A New Approach for Evaluating Differential Renal Function Utilizing a Mathematical Hypothesis.* (29102)

KATHLEEN E. ROBERTS AND C. ALLEN WALL (Introduced by M. Maxwell)
Maumee Valley Research Laboratories, Toledo, Ohio

The recognition that an increasing percentage of hypertensive patients have surgically correctible vascular lesions involving the renal artery has prompted an extensive reappraisal of methods currently employed to evaluate differential renal function. Dissatisfaction with present techniques has resulted in a study of the various methods employed and a critical analysis of the physiological merit of each procedure. Brought sharply into focus was the necessity to know with certainty the total urine excreted from each kidney(1,2). The notable problems attending the total ureteral urine collection have prompted an approach in which mathematical calculation of individual kidney urine flow is permitted when the concentration of a given substance is known from random sampling of urine from each ureter and total bladder collection is obtained. In this paper is presented the physiologic and mathematical hypothesis upon which this approach is based.

Mathematical formula. Theoretically, one can calculate the volume flow from each of 2 portals delivering to a common pool if the total pool volume and the concentrations of a solvent in the pool and in each portal are known. In the case of the kidney if the ureters are assigned as the portals and the total urine from both ureters and bladder is the volume of the collecting pool, it is possible to calculate differential ureteral flow of urine. When the flow is known, individual clearances reflecting renal plasma flow and filtration rate can be calculated. If R_f, and L_f and T_f equal rate of volume flow from right ureter, left ureter and the total urine respectively, and R_c, L_c and T_c equal solute concentration in urine from the right ureter, left ureter and bladder,† then

1. $R_c R_f + L_c L_f = T_c T_f$
2. since $L_f = T_f - R_f$, one can substitute
3. $R_c R_f + L_c(T_f - R_f) = T_c T_f$
   substituting
4. $R_f = T_f \left(\dfrac{T_c - L_c}{R_c - L_c} \right)$

If the solute measured is para-amino hippurate (in these studies radioactive iodinated hippurate was used) and inulin, the mathematical calculation can be done and then the measurement of renal blood flow and glomerular filtration rate can be measured by established technique. However, any solute can be measured except electrolytes which have been shown to show an independent flux across the bladder mucosa.

Experimental background. Fourteen experiments were carried out on anesthetized dogs. Both ureters were exposed, surgically, and all urine collected individually from each ureter. After baseline data were obtained, unilateral renal function was impaired by partial obstruction of the renal artery to one kidney. Within each collection period a small aliquot of urine from each ureter was collected for analysis of inulin and PAH concentration. The individual urine volume from each ureter was measured prior to pooling the 2 volumes as a total bladder specimen. Mathematic calculation of each volume flow from concentration data as well as total volume is then compared with the actual measured individual ureteral volume by utilizing the mathematic equation. The results of these experiments indicate an approximation of the calculated flow within 5%(5). An illustrative example of the results in dogs is

* Supported by USPHS grants.

† It is understood that the volume of all samples taken from the ureteral catheter is added to measured bladder content to obtain total urine (or T_f) during any given period. T_c can be analyzed by direct measurements on appropriate aliquots assuming that B_f is bladder flow and B_c concentration. Then T_c can be calculated as follows: $\dfrac{R_f R_c + L_c L_f + B_f B_c}{\text{Total flow}} = T_c$. In the experiments reported here this method was used.

TABLE I. Illustrative Examples of the Text as Applied to a Typical Patient and a Typical Animal Experiment.

	Measured (ml/min)	Calculated — From radioactivity — Counts (cpm/ml)	Urine flow (ml/min)	Calculated — From inulin — Conc (mg %)	Urine flow (ml/min)
A — Dog 12 (left renal artery partially occluded—indwelling catheter in each ureter which were tied proximal to bladder). Infusion of radioactive hippurate (RAI) and inulin—					
Total	10.5	17,600		212	
Right		16,900	8.2	200	8.0
Left		20,100	2.3	250	2.5
B — Patient M. B. (Partial right renal artery occlusion). Infuse RAI and inulin until urine flow is stable 2-3 hr after inserting bladder and ureteral catheters.					
Total	7.8	7122		85.2	
Right		8020	1.33	102	2.34
Left		6938	6.47	78	5.46

shown in Table I. A summary showing the relationship between calculated and measured urine output is also shown in Fig. 1.

Clinical data. Utilization of this approach in 20 patients following placement of No. 5 ureteral catheters and an individual bladder catheter has been employed. Total urine volume was collected from each ureteral catheter and the bladder. Measurement of individual kidney flow by established physiologic techniques has been compared with data obtained from mathematic substitution as shown in equations 1-4. Consistently accurate results have been obtained(4). This approach is also illustrated in Table I on one typical patient and one dog.

Discussion. A mathematical approach to the diagnosis of unilateral renal disease has been presented and found to be physiologically sound both experimentally and clinically. Intensive application of this approach to clinical diagnosis is currently in progress. Employment of this method to measure split renal function in evaluating the patient with renal artery occlusion affords a major advantage of simplicity for the accurate appraisal of the physiologic performance of each kidney.

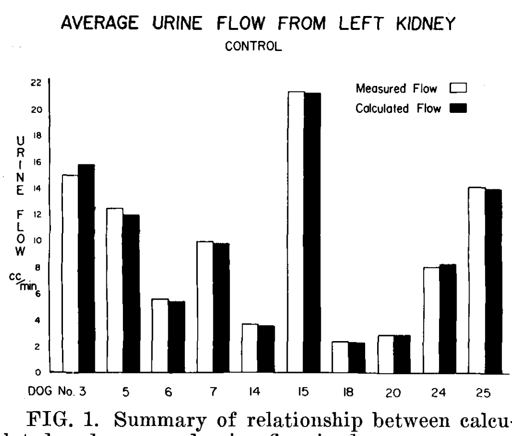

FIG. 1. Summary of relationship between calculated and measured urine flow in dogs.

Summary. A new approach to evaluate differential renal function is presented. It utilizes a theory that if total urine volume is known and concentration of a given substance within each ureter and bladder is known, it is possible to calculate, mathematically, the flow from each kidney. When the flow from each kidney is known, glomerular filtration rate and renal plasma flow can be calculated by the Fick principle. The major advantage of this test is that it obviates leakage, trauma and spasm of ureters which are the major obstacles when large, obstructive catheters are used.

1. Wall, C., Whalen, T. J., *Calif. Med.*, 1963, v98, 142.

2. Stamey, T. A., Needelman, J. J., Good, P. A., Schwentker, F. N., Hendrick, F., *Medicine*, 1961, v40, 347.

3. Peters, J. P., Van Slyke, D. D., *Quantitative Clinical Chemistry*, Williams & Wilkins, Pub.

4. Roberts, K. E., Wall, C. A., *J. Clin. Invest.*, 1963, v42, 971.

5. Wall, C., Roberts, K. E., *Surg. Forum*, 1963, XIV, 109.

Received June 25, 1963. P.S.E.B.M., 1964, v115.