presence of unilateral renal disease or bilateral renal disease predominantly affecting one side.

Intravenous pyelograms and ¹³¹I-hippuran renograms were assessed in a selected group of 107 patients together with other investigations, including aortograms in 38 cases.

Comparison of the pyelogram and renogram findings showed good agreement in 77% of cases.

Discrepancies occurred most often in renal artery stenosis; seven cases with unilateral arterial lesions were found, of which six showed abnormalities in the renogram indicating disparity in function between the two kidneys; however, in only three instances did the pyelogram suggest the possibility of this diagnosis.

In a few cases a unilateral abnormality in the renogram could not be explained by other methods of investigation.

¹³¹I-hippuran renography used in conjunction with intravenous pyelography is of considerable value in the selection of hypertensive patients for aortography and divided renal-function tests.

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VALUE OF ¹³¹I-"HIPPIRAN" RENOGRAPHY IN UROLOGICAL INVESTIGATION

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¹³¹I-"hippuran" renography is a simple and safe diagnostic procedure causing the patient minimal discomfort. The test involves the recording of radioactivity over the kidneys for a period of 10 to 15 minutes after a single intravenous injection of ¹³¹I-hippuran (sodium orthoiodohippurate). This paper illustrates the value of the test in the investigation of obstruction of the urinary tract, abdominal pain of suspected renal origin, and certain forms of renal disease. The apparatus and procedure are described in another paper (Doig *et al.*, 1963), the only modification being occasional performance of the test in the prone position when the patient could not adopt the usual sitting position.

Results

In the normal renogram (Fig. 1, right kidney) there is an initial steep ascent, the "vascular" phase, which is largely due to the arrival of blood containing ¹³¹I-hippuran in the kidney region; this is followed by a less acute rise, the "secretory" phase, which results mainly from tubular secretion of the labelled compound; finally the curve descends, the "excretory" phase, indicating drainage of the radioactive material from the field monitored by the scintillation counter.

The Table summarizes the results of radiohippuran renography and intravenous pyelography in 30 patients with disorders of the upper urinary tract which are grouped according to clinical presentation.

Renogram in Ureteric Obstruction

The renogram abnormalities in ureteric obstruction depend on the degree of obstruction and the function of the affected kidney; impairment in the latter may

FIG. 1.—Serial renograms from Case 1 with left renal colic illustrating spontaneous relief of obstruction. Tracings obtained over right kidney are normal.

be due to pre-existing disease or it may develop as a consequence of the obstruction. After recent ureteric occlusion the kidney continues to excrete hippuran, which is retained within the renal pelvis; this results in a prolongation of the secretory phase of the renogram with replacement of the excretory phase by a gradually ascending curve (Fig. 1, day 1). If obstruction has been of sufficient duration to cause impairment of renal function the amplitude of the vascular phase is decreased

and the secretory and excretory phases tend to become flat; a similar pattern may occur in recent obstruction where there has been pre-existing impairment of function. In partial ureteric obstruction the secretory phase is usually prolonged and may be increased in amplitude, while the excretory phase shows a slow rate of fall. Features of incomplete obstruction have occasionally been observed during renography, and these have disappeared after the patient has been asked

Results of Intravenous Pyelography and ¹³¹I-hippuran Renography

Case	Age	Sex	Clinical Data	Intravenous Pyelogram	Hippuran Renogram
1	52	F	Left renal colic. Hyperparathyroidism	Day 1: probable calculus at left ureterovesical junction; dilatation left collecting system	Day 1: severe obstruction (left). Day 2: (pain-free) severe obstruction (left). Day 3: partial obstruction (left). Day 11: normal
2	45	M	Right renal colic	Delayed emptying right side. ? non-opaque renal calculus	Day 1: severe obstruction (right). Day 9: partial obstruction (right)
3	36	M	Left " "	Irregular calculus, middle third left ureter	Day 1: severe obstruction (left). Day 14: partial obstruction (left) (pain-free)
4	35	M	" " " Day 5: small calculus passed	Small calculus, lower end of left ureter	Partial obstruction (left)
5	55	F	" " " Day 5: small calculus passed	Day 3: relative delay in excretion (left side)	Day 11: no evidence of obstruction
6	34	M	Right renal colic	Day 1: slight caliceal hydronephrosis (right). Day 9: normal	Day 1: severe obstruction (right). Day 7: slight delay in excretion (right)
7	33	M	" " " Day 11: calculus passed	Day 1: right kidney, faint nephrographic effect only. Day 10: normal	Day 1: severe obstruction (right). Day 7: partial obstruction (right)
8	50	F	Right renal colic. Right pyonephrosis. Stone impacted at pelvi-ureteric junction	—	Gross impairment of function and severe obstruction (right)
9	69	M	Recurrent pain in right loin for five years	Right hydronephrosis	Obstruction, poor function (right)
10	53	F	Recurrent left-sided abdominal pain and chills for five years	Left hydronephrosis with calculi	" impaired function (left)
11	72	F	Right flank pain	Right hydronephrosis. Early left hydronephrosis	Obstruction, impaired function (right). Delayed excretion (left)
12	16	M	Polyuria. Gross right hydronephrosis	Right hydronephrosis (poorly defined). Hypertrophied left kidney	Obstruction, impaired function (right). Hypertrophy (left)
13	22	M	Right abdominal pain. ? Renal colic. ? Malingering	Day 3: normal (pain-free)	Day 1: obstruction (right). Day 3: normal
14	54	M	Right abdominal pain. ? intestinal obstruction. ? Renal colic	? Pyelonephritis (right)	Partial obstruction (right)
15	56	M	Diabetic ketosis. ? Left renal colic	Normal	Normal
16	66	F	Long-standing bilateral loin pain. Subsequent negative laparotomy	"	"
17	54	M	Right loin pain	Day 10: relative delay in excretion (left)	Obstruction (left)
18	17	F	Lumbar pain. ? Trauma. ? Pyelonephritis	Small calculus and slight clubbing of calices at lower pole of right duplex kidney	Normal
19	29	F	Right loin pain. Pyelonephritis involving lower pole of right duplex kidney	? Hypernephroma	Slight increase in amplitude (right) otherwise normal
20	48	M	Right loin pain. Perinephric abscess	Right pyelonephritis	Impaired function (right)
21	28	F	Right flank pain for three years. Right pyelonephritis	Medullary sponge calcification (Ekström <i>et al.</i> , 1959). Large left kidney (17 cm.)	Decreased function (right). Hypertrophy (left)
22	29	F	Right flank pain. Medullary sponge kidneys. Right pyelonephritis	—	Bilateral complete obstruction. Normal secretory phases
23	53	F	Anuria. Bilateral ureteric obstruction	—	Day 5: gross impairment of function. Features of obstruction. Day 11: gross impairment of function. Day 21: normal
24	18	M	Oliguria. Acute renal failure. (Renal biopsy: acute tubular necrosis)	Normal	Normal
25	26	M	Assessment of donor for renal transplantation	Normal	Minimal residual function (left). Hypertrophy (right)
26	62	F	Calcified tuberculous left kidney. ? Non-functioning	Calcified, non-functioning left kidney. Hypertrophied right kidney	No evidence of renal function (left)
27	26	M	Proved renal agenesis	Right kidney normal. Absent left renal outline	Obstruction; impaired function (left). No function (right)
28	38	F	Recurrence of retroperitoneal sarcoma; left ureteric obstruction; ligation right ureter 5 years previously	—	Normal tracing (right). Obstruction; impaired function (left)
29	45	F	Carcinoma of cervix. Extensive local recurrence	Right kidney normal. Left kidney small; poor excretion of dye, hydronephrosis, and hydroureter. Extrinsic pressure on left side of bladder	Partial obstruction (right)
30	56	F	Large pancreatic tumour	—	—

FIG. 2

FIG. 3

FIG. 4

FIG. 2.—Apparent right ureteric obstruction relieved by standing. FIG. 3.—Renogram in Case 12, with right hydronephrosis and hypertrophy of left kidney. FIG. 4.—Renogram in Case 23, with acute bilateral ureteric obstruction.

to stand and again resume the sitting position (Fig. 2). This manoeuvre is performed routinely whenever an obstructive pattern is being recorded.

Renal Colic (Cases 1 to 8)

The renogram is of particular value in the diagnosis and management of renal colic. Fig. 1 illustrates a series of renograms from a patient with left renal colic. The initial tracing showed features of obstruction on the left side; these persisted unchanged on the second day, although the patient had been free of pain for 18 hours; on the third day the obstructive pattern was much less marked, while eight days later (11th day) the renogram was normal.

When a patient suffering from renal colic is admitted to hospital, immediate intravenous pyelography may be impracticable and a plain x-ray film of the abdomen is often negative. Under these circumstances the renogram is of considerable diagnostic assistance; further progress may then be assessed by serial renograms; these expose the patient to only a small fraction of the radiation dose received during an intravenous pyelogram. Surgical treatment may be indicated in cases where the renograms show evidence of persistent obstruction with progressive deterioration in the function of the affected kidney.

Hydronephrosis (Cases 9 to 12)

The renogram shows an obstructive pattern usually associated with evidence of impaired renal function (Fig. 3). In most instances the renogram adds little to the information obtained from pyelography, although occasionally, where the pyelographic evidence of dilatation of the renal pelvis is equivocal, the renogram may reveal a more definite abnormality.

Pain of Suspected Renal Origin (Cases 13 to 22)

As a simple brief test which gives an immediate result, renography has much to offer in patients complaining of abdominal or back pain where unilateral renal disease enters the differential diagnosis. A soldier aged 22 (Case 13) reported to the out-patient department on a Sunday morning complaining of right-sided abdominal pain; malingering was strongly suspected because of an unstable personality and an attempt at suicide two weeks previously. Although microscopical examination of the urinary sediment was negative, the renogram showed frank features of ureteric obstruction on the side of the pain. Two days later, when he was pain-free, both an intravenous pyelogram and a further renogram gave normal results.

Oliguria

Cases 23 and 24 illustrate the renogram findings in patients with oliguria or anuria due to acute renal failure and bilateral ureteric obstruction. A woman aged 53 (Case 23) developed anuria after retrograde pyelography which had been carried out during anticoagulant therapy. Although it was thought probable that bilateral

ureteric obstruction had resulted from submucosal haemorrhage and intraluminal blood clot further ureteric catheterization was undesirable and the possibility of acute renal failure could not be excluded entirely. The renogram (Fig. 4) showed a pattern of obstruction with rapidly rising secretory phases which indicated good extraction of ^{131}I -hippuran, thus confirming the initial diagnosis. Conservative management was associated with a gradual return of the renogram findings to normal over a period of 10 days.

These findings may be compared with those in Case 24, where the oliguria was due to acute tubular necrosis (diagnosis confirmed by renal biopsy). The patient, a young merchant seaman, developed oliguria after severe abdominal pain which occurred during a drinking bout. On admission to hospital five days later retrograde pyelography demonstrated gross swelling of the renal parenchyma, obliterating the calices; the first renogram (Fig. 5), also performed on the fifth day, using

FIG. 5.—Serial renograms (left kidney) in Case 24, with acute tubular necrosis. Tracings obtained over right kidney were similar.

twice the average dose of ^{131}I -hippuran ($15\text{ }\mu\text{c}$), showed severe impairment of renal function with replacement of the secretory and excretory phases by slowly rising curves; the latter was interpreted as indicating accumulation of hippuran in the swollen kidneys after its extraction by surviving tubular cells. Dialysis was required on the sixth day and the diuretic phase began on the ninth day. A renogram performed on the 11th day, when the blood-urea nitrogen (B.U.N.) was 102 mg./100 ml. and urinary output 2.9 litres/day, showed severe impairment of renal function without evidence of obstruction. A further renogram on the 21st day

FIG. 6.—Renogram in left renal agenesis (Case 27). FIG. 7.—Renogram and simultaneous tracing of heart radioactivity in Case 26, with calcified tuberculous pyonephrosis of left kidney.

revealed curves of normal contour with a slight decrease in amplitude; at this stage the B.U.N. was 19 mg./100 ml. and the creatinine clearance 105 ml./minute.

Non-functioning Kidney and Renal Agenesis (Cases 26 to 28)

The recognition of a non-functioning or absent kidney may be of importance—for example, when emergency nephrectomy is contemplated. In this situation renography is the simplest investigation for detecting the presence of functioning renal tissue. Should the renogram suggest an absent or non-functioning kidney, intravenous pyelography is indicated to exclude an ectopic kidney. Fig. 6 shows the renogram from a patient with left renal agenesis. These tracings should be compared with those illustrated in Fig. 7; the intravenous pyelogram from this patient showed a calcified tuberculous pyonephrosis of the left kidney without evidence of renal function; although the renogram showed gross depression of function on the left side, comparison with a simultaneous record obtained over the heart failed to show the progressive downward gradient of the heart curve, thus indicating persistence of some function. In Case 25, a prospective donor for renal transplantation, the finding of normal symmetrical renogram tracings in addition to normal total renal clearances and normal nephrograms and pyelograms was further evidence for the presence of two normally functioning kidneys.

Discussion

¹³¹I-hippuran renography is shown to be a rapid method of detecting obstruction of the upper urinary tract. Although delay in the disappearance of radioactivity from the renal area is invariably present in obstruction, it may also occur when there is dilatation of the collecting system or a marked diminution in urine flow; thus the renogram may show the features of obstruction in chronic pyelonephritis with caliceal clubbing and in acute circulatory failure.

In their original description of radioisotope renography using ¹³¹I-"diodrast," Taplin *et al.* (1956) illustrated tracings obtained from animals with ureteric obstruction and described similar curves in patients with renal colic. The renographic findings associated with dehydration, renal ischaemia, and acute renal failure have also been described in animals using ¹³¹I-diodrast (Taplin *et al.*, 1956; O'Connor *et al.*, 1961). Among the various ¹³¹I-labelled compounds which have been used for renography hippuran has proved most satisfactory (Nordyke *et al.*, 1960; Whitley *et al.*, 1961; Johnson *et al.*, 1961); investigators using this compound have described characteristic changes in the renograms of experimental animals and man with induced physiological changes or structural lesions (Nordyke *et al.*, 1960; Meade and Shy, 1961; Klapproth *et al.*, 1962). In this study similar renographic findings have been described in analogous clinical situations, and these are shown to be of diagnostic importance.

Summary

The results of ¹³¹I-hippuran renography are reported in 30 patients with various urological disorders.

In renal colic ureteric obstruction is shown by delayed excretion of the radioisotope-labelled compound, and the subsequent course of the obstruction can be followed by serial renograms. When persistent obstruction causes impairment of renal function this is also shown by changes in the renogram.

By revealing a renal abnormality the renogram often yields diagnostic assistance in patients with abdominal or back pain of indeterminate cause. The differentiation of anuria due to recent ureteric obstruction from that of acute renal failure can be made readily by renography; the rising curves of normal or increased amplitude characteristic of obstruction contrast with the flat curves of low amplitude found in acute renal failure. The renogram can assist in the recognition of a non-functioning or absent kidney.

It is concluded that ¹³¹I-hippuran renography is a convenient simple test of considerable value in the investigation and management of patients with a variety of urological disorders.

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INSULIN ASSAY IN INSULINOMAS

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The pre-operative diagnosis of insulin-secreting islet-cell tumours of the pancreas (insulinomas) has in the past depended on a number of empirical tests. The demonstration of Whipple's triad and the tolbutamide, glucagon, and leucine tests contribute to the diagnosis, but errors still occur.

It was hoped that a reliable insulin assay would permit the detection of insulinomas with certainty, but methods measuring insulin-like activity (I.L.A.) have given inconsistent results (Wright, 1960). Recently a specific immunoassay for insulin (Yalow and Berson, 1960) has become available. In this paper we record our observations on the use of this specific insulin assay in patients with insulinomas.

Materials and Methods

The normal range for plasma insulin was determined in 100 fasting control subjects and the normal plasma insulin response to tolbutamide in 30 control subjects.