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A Simplified Clinical Procedure for Measurement of Glomerular Filtration Rate and Renal Plasma Flow.*

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The measurement of discrete renal functions by means of "clearance" technics has been of great value in the study of both normal and abnormal kidney physiology. However, the technics[1] required for the accurate measurement of glomerular filtration rate, renal plasma flow and tubular function have several disadvantages, especially when applied to human subjects. Since inaccurate collection of urine constitutes the main source of error, an indwelling catheter, bladder washouts, and 3 or more serial collections of urine are required to yield reasonable accuracy. The amount of time devoted to the collection of blood and urine samples and to the chemical analyses prevents the standard method of measurement of the discrete renal functions from being a simple routine clinical procedure.

Several investigators[2-5] have devised technics which make the collection of urine unnecessary. These methods depend upon the rate of disappearance of inulin (or mannitol) and diodrast (or *p*-amino hippuric acid) from the blood after intravenous injection. These technics require serial blood samples to insure accuracy, and are not suitable for repeated observations at intervals of less than one day.

A simple procedure for the measurement of glomerular filtration rate and renal plasma flow has been devised that requires only a "blank" plasma sample and a single plasma sample for each estimation of the renal functions. This procedure is based on the assumption that, at equilibrium, the amount of a non-metabolized substance injected intravenously per minute should equal the amount excreted by the kidney per minute; *i.e.* providing this is the only excretory route. The measurement of glomerular filtration rate (inulin clearance) simply requires an intravenous infusion pump† that delivers fluid containing a known amount of inulin at a very constant rate, and a sample of plasma obtained after equilibrium between the rates of injection and excretion of inulin and its distribution in the body fluids is established. The clearance is calculated by dividing the amount of inulin injected per minute by the plasma inulin concentration. (Clearance equals

$$\frac{\text{Inulin excreted per minute, mg} \times 100}{\text{Plasma inulin concentration, mg per 100 ml}}$$

and at equilibrium, equals

$$\left(\frac{\text{Inulin injected per minute, mg} \times 100}{\text{Plasma concentration, mg per 100 ml}}\right)$$

The renal plasma flow (*p*-amino hippuric acid‡ clearance) can be measured simultaneously in the same way.

"Priming" intravenous injections of inulin and *p*-amino hippuric acid were given in amounts calculated, on the basis of their estimated volumes of distribution, to achieve plasma levels of 5 and 2 mg % respectively.

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1 Goldring, W., Chasis, H., Ranges, H. A., and Smith, H. W., *J. Clin. Invest.*, 1940, **19**, 739.

2 Barnett, H. L., PROC. SOC. EXP. BIOL. AND MED., 1940, **44**, 654.

3 Findley, T., and White, H. L., PROC. SOC. EXP. BIOL. AND MED., 1940, **45**, 623.

4 Newman, E. V., Bordley, J., III, and Winternitz, J., *Bull. Johns Hopkins Hosp.*, 1944, **75**, 253.

5 Landowne, M., and Alving, A. S., *J. Lab. Clin. Med.*, 1946, **31**, 453.

† The infusion pump used in these experiments consisted of a worm-driven rod that pushed on the plunger of a 50 ml syringe. This is excellent for short experiments, but not for any study extending over 3 or 4 hours.

‡ Since *p*-amino hippuric acid is acetylated by man it is necessary to determine "total" *p*-amino hippuric acid after hydrolysis.

TABLE I.

Glomerular Filtration Rate and Renal Plasma Flow as Measured by Infusion Pump Technic (A) and by Usual Clearance Technic (B).

Subject	Surface area (sq.m.)	Exp.	Time after start of infusion (min.)	Plasma inulin (mg %)	Glomerular filtration rate (ml/min) A	Glomerular filtration rate (ml/min) B	Plasma PAH (mg %)	Renal plasma flow (ml/min) A	Renal plasma flow (ml/min) B	Filtrate fraction % A	Filtrate fraction % B
An	1.80	1	70	4.44	130	129	1.62	659	618	19.8	20.9
			85	4.44	130	127	1.72	619	598	21.0	21.2
			99	4.47	129	122	1.78	598	570	22.6	19.9
					130	126		625	595	20.7	21.1
Br	1.93	2	67	5.29	145	161	1.46	899	942	16.1	17.1
			80	5.08	151	124	1.50	877	722	17.2	17.2
			90	5.19	148	155	1.56	835	806	17.7	19.2
					148	147		870	857	17.0	17.8
Ca	2.10	3	70	5.52	148	149	1.67	774	740	19.2	20.1
			83	5.52	148	152	1.68	770	798	19.2	19.1
			97	5.52	148	135	1.68	770	734	19.2	18.4
					148	145		771	757	19.2	19.2
		4	64	5.11	150	140	1.86	754	681	19.9	20.6
			80	4.87	158	152	1.79	784	742	20.2	20.5
			93	4.90	156	149	1.86	754	668	20.7	22.3
					155	147		764	697	20.3	21.1

The sustaining infusions delivered by the pump to maintain these levels were calculated on the basis of the estimated renal functions. Under these conditions, equilibrium was achieved with inulin shortly after 60 minutes and with *p*-amino hippuric acid within 30 minutes.

Glomerular filtration rate and renal plasma flow, as measured by the technics just described, were compared with simultaneous measurements by the usual method involving 3 serial urine collection periods. Four experiments in 3 normal young adult male subjects are summarized in Table I. Excellent agreement between the 2 technics was obtained when the averages of 3 periods are considered. The infusion technic, however, appears to yield more consistent individual values. The variations noted among the serial standard clearances are presumably the result of inaccuracies in urine collection.

Comment. A simple technic for the measurement of glomerular filtration rate and renal plasma flow has been devised. It requires a constant intravenous infusion pump and a minimum of blood samples and chemical analyses. It does not require urine collection and for this reason is simpler and more accurate. The method can be utilized for repeated serial observations during 24-hour periods.

Whether this technic can be adapted to the measurement of the maximal rate of tubular secretion or reabsorption of substances excreted only by the kidneys has not yet been established. It will also be necessary to determine how accurately the method can reflect acute changes in renal function and the effect of acute changes in the volume of body fluid compartments upon the measurements.

Finally, it may be noted that this method could be applied to the measurement of the "clearance" of other substances by other organs, provided the substance under study is excreted or metabolized only by the organ in question.

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Reaction of the Rat Peritoneum to Acid Colloidal Pigments.

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It is now well known that many types of foreign particulate matter are rapidly removed from the peritoneal cavity; this is particularly true of substances in acid colloidal form. Part of such a material is discharged into the lymph stream while the remainder is taken up by macrophages from adjacent connective tissues. MacCallum[1] and others have studied the free cells which appear in peritoneal fluid under these conditions, but most investigators have devoted but little attention to the peritoneum itself. In these investigations, an attempt is made to follow changes in the peritoneum and to note differences in its regional response to various acid-colloidal pigments.

Materials and Methods. Four groups of inbred albino rats, 67 in all, were used in these experiments, each group being composed of individuals of nearly the same age (within one week); all animals weighed 150-190 g at the time of the first injection. One group was intraperitoneally injected with each of the following pigments: trypan blue, Biebrich's scarlet, India ink, and Chlorazol black E (Erie black GXOO). These materials were made up as 2% solutions in distilled water. Animals were given daily injections of 1-3 cc over periods of time ranging from 1-75 days; they were killed 18-24 hours after the final injection. Tissues were fixed in Bouin, Helly or Regaud's solutions, dehydrated in alcohol

[1] MacCallum, W. G., *Bull. Johns Hopkins Hosp.*, 1903, **14**, 105.