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Urinary Clearance of ^{113m}In-DTPA and ^{99m}Tc-(Sn)DTPA Measured by External Arm Counting

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Summary. Single shot glomerular filtration rate measurements involving chelates (^{113m}In-DTPA, ^{99m}Tc-DTPA etc) assume direct loss from the plasma to urine via glomerular filtration and excretion. Inherent errors, due to considerable uptake of activity in tissue and uncertainty of complete bladder emptying are ignored and taking of half-hourly blood and urine samples involves patient discomfort. This paper describes a simple method of measuring urinary clearance of chelates using serial external arm counting which entails only an initial injection and takes into account tissue loss from plasma. The resultant plotted curve exhibits three phases, the first two depicting input and equilibration between plasma and tissue and the third and exponential part, which is a measure of the biological half-life of the chelate, being representative of the efficiency of renal glomerular filtration, the parameter to be measured. Results obtained, compared with single shot glomerular filtration rate measurements performed simultaneously, gave better correlation with clinical data including renography.

Key words: Glomerular filtration rate - Arm counting.

Measurement of the glomerular filtration rate (GFR) using a single injection of ^{51}Cr EDTA and serial blood and urine sampling was shown to be clinically feasible about a decade ago by several workers (1, 2, 3). Since then several other radionuclide labelled chelates have been shown to be equally effective (4). ^{113m}In-DTPA and, latterly ^{99m}Tc-DTPA(Sn) have been used in this department for a period of six years.

Although the 'single shot' technique is reasonably accurate and relatively simple to perform, it has inherent sources of error. These are, loss of radioactive label from plasma to tissue and, unless catheterisation is employed, incomplete bladder emptying when collecting urine samples. This leads to inaccuracy in estimating total urinary activity. In addition the taking of half-hourly blood samples can involve considerable patient discomfort and apprehension, especially in the case of young children.

In an effort to obviate the need for blood and urine sampling a simple method of measuring urinary clearance of chelates, using serial external arm counting has been evolved which entails only an initial injection and takes into account loss of active label from plasma to tissue. This method has been compared with the conventional 'single shot' GFR in selected control subjects and, subsequently, in patients referred with hypertension, who required measurements of renal efficiency. The method was found to be as accurate as the 'single shot' GFR, technically easier to perform and it involved minimal patient discomfort.

MATERIALS AND METHODS

Twenty control subjects were selected who had no evident disease of the urinary system. Following an intravenous injection of 1mCi ^{113m}In-DTPA or ^{99m}Tc-DTPA the subjects had their GFR measured by taking half-hourly blood and urine samples over a period of 2 hours and using the standard $\frac{UV}{P.t}$ calcula-

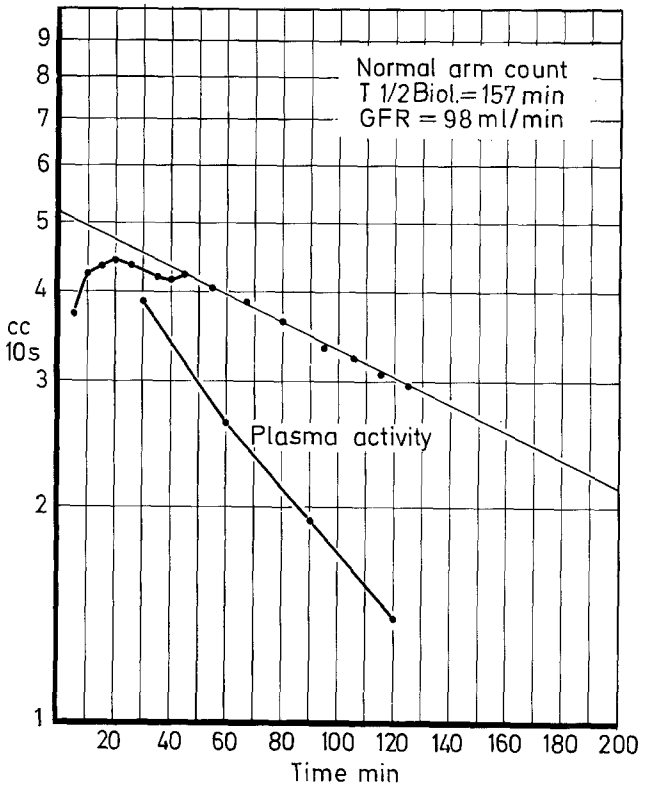


Fig. 1. Arm activity/time curve obtained from a control subject with corresponding plasma activity measured at 4 half-hourly intervals

Table 1. Series of 28 hypertensive patients investigated for the presence of renal disease

Investigation	Normal result	Equivocal result	Abnormal result
$T\frac{1}{2}$-biol	13	2	13
GFR	8	7	13
IVP	12	3	7
Renogram	10	2	14

Table 2. Fourteen hypertensive patients without evidence of renal disease

Investigation	Normal	Equivocal	Abnormal
$T\frac{1}{2}$-biol	13	1	0
GFR	8	6	0

tion where UV = the total weight in gms of urine x the % of the administered dose per gm collected in time t, and P = the average % of the administered dose per gm of plasma in the blood during time t. The GFR was calculated, using the above formula and samples of blood and urine taken at half hour intervals on four occasions. These were averaged and expressed in mls/min. Complete bladder emptying was verified by visualizing the bladder area, before and after urine collection, on the persistence scope of a Nuclear Chicago Pho-Gamma IV gamma camera.

In between the collection of blood and urine samples each subject had serial arm counts performed in a standard J & P Engineering (Reading) arm counter at ten minute intervals for two hours and, at varying time intervals thereafter, for a further three to four hours. Each arm count was performed over ten seconds (count rate range 30,000 - 40,000) repeated twice to ensure statistical accuracy, corrected for background and decay, and the result plotted on log linear paper to give arm activity/time curves.

Subsequently similar GFR and arm count measurements were made on a series of 28 patients who presented with hypertension and were being clinically screened to exclude renal involvement.

RESULTS

Arm activity/time curves obtained in the twenty control subjects were essentially similar in appearance (Fig. 1). During the first 45 minutes the curve is non-linear and reflects the uptake of activity to equilibrium in the tissues of the forearm. This accounts for a considerable part of the plasma activity loss, depicted in Figure 1 as the drop in plasma activity levels measured at half-hourly intervals. At 45 minutes the urinary excretion of activity exceeds the input to the tissues and from then on the loss of activity, as measured in the forearm, is exponential. The resultant decay corrected gradient, being simply related to the biological half-life of the chelate used, is then a direct measure of the urinary clearance of activity and the biological half-life ($T\frac{1}{2}$-biol) is the parameter used to express this clearance. The $T\frac{1}{2}$-biol value in minutes is found for each subject from the slope (Fig. 1) of the arm activity/time curves obtained either by using a minicomputer to fit a straight line successively through the later data points until a significant deviation is found or by drawing a best fit line by eye. By implication the longer the biological half-life the less efficient is renal function.

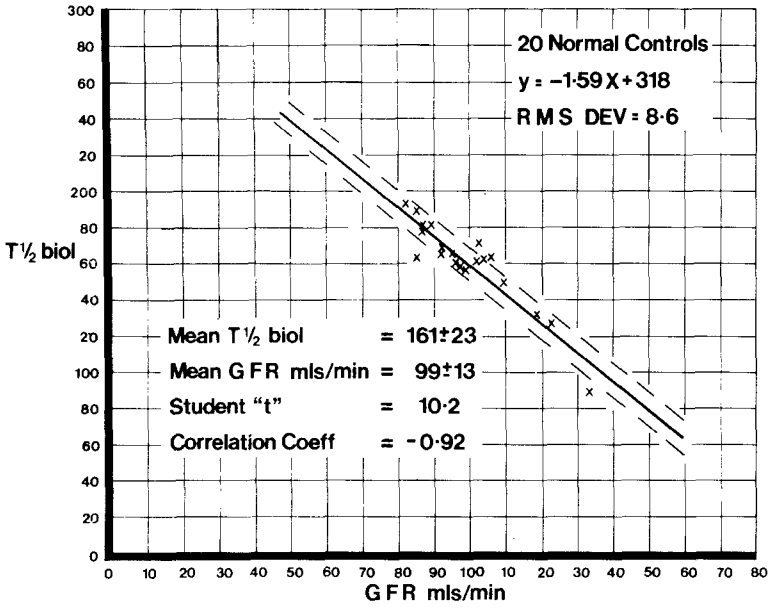
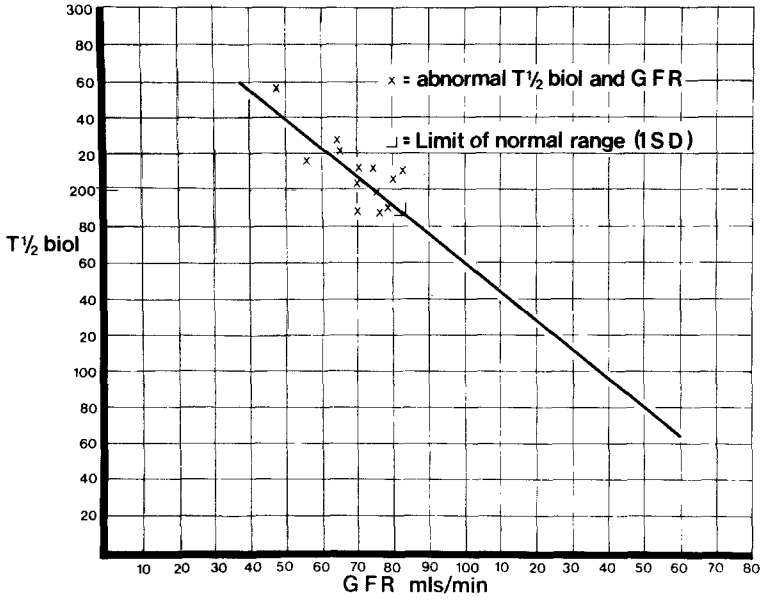
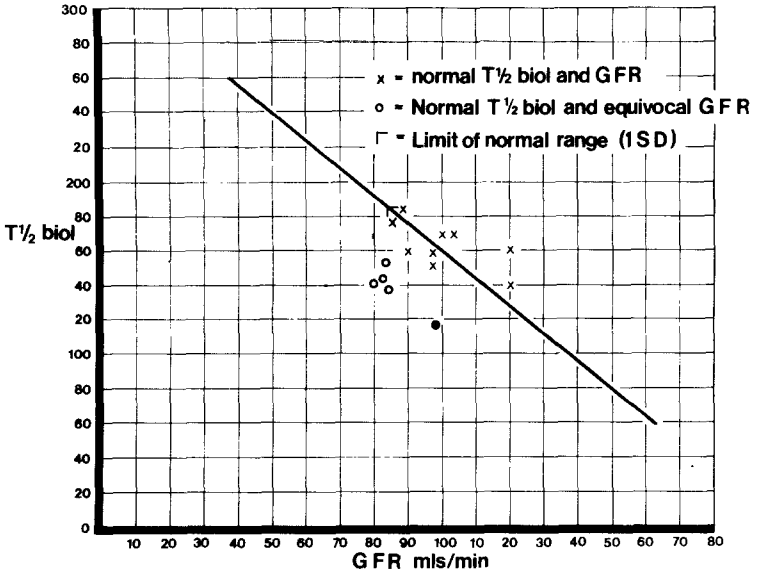


Fig. 2. Relationship between biological half-life ($T\frac{1}{2}$-biol) and glomerular filtration rate (GFR) in normal controls





Figs. 3 and 4. Relationship between biological half-life ($T\frac{1}{2}$-biol) and glomerular filtration rate (GFR) in patients with (x) and without (o) complete bladder emptying

When the $T\frac{1}{2}$-biol values for these twenty control subjects were compared with their simultaneously performed GFR, expressed as mls/min, a high degree of correlation was found (Fig. 2) the coefficient being-0.92 and the error margin taken as the root mean square deviation being 8.6 (depicted by broken lines on either side of the regression line). For these twenty control subjects the upper limit of normal for the $T\frac{1}{2}$-biol, taken as 1 S.D., is 184 min corresponding to a normal lower limit, (1 S.D.), for the GFR measurement of 86 mls/min.

Having established these relative limits of normality the results of single shot GFR and arm count measurements in the series of 28 patients referred for hypertension were compared. Each patient fulfilled the same protocol as the control subjects including a visual check on completeness of bladder emptying.

After a full clinical investigation, including arm count, single shot GFR, IVP and renography, 14 of these patients were fount to have no abnormality and 14 to have evidence of renal disease (Table 1). In the case of the 14 normal patients, 13 had a $T\frac{1}{2}$-biol within normal limits and one was equivocal. Compared to this, GFR estimation showed 8 within normal limits and 6 had equivocal or abnormal filtration rates (Table 2). Of these 6 patients with equivocal or abnormal GFRs, 4 were shown to have incomplete bladder emptying during the collection of urine samples for the GFR, thus introducing a variable source of error in the UV calculation. In this respect there was better correlation between the $T\frac{1}{2}$-biol and the results of the IVP and renograph. In addition among the normal patients the one with poorest correlation between GFR and $T\frac{1}{2}$-biol (Fig. 4, black circle) had demonstrable urinary retention.

Using the regression line established in normal controls (Fig. 2), good correlation between $T\frac{1}{2}$-biol and GFR in the 14 abnormal patients was obtained (Fig. 3) while in five of the 14 normal patients who had incomplete bladder emptying, the correlation was poor (Fig. 4).

CONCLUSION

In conclusion, this external arm counting method of measuring urinary clearance of ^{113m}In and ^{99m}Tc labelled chelates is simple and easy to perform. With an efficiently constructed and shielded chamber counter, errors arising from natural and body background can be minimised and accuracy of counting statistics established. The method does not involve patient discomfort in that no blood or urine sampling is necessary making it especially suited for use in children. It is not affected by loss of label to tissue or incomplete bladder emptying and thus gives a more accurate reflection of renal clearance than serial plasma sampling of 'single shot' GFR estimations when complete bladder emptying is uncertain.

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