Urological Research 3, 81-85 (1975)
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The Renogram and Individual ^{131}I-Hippuran Clearances in Experimentally Controlled Renal Perfusion*

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Received: February 25, 1975

Summary. The radioisotope renogram and renal clearances using ^{131}I-Hippurate were studied during experimentally controlled renal perfusion. In the first series of experiments, renograms were recorded during variations in renal blood flow produced by an extracorporeal pump circuit. There was a close correlation between renal blood flow and renogram parameters. These characteristics were also related to urine flow rates. - In the second series of experiments, unilateral renal damage was produced either by ischaemia or obstruction. Individual clearances using ^{131}I-Hippurate and the gamma camera were compared with standard clearances obtained during a steady state. There was a close correlation between these methods and the results emphasise the importance of subtracting background radioactivity. - It is concluded that the main value of the renogram is to provide a left to right comparison of renal tubular function whereas the value of corrected ^{131}I-Hippuran clearances is to provide an absolute measure of individual effective renal plasma flow.

Key words: Radioisotope renography, sequential renal scintigraphy, individual ^{131}I-Hippuran clearance, experimentally controlled renal perfusion.

The methods of nuclear medicine are being used on an increasing scale in the diagnosis of renal hypertension. These consist of a) Radioisotope renography and its development, sequential renal scintigraphy and b) Individual ^{131}-I-Hippuran clearances for determination of effective renal plasma flow (E. R. P. F.). We have studied the validity of these methods in two series of animal experiments in which renal perfusion and urine output were controlled. In the first series the characteristics of the renogram obtained by sequential scintigraphy were studied and in the second series ^{131}I-Hippuran clearances were measured.

* This research was undertaken with the support of the Federal Ministry for Research and Technology.

Series 1: Renogram Studies

Materials and Methods. Forty mongrel dogs were used; preliminary tests to establish the method were carried out on fifteen dogs and twenty-five dogs were used for the tests.

Renal perfusion: a unilateral nephrectomy was performed and a separate blood supply to the in situ kidney was established using silicone tubing from the ipsilateral common iliac artery.

The heparinised blood was returned to the kidney in a rigid glass catheter passed through the nephrectomy stump to the opposite renal artery (Fig. 1.). The extracorporeal (renal) blood flow was controlled by an adjustable pump; the flow rate was measured by an electromagnetic flow meter; the pressure was monitored by an electromanometer (Statham) and the temperature was controlled by an automatic water bath. The renal blood pressure and flow rate were monitored continuously and urine output was measured directly from a bladder catheter.

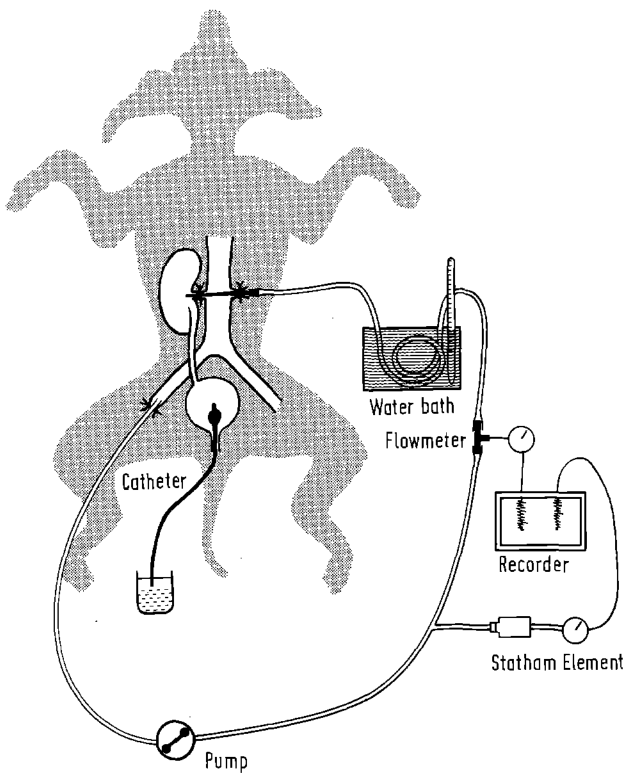

Fig. 1. Method for renal perfusion with one kidney left in situ after unilateral nephrectomy

Four renograms per test were recorded sequentially by means of a scintillation camera (Pho Gamma III, Nuclear Chicago) and transferred through a multichannel analyser into a computer (Siemens 305/306). Each renogram (recorded after intravenous injection of 300 μC ^{131}I-Hippurate) related to a different renal blood flow. The technique for processing these data has been reported elsewhere (4, 13).

The following renogram parameters were measured:

1. Amplitude of initial phase at 30 seconds after injection.
2. The total counts (pulse integral) obtained between 60 and 132 seconds after injection.
3. The time of maximum uptake activity (T_{max}).
4. The half-life (T/2) after T_{max}.

The percentage variations in these measurements were correlated with the percentage variation in renal blood flow. The effect of urine output on the renogram was also measured during a diuresis induced by hyperosmolar solutions and diuretics.

Results. A total of 49 renograms were obtained at varying rates of renal blood flow in 17 successful experiments. Four animals died during the procedure and four were abandoned because of circulatory collapse.

There was a close correlation between the percentage variation in renal blood flow and the total counts accumulated (pulse integral) between 60 and 132 seconds (Fig. 2). In the course of some experiments there was progressive renal damage, attributed to unphysiological pulse variations from the pump, which produced a greater reduction in renal blood flow relative to the other measurements (Fig. 3).

At normal urine flow rates there was a close relation between renal blood flow, T_{max} and T/2. Both values increased with reduced renal blood flow and urine flow rates. However, during a diuresis, T_{max} and T/2 were dependent on the urine flow rate (Fig. 4).

Series 2: ^{131}I-Hippuran Clearances

Materials and Methods. Forty mongrel dogs were studied. Preliminary ligation of a ureter in three dogs was used to produce unilateral tubular damage from hydronephrosis; in seventeen dogs the perfusion of one kidney was restricted by a ligature to a renal artery branch. The time between operation and clearance measurement varied from two to five days.

Individual ^{131}I-Hippuran clearences after both ureters were catheterised were determined on each animal. A scintillation camera and computer system were used to record and evaluate the results (4). This clearance test is based on the method described by Oberhausen (7, 8) with the addition of a subtraction of the activity in extrarenal body tissue and blood (extra parenchymal activity, E.P.A.) (3). Simultaneous with the first clearance test the secretion rate of radioactivity in the urine was also measured. Both results were then compared with the individual ^{131}I-Hippuran clearances carried out by a conventional steady state procedure.

Results. There was a close correlation (r = 0.969) between the corrected individual clearances obtained with scintillation camera and the simultaneously measured radioactivity in the urine (Fig. 6). When the clearances were not corrected for extraparenchymal activity the coefficient of correlation was 0.829; with the total body correction recommended by Oberhausen it was 0.855.

There was also a close correlation between the individual clearances obtained during the steady state and the secretion rate of radioactivity (r = 0.976).

Discussion

These results have shown that with normal renal tubular function, both the initial phase and the timed count rate (pulse integral) of the renogram provide an indication of renal blood flow. However, with abnormal renal tubular function these renogram measurements were altered and renal blood flow could not be deduced. Wax and McDonald (10) showed similar results in their analysis of the renogram.

The effect of background activity on the renogram is now well established and has been emphasized by Brown and Britton (1). It must therefore be taken into consideration in any evaluation. In the present studies a radiolabelled albumin correction procedure (11) was used so that the right/left ratio of the count rates (pulse integral) equaled the clearance ratio for the kidneys.

The influence of urine flow rate has been described by Farmelant et al. (2) and the importance of this factor on the interpretation of the renogram has been confirmed in the present studies.

In the second series of experiements we have shown the dependence of the pulse integral on the tubular clearance rate. The importance of a method for background correction was again demonstrated. The advantage of the corrected ^{131}I-Hippuran clearances without catheterization is that they provide absolute values for effective renal plasma flow, whereas corrected renograms can only provide clearance ratios. Short et al. (9) have described a method using ^{123}I-Hippurate and the gamma camera where a renogram uptake ratio and a measurement of total renal plasma flow are used to obtain absolute values for each kidney.

The results from the present studies with the gamma camera have shown that these non-invasive techniques provide reliable measures of renal function and can be applied to the study of renal hypertension as well as other kidney diseases.

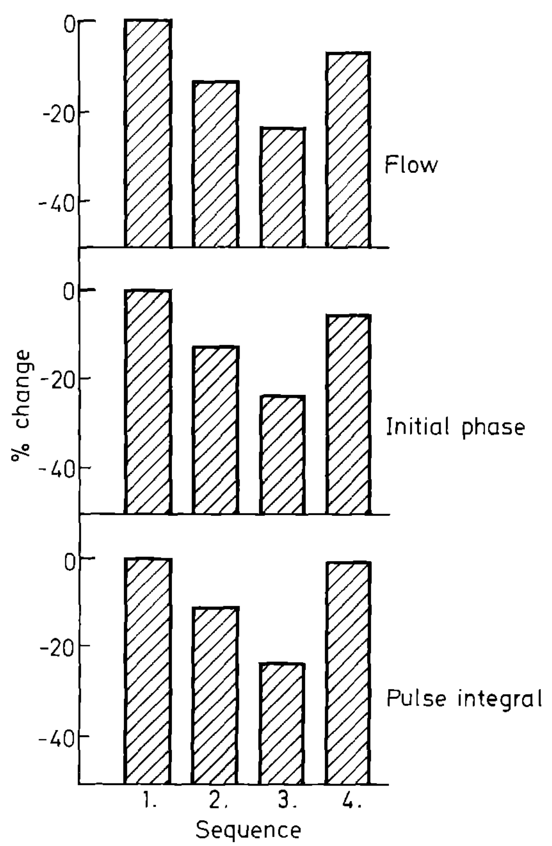

Fig. 2. Test No. 29: Uniform changes of renal flow, initial phase amplitude (30 secs post injection) and pulse integral of phase 2 of the renogram (60-132 secs post injection)

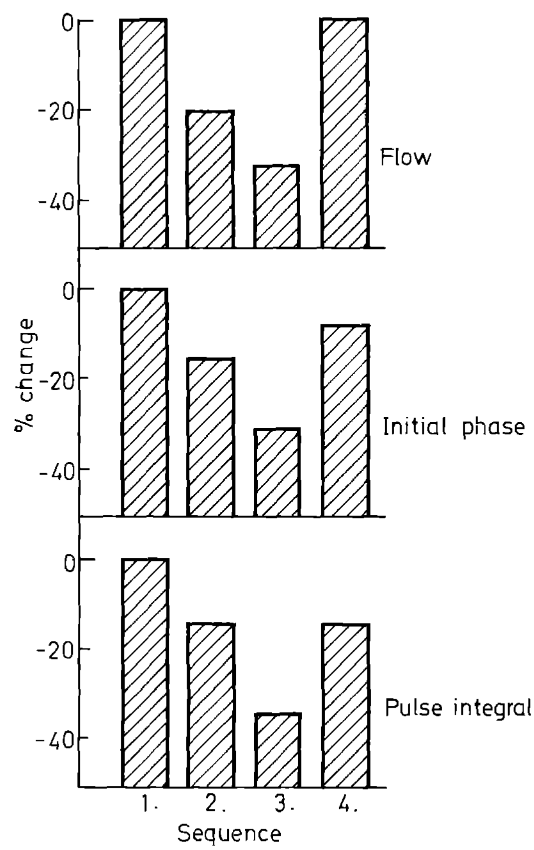

Fig. 3. Test No. 20: Uniform changes of renal flow, initial phase amplitude and pulse integral of phase 2 of the renogram up to the 3rd sequence. There is a relative reduction of the initial phase and pulse integral in the 4th sequence, the pulse integral being affected more markedly

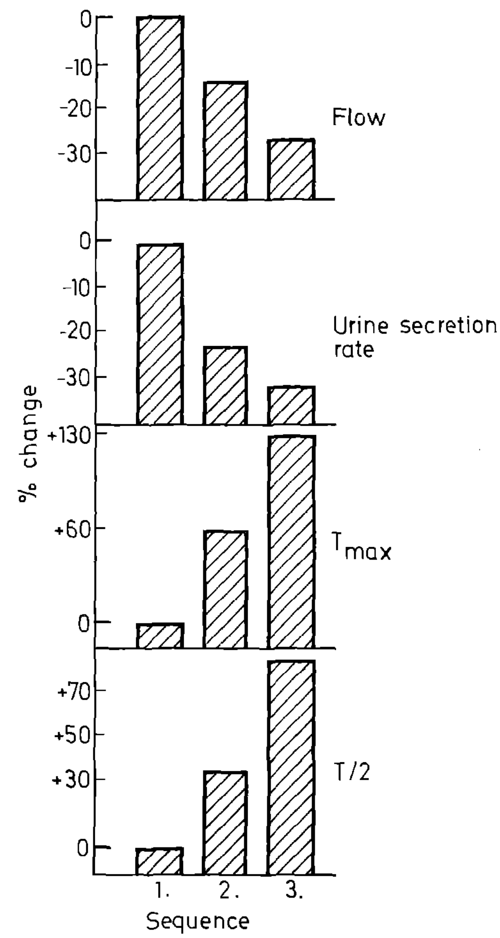

Fig. 4. Test No. 29: Similar changes of renal flow and urine secretion rate. Reverse changes of renal flow and T_{max} and T/2

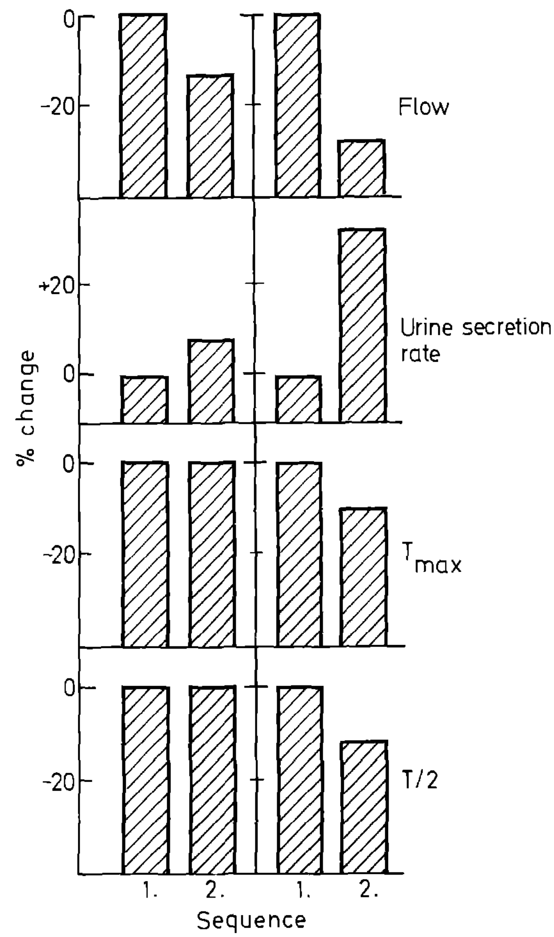

Fig. 5. Tests Nos. 25 and 39: Dependence of T_{max} and T/2 urine secretion rate when it behaves contrary to the renal flow. Despite the reduced flow there is no increase of the two renogram parameters, in fact in test no. 39 there is a decrease of these parameters

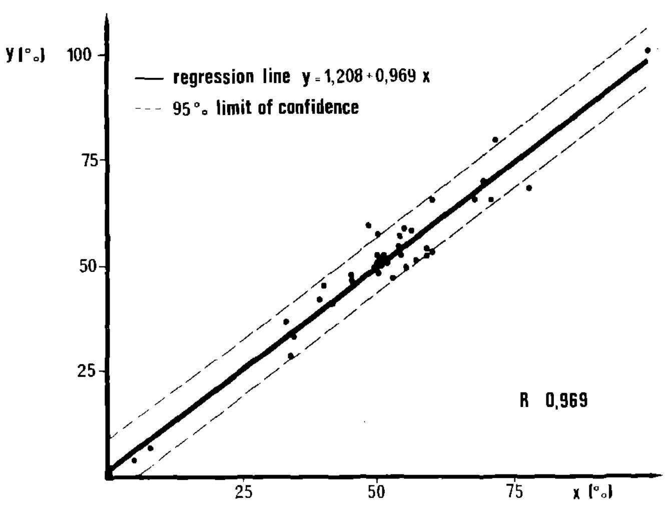

Fig. 6. Correlation diagram for the clearance rate of the left kidney. X = % function fraction based on the pulse integral between 60 and 132 secs. p. i. after EPA correction. Y = % function fraction based on rate of secretion in the urine

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