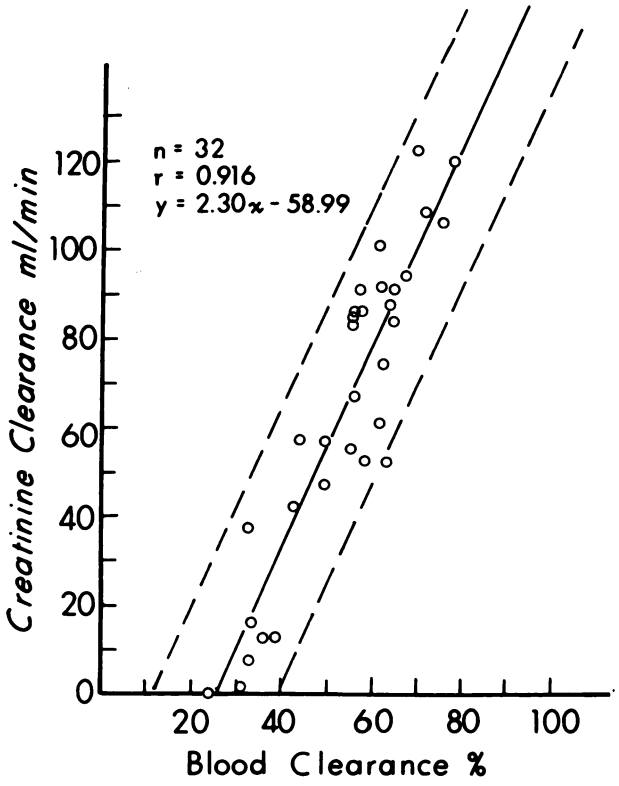
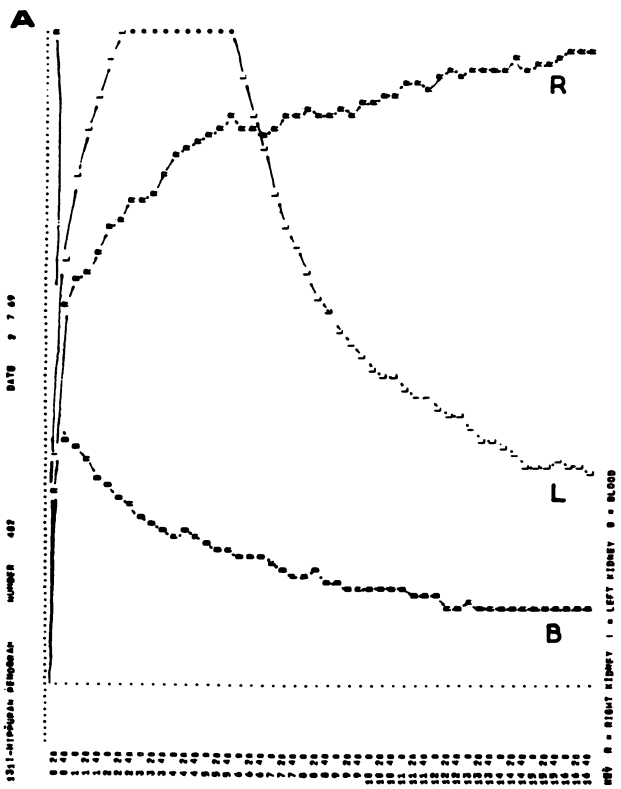
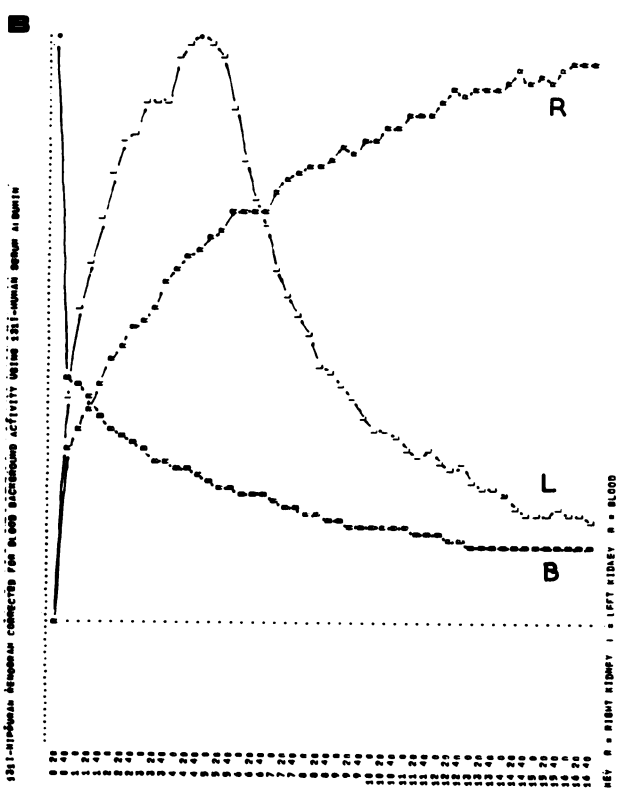


FIG. 6. Blood clearance of ^{131}I-Hippuran expressed as percentage fall in counts over the mediastinum from 2 to 15 min compared to creatinine clearance in 32 patients.

there is radiologically demonstrable complete obstruction, the computed ^{131}I-Hippuran outflow curve closely follows the baseline (Fig. 7), in keeping with the absence of urine flow. In partial obstruction the third phase may continue to rise or show a rounded delayed peak and a poor drainage phase. In these circumstances the computed outflow of ^{131}I-Hippuran rises above the baseline, starting at about the same time as, or shortly after, the unobstructed side and before the peak is reached (Fig. 8).

The renogram from a nonfunctioning kidney or over the site of a nephrectomy shows a curve which corresponds to the clearance of ^{131}I-Hippuran from this region (*12*). With the correction for blood and tissue background activity a horizontal tracing should be obtained along the baseline. Eight patients have been studied 3 months or more after unilateral nephrectomy. Five had relatively good renal function (i.e., a creatinine clearance greater than 40 ml/min) and in these patients the kidney trace from the nephrectomy site was horizontal although raised a little above the baseline (Fig. 9). Gamma camera views of this region in one of these patients showed no excess of background activity in this area. The correction underestimates blood and tissue background by about 10%. In the other three patients with more severe renal failure (all had creatinine clearances of less than 20 ml/min), the kidney trace from the nephrectomy site in addition to being above the baseline, rose slightly and this probably reflects our failure to take account of the continuing extravascular spread of ^{131}I-Hippuran for gamma camera views in two of them did not show any increasing activity in this region, although such a small rise might be difficult to appreciate visually.





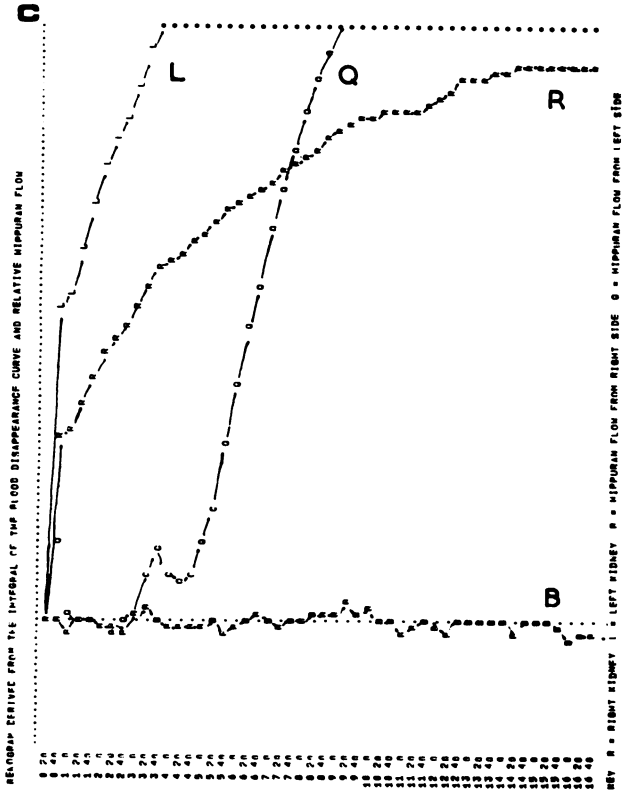


FIG. 7. A is computer printout of conventional renogram from male patient aged 25 with acute right-sided ureteric obstruction. Tracing from right kidney rises throughout test, but less steeply after 6 min. B shows kidney traces from same patient. Tracing on right is now a smooth curve. Relative function: right 38%, scan 28%. C shows integrated clearance curves and outflow of ^{131}I-Hippuran. Outflow from right side (B) closely follows baseline suggesting that there is practically no flow from this side. Relative outflow of ^{131}I-Hippuran: right 0.4%. Transport efficiency: right 0.3%, left 70.3%.

With a poorly functioning kidney, the conventional renogram also shows a falling graph which can be difficult to distinguish from no function at all. The kidney trace in these circumstances may indicate not only that function is present, but also whether this poor function is due to parenchymal disease or obstruction to the outflow of urine (Figs. 10 and 11). With severe parenchymal disease without obstruction the kidney trace still rises and falls, and both the accumulation and disappearance of ^{131}I-Hippuran are apparent, while in obstruction the kidney trace rises throughout.

However, kidney traces similar to those seen in obstruction may also be seen in the absence of any radiographic evidence of obstruction. This has been observed in two patients with severe unilateral chronic pyelonephritis, in one patient shortly after a massive embolus to the kidney (documented by subsequent arteriography), and in another patient with rapidly progressive oliguric renal failure due to polyarteritis nodosa.

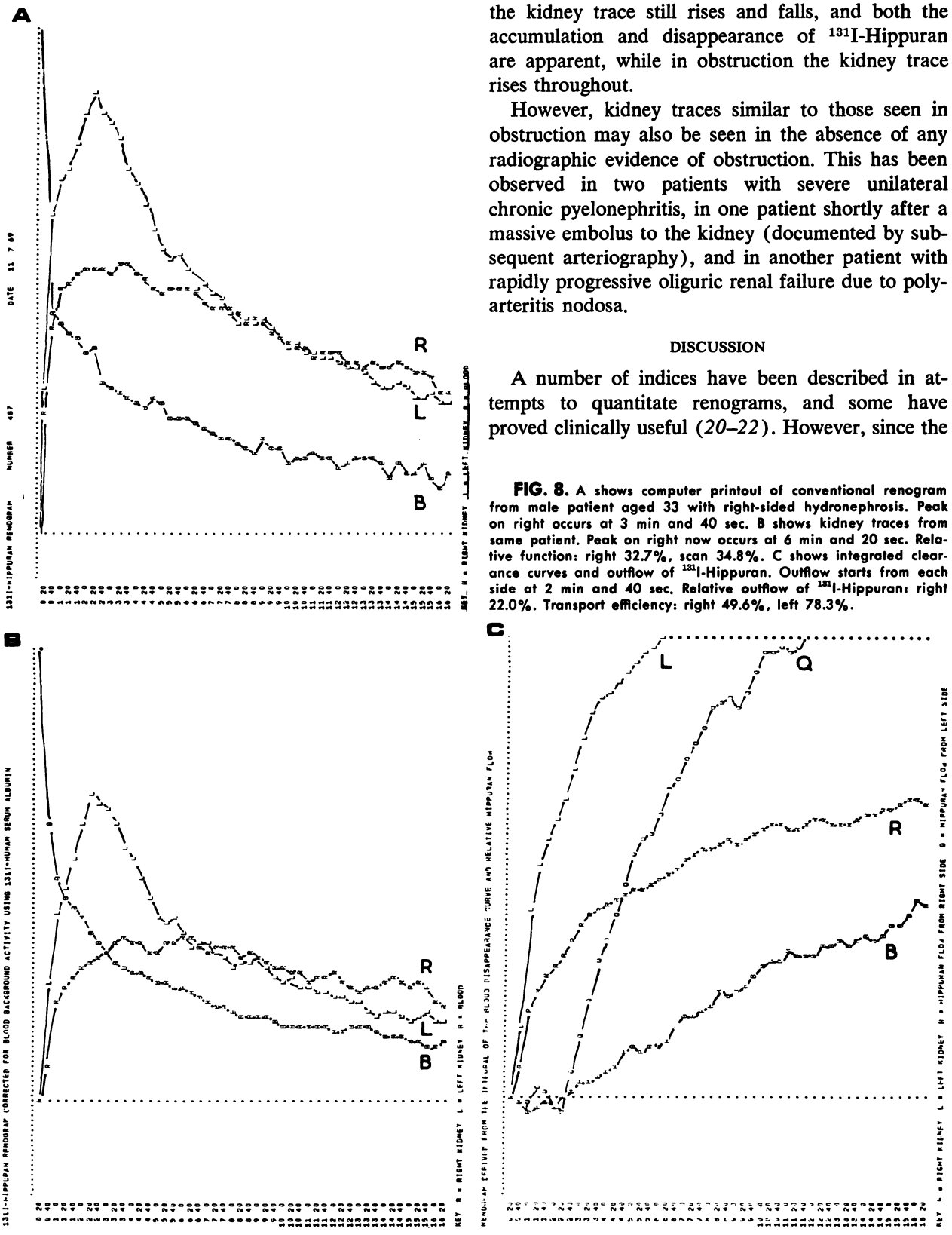


FIG. 8. A shows computer printout of conventional renogram from male patient aged 33 with right-sided hydronephrosis. Peak on right occurs at 3 min and 40 sec. B shows kidney traces from same patient. Peak on right now occurs at 6 min and 20 sec. Relative function: right 32.7%, scan 34.8%. C shows integrated clearance curves and outflow of ^{131}I-Hippuran. Outflow starts from each side at 2 min and 40 sec. Relative outflow of ^{131}I-Hippuran: right 22.0%. Transport efficiency: right 49.6%, left 78.3%.

DISCUSSION

A number of indices have been described in attempts to quantitate renograms, and some have proved clinically useful (*20–22*). However, since the

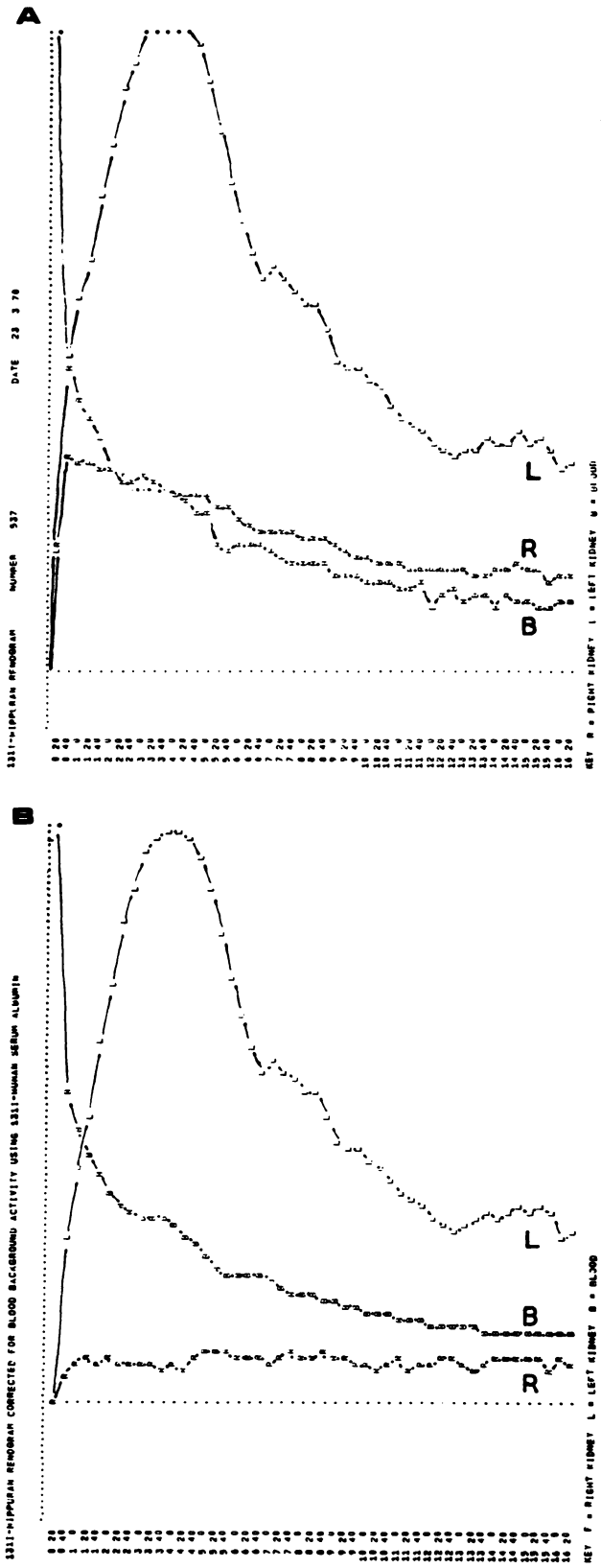


FIG. 9. A shows computer printout of conventional renogram from patient aged 9 who had had right nephrectomy. Tracing over nephrectomy site begins to follow mediastinal clearance curve after the first 2 min and resembles it closely after 6 min. B shows kidney trace from same patient. On right, tracing is almost horizontal although little above baseline.

renogram is a composite tracing of the changing activity within the kidney tubules, renal pelvis, and surrounding renal and extra-renal structures, it is not surprising that some observers have relied more on a visual assessment of the tracings than on any of the indices derived from them (*27*).

Computer-assisted renography, by providing a physiologically more realistic tracing, allows a more accurate determination of relative function and ^{131}I-Hippuran outflow than can be obtained from the conventional renogram.

For the blood and tissue background correction, several assumptions are made. It is assumed that the ^{131}I-IHSA remains within the vascular compartment during the renogram. After intravenous injection of ^{131}I-IHSA the counting rate recorded by an external detector reaches a steady figure within 3–4 min of injection and remains relatively constant for several hours even though some extravascular exchange takes place. In addition an essentially constant ratio is established between labeled red cells and labeled albumin for at least 15 min after the first circulation (*23*) so that this assumption is reasonable. Of more importance is the assumption that the clearance curve obtained from the mediastinum is a true representation of the ^{131}I-Hippuran clearance curve in the kidneys and surrounding tissues. Meade and his colleagues have observed that external counting over the precordium reflects blood clearance (*4*) while Van Stekelenburg and his colleagues (*15*) have shown that after the first 60–80 sec the clearance curve does reflect the changes in tissues surrounding the kidneys. In addition they point out that in normal kidneys a single factor alone is needed to correct for both the vascular and extravascular spread of ^{131}I-Hippuran. The horizontal kidney trace obtained over nephrectomy sites suggests that this assumption is also reasonable. However, it is clear that the extravascular spread of Hippuran is not entirely accounted for by the tissue background correction because the horizontal trace seen over a nephrectomy site runs along above the baseline and even rises slightly when the remaining kidney is poorly functioning.

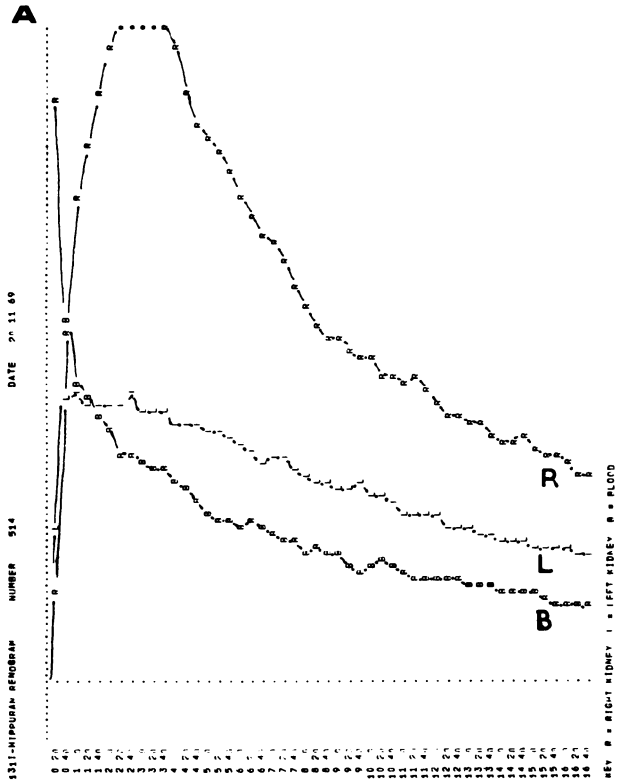
When determining relative function it is assumed that both kidneys are the same depth beneath the skin and also that each is viewed with equal sensitivity. It is unusual for kidneys to be more than 1 cm different in depth [Van Stekelenburg, quoted by Britton and Brown (*10*)]. Considerable care was taken in locating the detectors beneath each kidney from the tracer dose of ^{197}Hg-chlormerodrin, but with impaired renal function this method becomes unreliable for the right kidney due to increased hepatic uptake of the labeled chlormerodrin. More

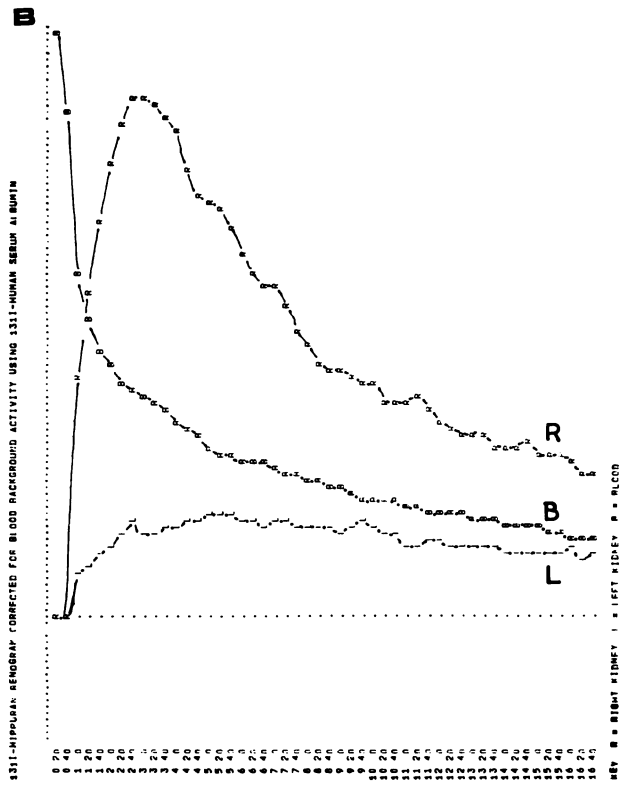
accurate measurements of renal function require depth detection, as suggested by Tauxe and his colleagues (*26*).

Additional assumptions are that blood flow remains constant during the test, and also that the patient remains still. This latter consideration led to the use of a couch similar to that described by Reba, McAfee, and Wagner (*25*) in which the patient lies comfortably supine with his head supported by two or three pillows and another pillow beneath his knees.

The program is based on a simple model of the kidneys described by Britton and Brown (*17*) and others (*25*). A large fraction of the injected ^{131}I-Hippuran is removed rapidly by the kidneys because they receive about one fifth of the cardiac output. About 20% of this is filtered at the glomerulus, and most of the remaining ^{131}I-Hippuran is extracted by the proximal tubules. This ^{131}I-Hippuran then passes down the tubules and collecting system, without mixing, until it reaches the renal pelvis. There it passes rapidly into the ureter to leave the field of view of the detector and so produces the sharp peak on a normal renogram.

The shape of the initial portion of the kidney trace, from 80 sec after the injection until just before





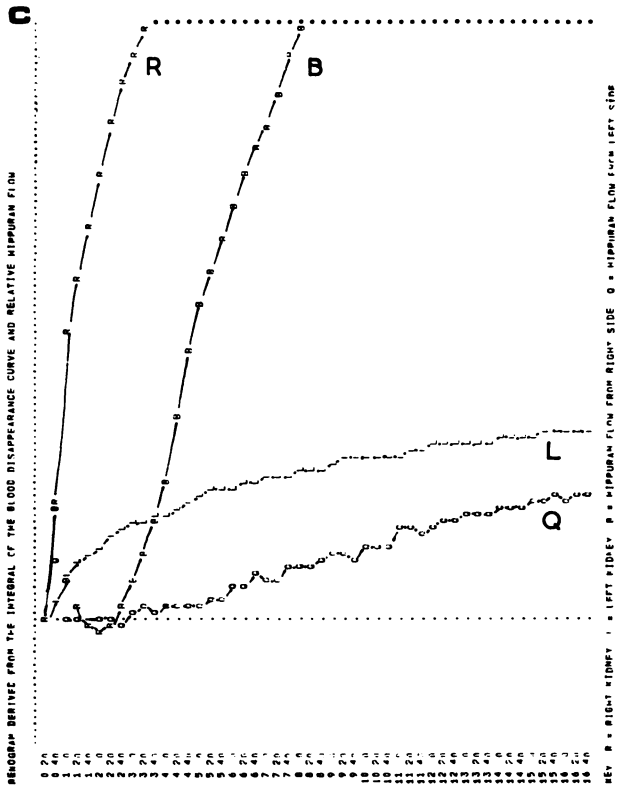


FIG. 10. A is computer printout of conventional renogram from female patient aged 32 with hypertension and left-sided chronic pyelonephritis. Tracing from left side falls throughout test, making interpretation difficult. B shows kidney trace from same patient. Tracing from left side now rises and falls suggesting parenchymal disease. Relative function: left 14.8%, scan 6.5%. C shows integrated clearance curves and outflow of ^{131}I-Hippuran. Outflow from left side starts within 20 sec of that on right. Relative outflow of ^{131}I-Hippuran: left 9.8%. Transport efficiency: right 75.5%, left 45.6%.

^{131}I-Hippuran begins to leave the kidney, reflects the rate at which ^{131}I-Hippuran is being taken up from the blood stream and hence is related to the integral of the blood clearance curve. The observed close correspondence obtainable between the early part of the kidney traces and the matched integrated mediastinal clearance curves supports this aspect of the model. Furthermore, since the plasma is almost completely cleared of ^{131}I-Hippuran in a single passage through the kidneys, the relative quantity of ^{131}I-Hippuran within each kidney, before any has left, reflects relative effective renal plasma flow. This forms the basis for using the relative areas under the kidney traces, before the first peak, as a measure of relative function. Our failure to completely correct for tissue background activity leads to some inaccuracy when assessing the relative contribution of a very poorly functioning kidney because some of the area beneath the kidney trace represents tissue background activity. By the same token some function might be ascribed to a nonfunctioning kidney or even an absent kidney, but in these circumstances the kidney trace reaches a plateau within 80 sec of the injection and remains at this level for the rest of the test (Fig. 9).

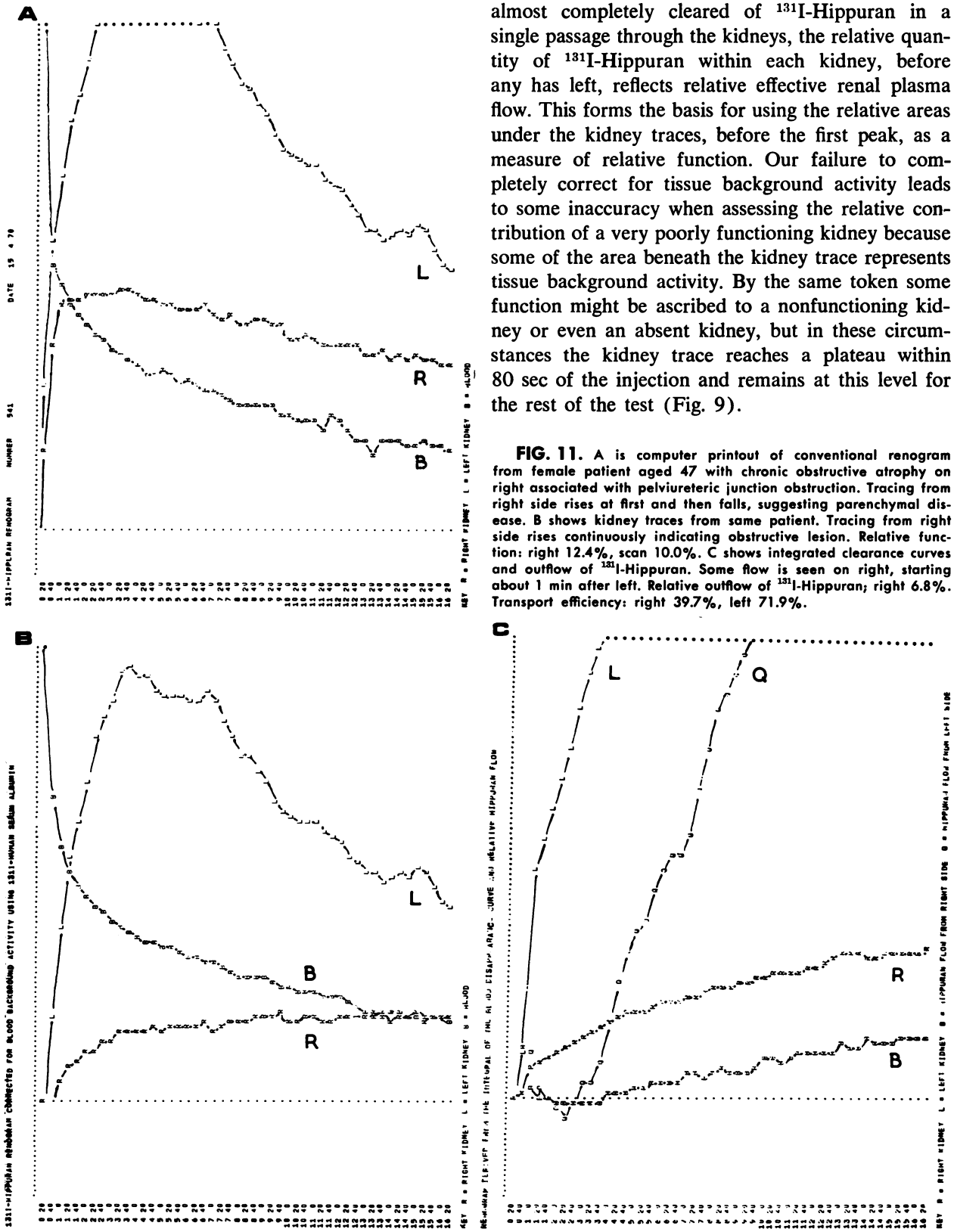


FIG. 11. A is computer printout of conventional renogram from female patient aged 47 with chronic obstructive atrophy on right associated with pelviureteric junction obstruction. Tracing from right side rises at first and then falls, suggesting parenchymal disease. B shows kidney traces from same patient. Tracing from right side rises continuously indicating obstructive lesion. Relative function: right 12.4%, scan 10.0%. C shows integrated clearance curves and outflow of ^{131}I-Hippuran. Some flow is seen on right, starting about 1 min after left. Relative outflow of ^{131}I-Hippuran; right 6.8%. Transport efficiency: right 39.7%, left 71.9%.

Experimentally in dogs, Farmelant and his colleagues have shown that the urine activity/time curves recorded from the bladder closely correspond to the integral of the blood clearance curve (*25*). The matched integrated clearance curves represent the way in which ^{131}I-Hippuran enters each kidney, while the kidney traces show both its entrance and departure. The difference between these curves gives the outflow of ^{131}I-Hippuran. In normal patients, the similarity in shape observed between the integrated curves and the ^{131}I-Hippuran outflow curves suggests that this method of computing ^{131}I-Hippuran outflow is valid. It gains further support in the patients with radiologically complete obstruction to the outflow of urine for in these the computed outflow of ^{131}I-Hippuran was almost zero.

The good correlations between the efficiency of ^{131}I-Hippuran transport, in the absence of obstruction to the outflow of urine, and both creatinine clearance and blood urea suggest that the transport efficiency may be a useful measure of a kidney's integrity. In the presence of obstruction to the outflow of urine the transport efficiency reflects both parenchymal damage and delay in the passage of ^{131}I-Hippuran across the renal pelvis.

None of the patients who had computer-assisted renograms, had divided clearance studies, so that there is no direct corroborative data to support either the relative function or the ^{131}I-Hippuran outflow estimations. However, Britton and Brown have compared this type of renography with divided clearance and find that the error in their estimation of relative function is less with the kidney traces than with the divided clearance technique (*17,18*). In our study estimations of relative function from the ^{197}Hg-chlormerodrin scans, in which the relative quantity of radioactivity within each kidney has been shown to correspond to relative effective renal plasma flow (*16*), were in good agreement with the kidney traces and each depends on a different method of uptake of the two radioisotopes. The rather greater difference between them in acute obstruction suggests that the mechanisms responsible for the uptake of ^{197}Hg-chlormerodrin are more sensitive to the acute effect of back pressure than are those involved in the handling of ^{131}I-Hippuran.

In patients with one normal kidney and one very poorly functioning kidney and in those with considerable overall impairment of renal function with oliguria, the kidney traces do not reliably distinguish between parenchymal disease alone and obstruction to the outflow of urine as a cause of parenchymal dysfunction.

Computer-assisted renography provides a reproducible method of estimating relative renal function and also a measure of the efficiency with which the whole kidney transports ^{131}I-Hippuran. In hypertension, it may be used to determine the relative function of each kidney in patients with unilateral renal disease, but of even more importance the efficiency of the apparently unaffected kidney can be determined, for the outcome of surgery may depend more on the integrity of the "good kidney" than on the difference in function between them (*28*). In patients with ureteric colic it can be used to assess the completeness of obstruction and also to measure the loss of functioning kidney that follows prolonged obstruction. In these circumstances the intravenous pyelogram gives a false sense of optimism (*19*). In patients with pelviureteric junction obstruction and ureteric strictures it may be used to assess relative function prior to surgery and to study the changes in relative function and efficiency that follow the surgical procedures.

SUMMARY

Computer-assisted renography has been carried out on more than 100 patients. In order to estimate blood and tissue background radioactive ^{131}I-IHSA was given first, followed 6 min later by ^{131}I-Hippuran, and the changing quantity of activity over each kidney and the upper mediastinum was recorded on punched paper tape.

The data tapes were analyzed by a program written in Fortran V which runs on the University of London Atlas Computer. Kidney traces, derived from the conventional renograms by blood and tissue background subtraction, were used to estimate relative renal function. They were also compared to matched integrated mediastinal clearance curves to yield the relative outflow of ^{131}I-Hippuran and the efficiency of transport of ^{131}I-Hippuran through the kidney and renal pelvis.

Good correlations ($r > 0.9$) were found between (A) the relative function calculated from the kidney trace and that determined from ^{197}Hg-chlormerodrin kidney scans; (B) the relative function from the kidney trace and the relative outflow of ^{131}I-Hippuran in the absence of obstruction; (C) the average efficiency of ^{131}I-Hippuran transport and creatinine clearance; and (D) mediastinal clearance between 2 and 15 min and creatinine clearance.

The mean transport efficiency of patients with normal kidneys was significantly greater than that of hypertensive patients and patients with polycystic kidneys, and reflected the difference in renal function between these groups. The mean transport efficiency of kidneys with pyelonephritic scarring, back pressure atrophy, and acute obstruction were significantly different from each other and from the normal group.

The method provides a reproducible way of assessing individual kidney function in patients with hypertension and can be used to determine the loss of kidney function that accompanies acute or chronic ureteric obstruction and to follow the changes in individual renal function that occur after surgical intervention for these conditions.

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