THE DISTRIBUTION AND EXCRETION OF INULIN IN MAN

by

HUGH MILLER, M.B.,Ch.B.

Thesis presented for the Degree of Doctor of Medicine, University of Edinburgh.

April 1941.

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I. INTRODUCTION.

When Sir William Bowman demonstrated the continuity between the glomerulus and the uriniferous tubule in 1842 the unity of the nephron as a glomerulo-tubular unit was once and for all established. From the demonstration of this anatomical fact arose the vitalistic and mechanical schools of renal physiology with their opposing theories, which have for so long been hotly contested.

Despite the divergence of their views both schools were confronted by a common obstacle, namely, the study and measurement of the activity of the glomerular and tubular portions of the nephron separately. The methods which have been designed to do this are legion, and many are masterpieces of ingenuity and physiological technique. Particularly worthy of mention is the work of A.N. Richards and his co-workers, which was carried out principally on the frog, in which the glomerulus and tubule receive a separate blood supply, and are readily accessible to micro-dissection technique. Much of our present conception of renal function in man is based on this work. Studies of the mammalian kidney have presented much greater difficulties on account of its/

its complex structure. The methods which have been used consist of attempts to remove the medulla, thus cutting out the loops of Henle, observing the deposits of various dyes injected during life in fixed microscopic preparations, a few direct microscopic observations of the excretion of fluorescent substances in the living intact animal, and perfusion experiments with poisoning of the tubule cells with cyanide.

From these animal experiments it was found that an ultra-filtrate of the plasma is formed in the glomerulus. Certain substances present in this filtrate are absent from the bladder urine indicating that they have been reabsorbed by the tubules. That the tubules are capable of active secretion of certain substances into their lumen has also been demonstrated.

Though affording useful and interesting information these methods were not applicable to studying deranged renal function in man. This at best could be expressed by the ability of the kidney to reabsorb water in producing a concentrated urine, or by measuring the rate of excretion of some known substance. The obstacles in the way of conducting such studies in man, and the means whereby they may be overcome cannot be expressed

better/

better than to quote the words of Homer Smith (1939), who with his associates has been largely responsible for evolving a means of measuring independently the functions of the constituent parts of the mammalian nephron:- "By the filtration-reabsorption mechanism of the nephron postulated above, the glomerular filtrate undergoes a variable degree of concentration by the reabsorption of water. It is thus impossible to determine directly from the composition of the blood and urine whether the excretion of any one of several substances involves filtration alone, or filtration plus either tubular reabsorption or tubular excretion. Once tubular excretion was admitted as a possibility, it was clear that the unravelling of the problems of renal function could not advance beyond the stage of speculation, whether nephrons were investigated individually or en masse, until there was available at least one substance which was known for certain to be neither excreted nor reabsorbed by the tubule cells. Once such a substance had been discovered it could be used as a standard of reference with which to measure the tubular reabsorption of water, and hence to examine the mechanism of excretion of any other substance". For the discovery of this substance/

substance we are indebted to the work of Homer Smith (1937).

He started from the known fact that glucose was neither reabsorbed by the tubules of the phlorizinised kidney, nor excreted by the aglomerular kidneys of certain fish. Hence he decided to investigate the mode of excretion of certain non-metabolised sugars. These he considered the most suitable substances for measuring the tubular reabsorption of water for, though inert, they are copiously excreted by the kidney. Renal clearances were carried out using sucrose, xylose, raffinose and inulin on various species including dogfish, dog and man.

The renal clearance of a substance may be defined as "the virtual volume of blood which is completely cleared of that substance by the kidneys in one minute's time". It is given by the expression UV/B, where U equals the concentration of that substance in the urine, V equals the number of c.c. of urine formed per minute, and B equals the concentration of the same substance in the blood. Since U x V equals the quantity of the substance excreted per minute, if one divides this quantity by the amount B, contained in each volume of blood, the result gives the virtual volume of blood

cleared/

cleared, or clearance. Conversely, it may be defined as "the minimum volume of blood required to furnish the quantity of substance excreted in the urine in one minute's time".

The clearance of a substance which is freely filterable through the glomerular membrane in the same concentration as in the blood, and is neither reabsorbed nor excreted by the tubules, is a measure of the tubular reabsorption of water and is at the level of glomerular filtration. Homer Smith (1927) has discussed the criteria with which a substance must comply to be a measure of glomerular filtration, both generally and with special reference to inulin, which, of all the substances examined, appeared to be the most suitable for measuring glomerular filtration. These criteria may be summarised as follows:-

1. Any substance, X, to be completely filterable through the glomeruli must be completely filterable from the plasma through artificial membranes impermeable to plasma proteins but permeable to smaller molecules.

2. As presumptive evidence against tubular excretion, X should not be excreted by the aglomerular fish/

fish kidney.

3. (a) The rate of excretion of X (UV) should increase over wide limits in simple, direct proportion to the plasma concentration (P); i.e. the clearance UV/P, should be independent of the plasma concentration. This condition in a large measure excludes the possibility of tubular excretion and tubular reabsorption.

(b) Where 3(a) cannot be demonstrated, because of inconstancy in the rate of filtration itself, it is of equal force to show that the clearance of X is constant, relative to the clearance of some other substance, at various plasma levels of X.

4. Assuming that adequate doses of phlorizin completely block the tubular reabsorption of glucose, then in the phlorizinised animal the clearance of X should be equal to the glucose clearance. (This, of course, is not evidence that phlorizin does not block the tubular excretion or reabsorption of X itself).

5. Where the simultaneous clearance of two or more substances are identical under a wide variety of conditions (plasma level, urine flow, etc.), this may be taken as evidence that both substances are excreted/

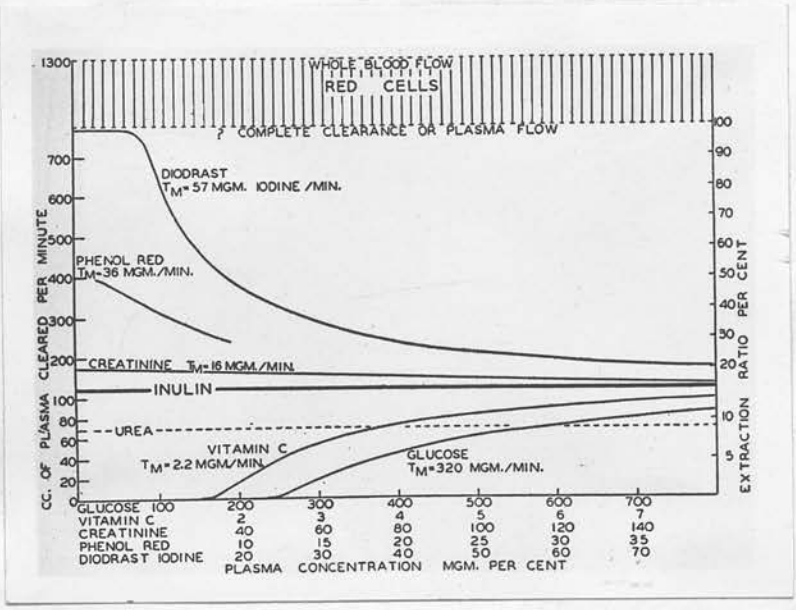


Fig. 1. Diagrammatic summary of excretion of various types of compounds by the human kidney. (From Homer W. Smith, "Studies in the Physiology of the Kidney, 1939. Porter Lecture Series IX. University of Kansas. p.18).

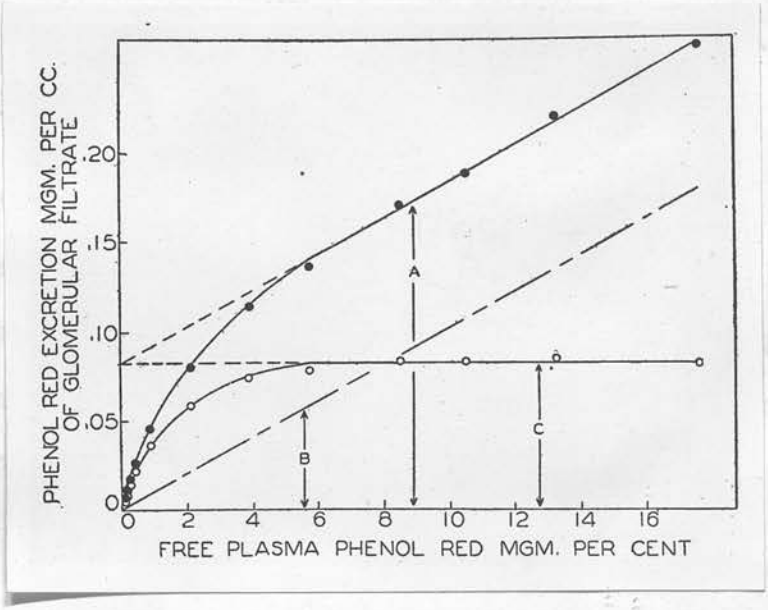


Fig. 2. Filtration and tubular excretion of phenol red in the dog. (A) total phenol red excreted; (B) phenol red filtered; (C) phenol red excreted by the tubules. The above data are from a single experiment. The rate of excretion of dye by the tubules does not increase in direct proportion to P, but approaches and ultimately reaches an upper, maximal, limit. For this reason the total excretion by tubules and glomeruli, UV, does not increase inproportion to P; i.e., the clearance, UV/P, is depressed as the plasma level of dye is raised above a critical value. (From Homer W. Smith, "The Physiology of the Kidney. 1937. Oxford Univ. Press. p.85)

excreted by the glomeruli, without interference from the variable factors of tubular reabsorption or tubular excretion.

6. Where a completely filterable substance is excreted in part by tubular activity, the clearance of that substance when depressed by elevating the plasma level should approach the clearance of X as the limiting asymptote.

It has been found that inulin clearance is at the level of glomerular filtration. From this it will be seen that substances which have a clearance higher than inulin are secreted by the tubules, whereas these with a clearance lower than inulin, are either reabsorbed by the tubules, or diffuse through the tubules. The majority of the substances whose mode of excretion has been investigated appear to be either secreted or re-absorbed by the tubules at a fairly constant rate once their blood concentration has reached a certain critical level. (Fig.2) It is for this reason that, when the blood concentration of these substances is elevated, their clearance is either depressed or raised towards the level of inulin clearance and the glomerular filtration rate. (Fig.1) Another

interesting/

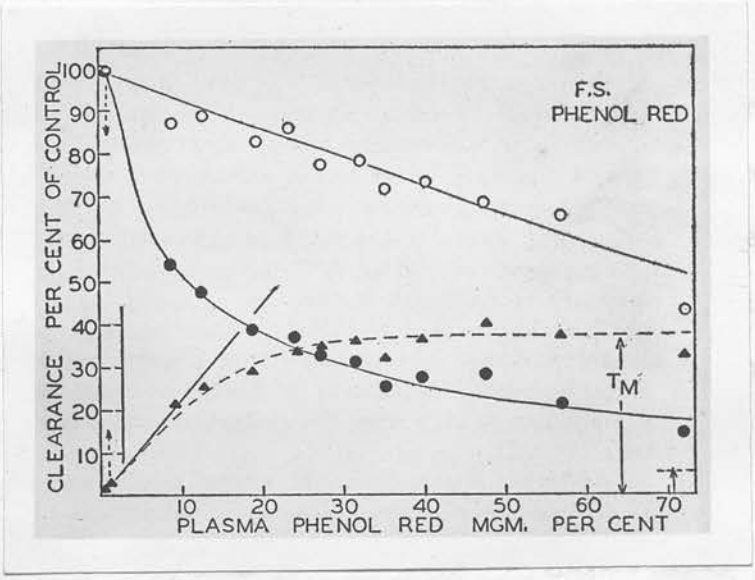


Fig. 3. Effect of elevated plasma concentration of phenol red on the self-clearance (dots) and on the diodrast clearance (circles), all clearances being expressed in terms of the average of two control periods at low plasma levels of phenol red. (From Homer W. Smith, Wm.Goldring and Herbert Chasis. J. Clin. Invest. 1938, 17, 261)

interesting point in regard to the behaviour of the tubules is that if, while they are excreting one substance, another substance is presented to them which is likewise secreted by the tubules, the normal amount of one or other of these substances which is secreted by the tubules is lowered. (Fig. 3).

Knowing the amount of glomerular filtrate from the inulin clearance, it is quite easy to calculate from the clearance of any other substance which is secreted by the tubules, the amount of that substance secreted exclusively by the tubules, e.g.:- if the inulin clearance were 120 c.c./min., the clearance of a substance X were 160 c.c./min., and the blood concentration of X were 10 mg./100 c.c., then the amount of X secreted per minute by the tubules equals:-

$$\frac{\text{Clearance of X} - \text{Clearance of Inulin}}{100} \times \text{Blood concentration of X}$$

$$= \frac{160 - 120}{100} \times 10 = 4 \text{ mg./min.}$$

This gives an accurate measure of the amount of work being performed by the tubules and is known as "tubular excretory mass" or T.M. (Fig. 2).

As/

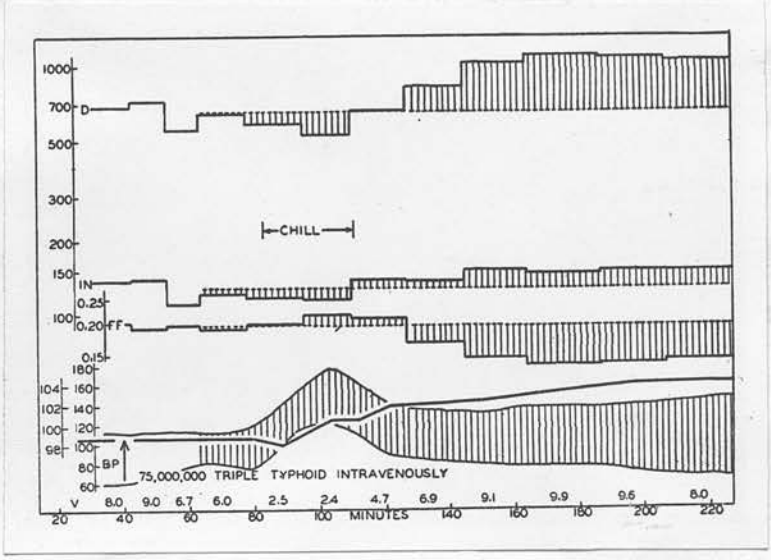


Fig. 4. Action of T.A.B. vaccine on effective renal plasma flow, (D = diodrast clearance in c.c. per minute), filtration rate(IN = inulin clearance in c.c. per minute), filtration fraction (FF = inulin/diodrast clearance ratio), blood pressure (BP in mm. Hg) and urine flow (V in c.c. per minute). (From Homer W. Smith. "Studies in the Physiology of the Kidney. 1939. Porter Lecture Series IX. University of Kansas. p.81).

As a further development of this work, a substance was sought which would be completely removed from the blood in one circulation through the kidney. The clearance of this substance would be a measure of the plasma flow through the kidney. The organic iodine compound "Diodrast", used in intravenous pylography, has been found to fulfil these requirements. By studying plasma flow and glomerular filtration together much useful information has been obtained about the behaviour of the renal vaso-motor system. (Fig.4)

I have called attention to the preceding methods of studying kidney function, not so much on account of their direct bearing on this thesis, but for the purpose of emphasising the importance of the accurate measurement of glomerular filtration by inulin clearance, which is the main theme of this thesis, and which forms a base line for an entirely new conception of renal physiology. Inulin clearance itself and in conjunction with the clearances of other substances enables us to make accurate measurement of (1) the volume of glomerular filtrate formed, (2) the/

(2) the exact amount of various substances which the tubules are capable of secreting or re-absorbing, (3) the amount of substances which diffuse back into the circulation from the tubules during their passage through them, (4) the state of the renal vaso-motor system.

No one can deny that such accurate measurements of renal function are of greater scientific and clinical value than the existing tests of renal function in general use; therefore, though they present greater technical difficulties, they should not be allowed to remain as experimental procedures, but every effort should be made to simplify the methods of carrying them out for clinical use, so that they may become part of the every-day routine of investigating any case of suspected renal disorder.

I was so impressed with the possibilities of this new method of studying renal function in man that I decided, in October 1938, to conduct some experiments on similar lines. My ultimate objective was to have been a study of the vaso-motor mechanism of the kidney, as all previous investigations/

investigations indicated a marked constancy of the rate of glomerular filtration. Unfortunately my observations never reached this stage as they were interrupted by the onset of the war. I am glad to state, however, that this problem has since been elucidated by Chasis, Ranges, Goldring and Homer Smith (1938), who have demonstrated the presence of a local automatic regulating mechanism in the kidney, which maintains the rate of glomerular filtration constant, irrespective of the renal blood flow. This idea is certainly very revolutionary, especially to those who have based their ideas of renal function in man on experiments in the frog, where the glomeruli exhibit functional intermittency and operate in relays.

At the start of my work it was necessary to perfect a technique for performing inulin clearances, which form the basis of all other observations of this nature. Hence this thesis is largely concerned with a study of the methods of carrying out this procedure, and the manner in which inulin is handled by the human body.

The following aspects have been studied:-

1. Purification and preparation of inulin for intravenous injection.

2./

2. Quantitative methods for the estimation of inulin.
3. The distribution of inulin in the human body.
4. Inulin clearance.
5. Comparison of simultaneous urea and inulin clearances.
6. The mode of excretion of inulin.

1. The Purification and Preparation of Inulin for Intravenous Injection.

(a) Purification.

Inulin unless specially treated contains toxic substances which cause pyrexial upsets. Crude inulin may be obtained from British Drug Houses Ltd. I have treated two 500 gm. lots of crude inulin by the method recommended by Homer Smith et al. (1938), and obtained satisfactory non-toxic inulin, suitable for intravenous injection in man. There was a loss of about 30% by this process. In preparing a subsequent lot of 1000 gm. I discovered that one must pay special attention to the brand of charcoal used. With this particular batch "B.D.H. decolorising charcoal" was used, and so powerful was its action that the entire lot was completely hydrolysed to fructose. Merck's charcoal has been found to be satisfactory.

It is advisable that inulin should be prepared in fairly large quantities, as about 30 gm. are used for each experiment, and each lot prepared must be tested clinically for toxicity. On account of the difficulties of handling such large quantities/

quantities as 1000 gm. with ordinary laboratory apparatus, I had the later lots prepared by British Drug Houses Ltd. in 2000 gm. batches. This inulin was non-toxic, and though it cost about twice the amount of the crude inulin, it was probably more economical than preparing it oneself, when one considers the loss and the cost of the reagents.

(b) Preparation of inulin for injection.

The purified inulin is stored dry in solid form, but recently a method (Homer Smith, personal communication) of storing it in liquid form ready for use has been evolved.

Inulin is administered by intravenous injection. It is sparingly soluble and to produce a suitable blood concentration it is usually injected warm as a super-saturated solution. Some workers give a large priming dose followed by a slow infusion to maintain the concentration. This requires rather an elaborate apparatus to regulate the temperature of the inulin solution being injected. In my experiments I have given a single large dose.

The/

The solution is prepared by dissolving in distilled water the approximate quantity of inulin necessary to produce the required concentration. The solution is sterilised by boiling it for 5 minutes in a conical flask lightly plugged with cotton wool. The temperature is allowed to fall to body temperature, when the solution is ready for injection.

The injection is performed with a two-way syringe, so that the volume ~~of~~ given can be measured accurately. The cotton wool plug is removed from the flask, and a rubber bung inserted, which is bored with two holes. Through one hole a piece of glass tubing passes to the bottom of the flask. The end of the glass tubing projecting through the bung is connected by rubber tubing to the side tap of the syringe. It is thus possible to aspirate from the flask and inject into the subject accurately measured volumes of the inulin solution. When it is desirable to know the exact amount of inulin administered, the inulin concentration of a sample of the solution injected is estimated and the amount calculated from the volume of the injection.

2. Quantitative Methods for the Estimation of Inulin.

Inulin, which occurs in nature as dahlia starch, is a polysaccharide consisting of thirty-two hexose molecules, mostly fructose. It is estimated quantitatively as fructose.

In blood estimations difficulty arises in differentiating fructose from glucose, which gives the same reactions by the quantitative methods usually employed. There are two ways of overcoming this difficulty. In the first of these the blood glucose is estimated by Folin's method, and following hydrolysis of the inulin to fructose the total amount of reducing substance is estimated. From this the amount of glucose is subtracted, giving the amount of fructose or inulin. In the second method, which is designed to overcome the errors associated with a differential calculation, the glucose is removed from the blood by fermentation with yeast prior to hydrolysis and the inulin then estimated as fructose.

When I commenced my studies of inulin one or other of the two methods mentioned in the above paragraph were in general use. In view of their complexity/

complexity and possible sources of error, I adapted Herbert's diphenylamine method for the estimation of fructose in the presence of glucose (1938) to the estimation of inulin, at the suggestion of Dr C.P.Stewart. Since that time at least two papers have been published giving improved methods for the direct estimation of fructose in the presence of glucose, as a method of estimating inulin.

The method of all my experiments was absolutely identical with that of Herbert for the estimation of fructose. All blood estimations were carried out on plasma. The proteins were precipitated by the zinc hydroxide method of Somogyi (1930). To 2 c.c. of the filtrate so obtained were added 6 c.c. of "acid-alcohol-diphenylamine reagent", in a Pyrex tube. The tube was placed in a boiling water bath for exactly 15 minutes. It was then removed and rapidly cooled, and the volume made up to 10 c.c. with absolute alcohol. The blue colour which had developed was then compared in a colorimeter with that produced by a standard fructose solution (10 or 20 mg./100 c.c.) which had been treated in exactly the same way. Both urines and blood were estimated by this method.

The method has certain great advantages over the two previous ones. The breakdown of the inulin to fructose, and the development of the blue colour reaction take place at the same time during hydrolysis with the "acid-alcohol-diphenylamine reagent", thus eliminating one step from the estimation. At the end of 15 minutes, 88% of the colour due to fructose has developed. This develops in a rectilinear fashion. The colour due to glucose at this time is negligible unless there is a very marked hyperglycaemia. Thus it is unnecessary to remove the glucose from the blood by fermentation with yeast. The accuracy of the method is ± 1 mg./100 c.c.

Of the two papers mentioned above, on new methods of estimating inulin, one by Alving, Rubin and Miller (1939) deals with a diphenylamine method, and this method seems since to have come into fairly general use among workers on inulin clearance. Their method is designed to give a high degree of accuracy at low blood inulin levels. Cadmium precipitation is used, and the proportions of the various reagents differ considerably from the method of Herbert. The colour develops during

60/

60 minutes in a boiling water bath, and the comparison of the intensity of the colours is carried out in a photometer. Using this method it is essential to remove the glucose by fermentation with yeast for estimating concentrations below 30 mg./100 c.c., thus losing one of the greatest advantages of the new method, whose principal object is to simplify the procedure by estimating the fructose in the presence of glucose.

As a result of this method, inulin clearance is rapidly passing from the stage of a laboratory experiment to a routine clinical procedure, as it can now be performed with a single injection of 10 gm. of inulin, instead of a large priming injection followed by a slow sustained infusion.

The evolution of this method is of interest. The blue colour reaction which fructose gives with diphenylamine was first observed as long ago as 1885 by Ihl and Pechman. This formed the basis for Van Creveld's method of estimating fructose. The blue colour which developed was, however, insoluble in water, and had to be dissolved in an organic solvent. Herbert obviated this difficulty by the addition of an excess of ethyl alcohol.

The/

The second of the newly evolved methods for the quantitative estimation of inulin is that of K.Steinitz (1939) which uses Roe's modification of Seliwanoff's resorcinol method for estimating fructose in the presence of glucose.

3. Distribution of Inulin in the Human Body.

(a) Method.

A carefully measured volume of inulin is injected intravenously by the method previously described. An interval is allowed to elapse so that the inulin may become distributed throughout the body. This is usually about 30 minutes. At the end of that time the subject empties his bladder and a sample of blood is taken. The volume of urine passed is measured and a sample is taken for estimation.

Estimations are now carried out on a sample of the inulin solution which was injected, on a sample of oxylated venous blood, and on a sample of the urine.

From these data the amount of inulin injected and excreted in the urine can be calculated. By subtracting one from the other, the amount remaining in the body is arrived at. The blood sample gives the plasma-~~and~~ inulin concentration when the body contains this amount of inulin, and by dividing the first by the second we get the volume of fluid in which the inulin remaining in the body is dissolved, i.e. the distribution of inulin in the human body. This is expressed as a fraction of

the/

the body weight.

(b) Results.

The fraction of the body weight in which inulin is distributed was measured in ten subjects selected at random from hospital patients. The results of these observations are given in Table I. They suggest that inulin was distributed in the extracellular fluids of the body, and compare favourably with those obtained by Leviates (1935) using sucrose. Inulin is completely inert in the human body, totally recoverable and non-toxic and thus appears to be a very suitable substance for measuring the volume of the extracellular fluids of the body clinically.

Table I.

Analysis of Distribution of Inulin in Human Body per Body Weight in Ten Subjects.

Subject	Distribution of inulin/body weight.	Reciprocal	Deviation of each observation from mean Mean = 0.214	Square of each deviation from mean
Mr H.S.	1/7	0.143	-0.071	5.041
Mrs P.	1/6.8	0.147	-0.067	4.489
Mr R.B.	1/5.3	0.189	-0.025	0.625
Mr L.	1/4.8	0.208	-0.006	0.036
Mr S.	1/4.5	0.222	+0.008	0.064
Mr M.	1/4.4	0.227	+0.013	0.169
Mr A.McL.	1/4.2	0.238	+0.024	0.576
Mr F.C.	1/4.1	0.244	+0.03	0.900
Mr D.W.	1/4.1	0.244	+.0.03	0.900
Mr A.A.	1/3.6	0.278	+0.064	4.096
		2.140	0.	16.896

1. Mean = 1/4.67 = 0.214.

2. Range = 1/7 - 1/3.6 = 0.143 - 0.278.

3. Symetry = 6/4.

4. Standard deviation σ $= \sqrt{\frac{\text{Sum of squared deviation from mean}}{n - 1}}$

$= \sqrt{\frac{16.896}{10-1}}$

$= 0.013.$

5. Coefficient of variation $= \frac{\sigma}{\text{mean}} \times 100$

$= \frac{0.013}{0.214} \times 100$

$= 6.1\%$

4. Inulin Clearance.

(a)Method.

Urine specimens are collected over accurately measured periods. Blood samples are withdrawn at the exact "mid-point" of those periods. This is especially important when using foreign substances whose concentration is falling rapidly, and presents difficulties in nervous subjects who may be unable to pass urine with clockwork regularity. It was my chief difficulty using students as subjects since they appear to be very introspective. If blood specimens are taken at random and the concentration plotted logarithmically against time, the "mid-point" concentration can be worked out by interpolation. This appears to be a better method although I have not used it in these experiments. I would nevertheless recommend its use as it is particularly exasperating to see the labour of an experiment going to waste because the subject is nervous and unable to micturate at the required time. I did not consider that catheterisation and washing out of the bladder with saline was a justifiable procedure to/

to overcome this difficulty in a clinical experiment despite the fact that it was used by American workers. A method of carrying out inulin clearance in infants, designed to obviate this difficulty, has been devised recently by Barnett (1940). The method utilises the rate of fall of blood concentration following a single injection as a measurement of inulin clearance and only blood samples are required.

In the following experiments the calculation of inulin clearance is performed as described in the Introduction.

Results. 18 clearance estimations were carried out in 10 subjects, and these results are given in Table II. A study of this will show that there is a wide variation and they are somewhat disappointing when compared with the very uniform figures obtained by Homer Smith. In 12 of these observations data of the subjects' surface area were available and these clearances were standardised to 1.73 sq. metres. The effect of this correction can be studied by comparing Tables III and IV. There was very little difference between them and the correction/

Table II.

Analysis of Eighteen Inulin Clearances in Ten Subjects.

Subject	Eighteen observations of inulin clearance	Deviation of each observation from mean. Mean = 116.2	Square of deviation from mean
Mrs L	66.0	- 50.2	2520.0
Mr J.B.	71.3	- 44.9	2010.0
Mr F.C.	86.8	- 29.4	863.0
Mr S.	87.5	- 28.7	820.0
Mr M.	95.0	- 21.2	449.0
Mr J.B.	95.1	- 21.1	445.0
Mr H.S.	97.6	- 18.6	345.0
Mr H.S.	110.7	- 5.5	30.3
Mr J.B.	111.2	- 5.0	25.0
Mr H.S.	118.0	+ 1.8	3.2
Mr J.L.	121.5	+ 5.3	28.1
Mr J.L.	128.6	+12.4	152.0
Mrs P.	134.3	+18.1	328.0
Mr H.S.	137.0	+20.8	432.0
Mr J.L.	147.5	+31.3	980.0
Mr H.S.	151.0	+34.8	1210.0
Mr A.A.	158.0	+41.8	1740.0
Mr R.B.	174.0	+57.8	3350.0
	2091.0	x 0.5	15730.6

x As only one decimal point is taken, the sum of the deviations may not be exactly zero.

1. Mean = 116.2
2. Range = 66-174
3. Symetry = 9/9
4. Standard deviation $\sigma = \sqrt{\frac{\text{Sum of squared deviation from mean}}{n-1}}$

$$= \sqrt{\frac{15730.6}{18-1}} = 30.2.$$

5. Coefficient of variation $= \frac{\sigma}{\text{mean}} \times 100 = \frac{30.2}{116.2} \times 100$

$$= 25.9\%$$

Table III.

Analysis of Twelve Inulin Clearances in Eight Subjects corrected to 1.73 sq. metres surface area.

Subject	Twelve observations of inulin clearance reduced to 1.73 sq.m.	Deviation of each observation from mean. Mean = 128.1	Square of each deviation from mean.
Mrs L.	82.0	- 46.1	2130.0
Mr F.C.	85.0	- 43.1	1860.0
Mr S.	87.5	- 40.6	1650.0
Mr M.	102.4	- 35.7	660.0
Mr H.S.	110.0	- 18.1	327.0
Mr H.S.	125.0;	- 3.1	9.6
Mr H.S.	134.0	+ 5.9	34.8
Mrs P.	149.0	+ 20.9	436.0
Mr H.S.	155.0	+ 26.9	723.0
Mr A.A.	155.0	+ 26.9	723.0
Mr H.S.	171.0	+ 42.9	1840.0
Mr R.B.	181.0	+ 52.9	2790.0
	1536.9	x 0.3	13163.4

x As only one decimal point is taken, the sum of the deviations may not be exactly zero.

1. Mean = 128.1
2. Range = 82-181.
3. Symetry = 6/6.
4. Standard deviation $\sigma = \sqrt{\frac{\text{Sum of squared deviation from mean}}{n - 1}}$

$$= \sqrt{\frac{13163.4}{12.1}}$$

$$= 36.1.$$

5. Coefficient of variation $= \frac{\sigma}{\text{mean}} \times 100$

$$= \frac{36.1}{128.1} \times 100$$

$$= 28.3\%$$

Table IV.

Analysis of Twelve Inulin Clearances in Eight Subjects.

Subject	Twelve observations of inulin clearance	Deviation of each observation from mean. Mean = 118	Square of each deviation from mean.
Mrs L	66.0	-52.0	2700.0
Mr F.C.	86.8	-31.2	970.0
Mr S.	87.5	-30.5	930.0
Mr M.	95.0	-23.0	530.0
Mr H.S.	97.6	-20.4	415.0
Mr H.S.	110.7	- 7.3	53.3
Mr H.S.	118.0	0.0	0.0
Mrs P.	134.3	+16.3	265.0
Mr H.S.	137.0	+19.0	360.0
Mr H.S.	151.0	+33.0	1090.0
Mr A.A.	158.0	+40.0	1600.0
Mr R.B.	174.0	+56.0	3150.0
	1415.9	x 0.9	12063.3

x As only one decimal point is taken, the sum of the deviations may not be exactly zero.

1. Mean = 118
2. Range = 66-174.
3. Symetry = 5/6
4. Standard deviation σ $= \sqrt{\frac{\text{Sum of squared deviation from mean}}{n - 1}}$

$$= \sqrt{\frac{12063.3}{12.1}} = 33.1$$

5. Coefficient of variation =

$$\frac{\sigma}{\text{mean}} \times 100 = \frac{33.1}{118} \times 100$$

$$= 28.1\%.$$

Table V.

No. of subjects	No. of observations	Range	Mean
10	18	108	116.2
8	12	108	118.0
8	12	99	128.0
Mr H.S.	5	53	122.9
Mr J.B.	3	40.2	92.5
Mr J.L.	3	26.5	132.5

correction only appears to have slightly raised the mean as most of the subjects investigated seem to have had a surface area slightly less than the standard.

The number of observations from single subjects is small consisting of two sets of three observations and one of five, (Table V) but it seems significant that the variation is not quite so great as in comparing the clearances in a series of different subjects.

Though much of the variation may be due to the difficulty experienced by subjects in completely emptying the bladder at a fixed time, I am of the opinion that this is not the entire cause of the variation, as the "measurements of the fraction of body weight in which the inulin is distributed" which also involve the collection of urine specimens are remarkably constant.

Many of the subjects were not physiologically normal. From the experiences of other workers I was doubtful about the toxicity of inulin and consequently the initial observations were made on subjects with advanced malignant disease in the Eastern General Hospital. This appears to be a likely cause of the variation in the groups of subjects.

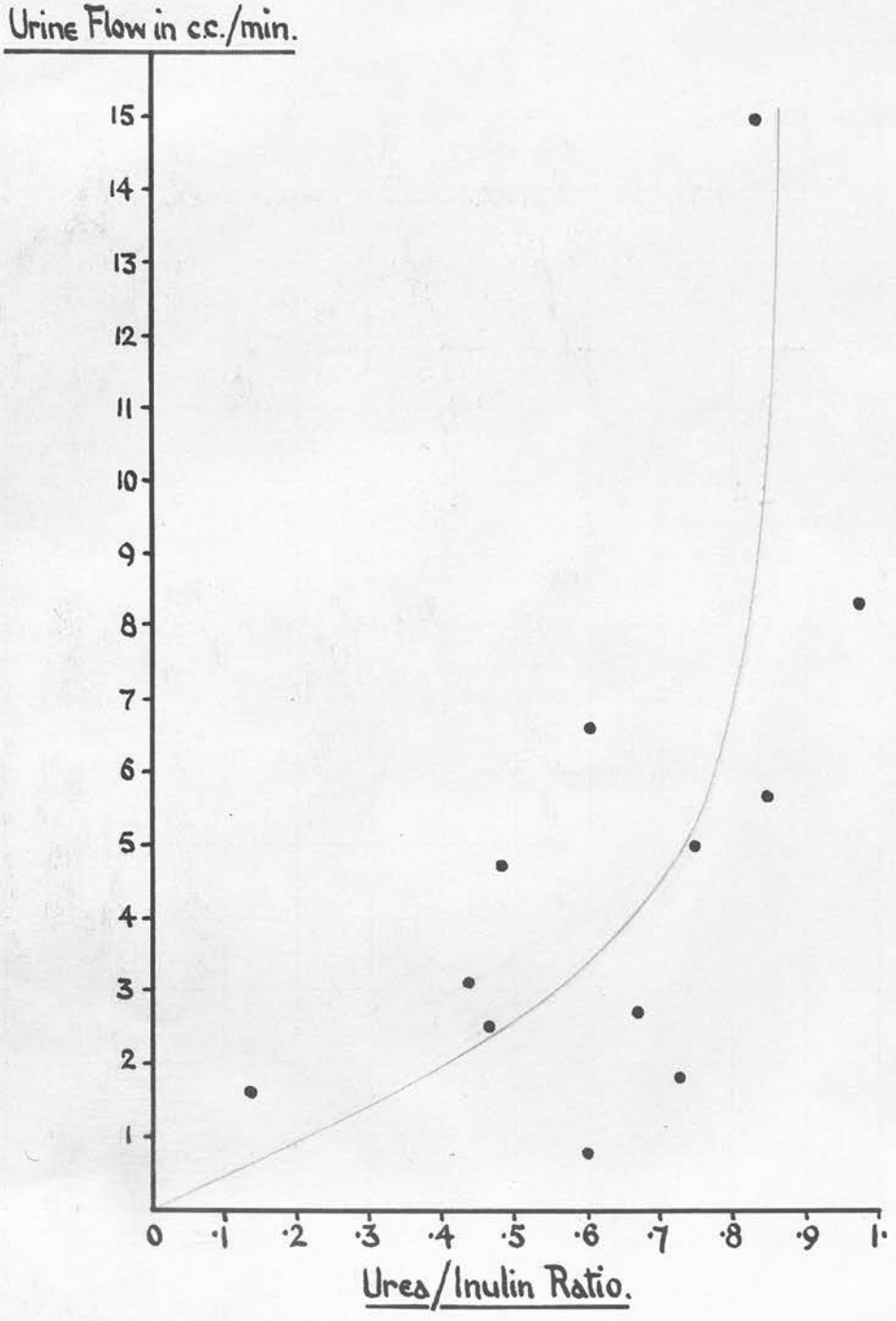
5. Comparison of Simultaneous Urea and Inulin Clearances.

Twelve estimations of urea clearance were carried out simultaneously with the inulin clearances in six subjects.

The ratios of urea to inulin clearance are compared with the urine flow (graph 1). Though the points are widely scattered, the results are comparable to those obtained by Chasis and Smith (1938), and the divergence is only to be expected on account of the wide range of inulin clearances. These workers have noted that when the urine flow is increasing urea clearance may be raised to abnormally high values relative to the rate of urine formation which will also account for any discrepancy.

At high urine flows the urea clearance should approach to about 60% of the inulin clearance.

Graph to show Relationship between Urea/Inulin Ratio and Urine Flow.



The data are from 12 observations in 6 different subjects. (See tables for figures.)

Graph 1.

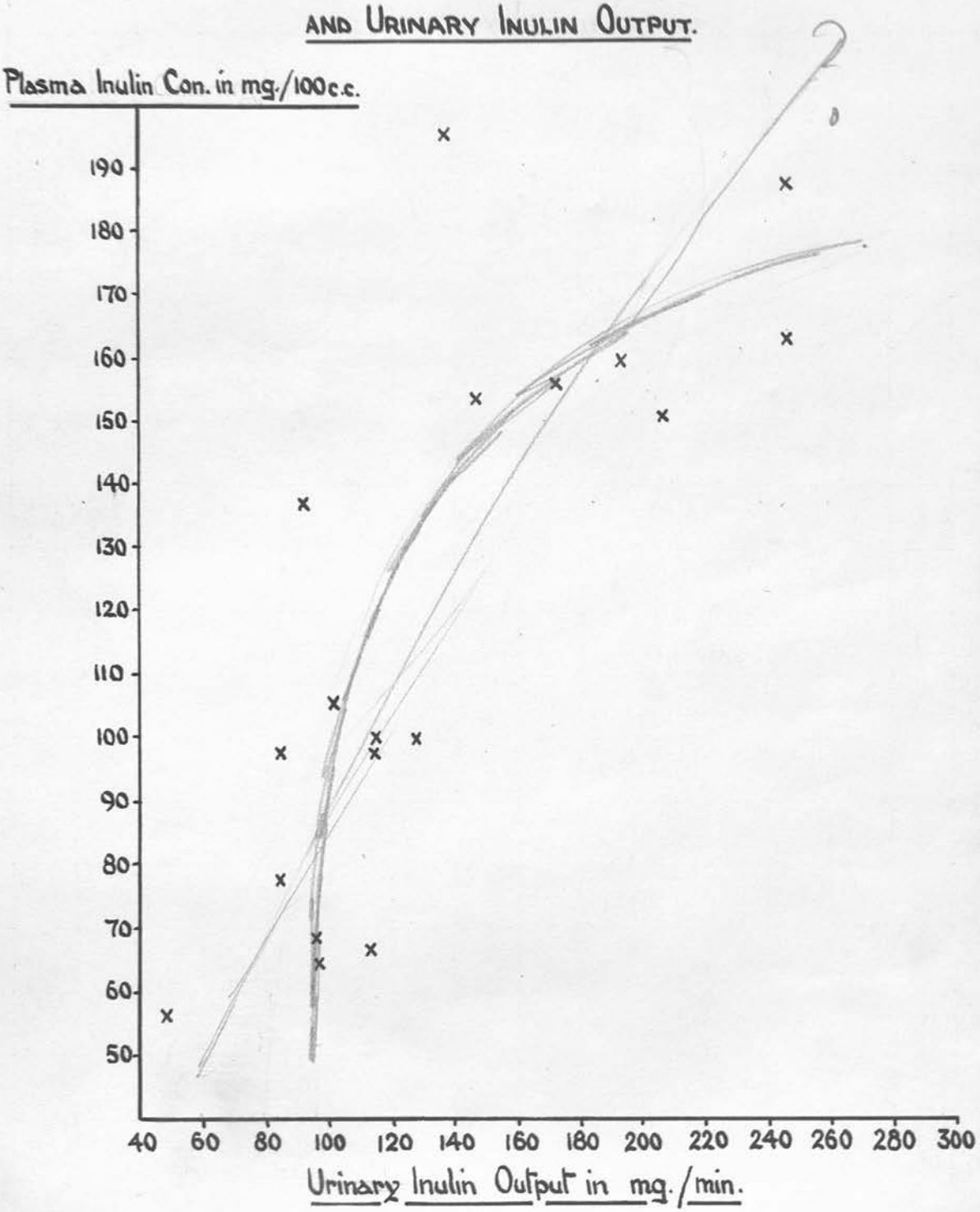
6. The Mode of Excretion of Inulin.

Inulin is excreted by a purely physical process of filtration by the kidneys. Two sets of observations have been made to demonstrate this fact. Employing the same data as used for calculating inulin clearance the amounts of inulin excreted per minute is calculated. This is plotted against the blood inulin concentration (Graph II). It will be seen that the amount of inulin excreted per minute increases as the blood inulin concentration is raised.

Secondly, following large single injections of inulin, blood specimens are withdrawn at varying intervals and the inulin concentration estimated. The logarithm of the blood/inulin concentration is then plotted against time.

Seven such observations have been made, each consisting of three or more blood specimens (see Graph III). It will be seen that the fall of concentration follows an almost rectilinear relationship.

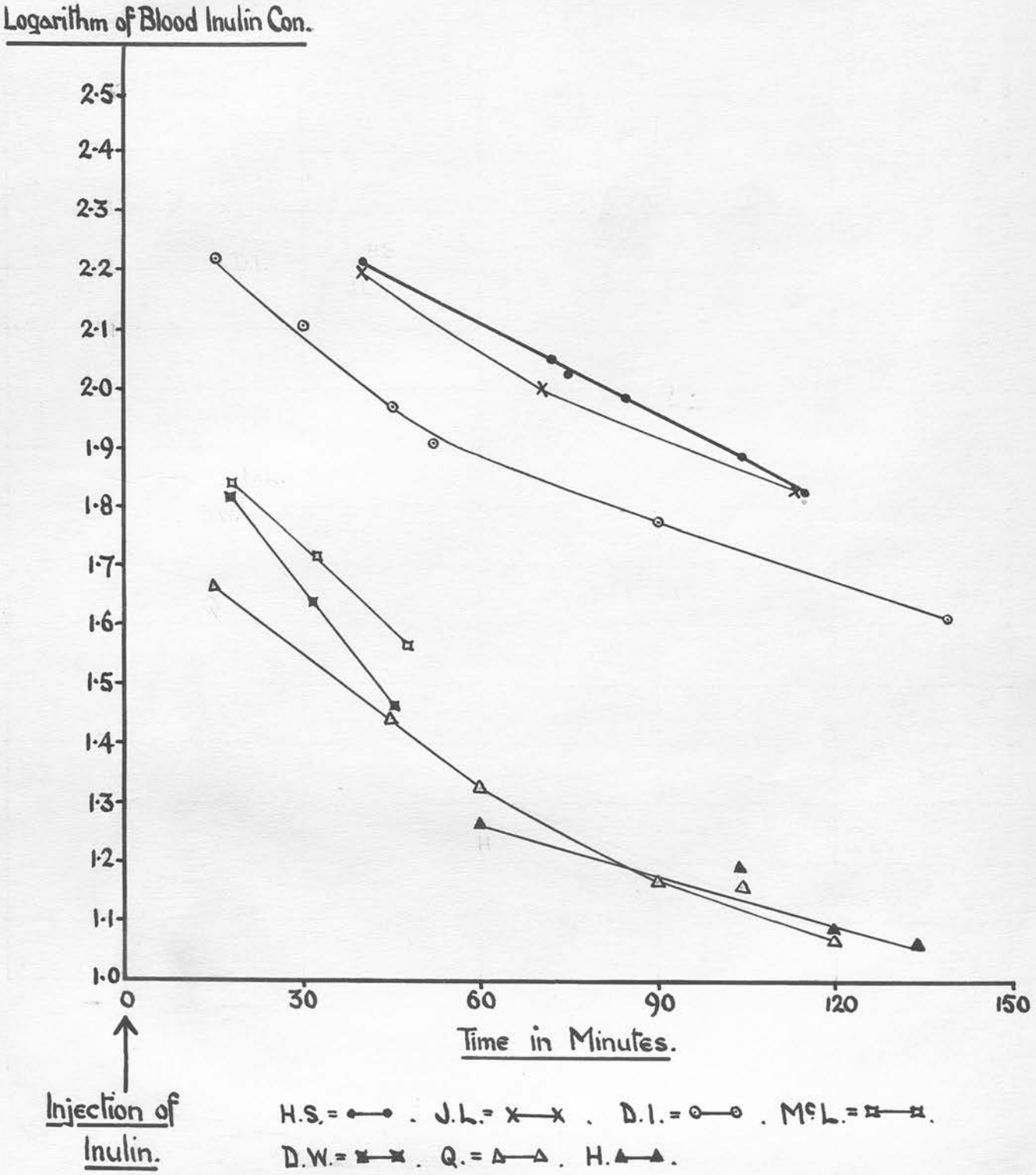
Graph to show Relationship between Plasma Inulin Concentration and Urinary Inulin Output.



The data are from 18 observations in 10 different subjects.
(See tables for figures.)

Graph II.

Fall of Blood Inulin Concentration in 7 Subjects following a Single Injection of Inulin.



Graph III.

III. SUMMARY AND CONCLUSIONS.

A technique has been devised for performing inulin clearances in man, which is a great simplification on the method used by earlier workers.

The simplification is threefold.

A single injection is used in lieu of a large priming injection followed by a sustained infusion to maintain the blood inulin concentration. As a result of this the blood concentration is constantly falling throughout the experiment, so that some difficulty may be experienced in getting the exact mean blood concentration for each observation.

Urine specimens were voided in the natural way, and catherisation of the bladder followed by washing out with saline was not practised. It was felt that such a drastic procedure was not warranted by a clinical experiment.

This is an obvious source of error on account of large differences between blood and urine concentration, but if the urine flow is kept at a high level by giving the subject large quantities of water to drink this can be minimised.

A/

A marked improvement in the manner of estimating blood inulin has been introduced. This method is both simpler and of greater accuracy than the original ones used in the estimation of inulin. It is on account of the greater accuracy that a relatively small single injection can be used.

This method is much simpler than a similar one which has been introduced by Alving, Rubin and Miller in America and which is fairly generally used in that country now. It is possible, however, that their method may be of slightly greater accuracy. I am sceptical of the use of this method without removing the blood glucose. The authors state that it is applicable at blood concentrations of over 30 mg./100 c.c.

The colour due to fructose in Herbert's method is 88% developed after 15 minutes, and this follows a rectilinear relationship. At this time the colour due to glucose is negligible. By the other method, however, the specimens are incubated for 1 hour, and though the proportions of the reagents are different, one feels that there must be a considerable colour development due to glucose.

The/

The results obtained in a series of subjects by this method are analysed and discussed, and certain of the observations are compared with synchronous urea clearances.

In the course of these investigations the distribution of inulin in the human body is also studied, and the fact that inulin is excreted by a simple physical process of filtration is demonstrated by observations showing that the rate of excretion increases proportionally to the blood inulin concentration. As further proof of filtration, it has also been shown that when the fall of blood concentration is plotted logarithmically against time, a rectilinear relationship results.

This work was carried out in 1938-39 during the tenure of a Crichton Research Scholarship.

I am indebted to Professors D. Murray Lyon and D.M.Dunlop for the use of patients in the Royal Infirmary, Edinburgh, and to Dr R.B.Macmillan for the use of patients in the Eastern General Hospital, Edinburgh.

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Alphabetical Table of Results.

Subject	Urine flow. c.c./ min.	Blood inulin mg./ 100 c.c.	Inulin output mg./ min.	Inulin clear-ance c.c.	Urea clear-ance c.c.	Urea/ inu-lin ratio times	Distri-but-ion of inulin/ body wt.	Inulin clear-ance/ 1.73 sq.m.	Fall of blood inulin conc.
Mr A.A.	5.8	151	228	158	-	-	1/3.6	155	
Mr J.B.	6.1	153.8	147	95.1	-	-	-	-	
	5.8	195	139	71.3	-	-	-	-	
	8.3	156	173.8	111.2	-	-	-	-	
Mr R.B.	1.8	66	113	174	127	0.73	1/5.3	181	
Mr F.C.	2.2	56	49	86.8	-	-	1/4.1	85	x
Mr H.									x
Mr D.I.									x
Mrs L.	5.7	137	92	66	56.5	0.85	1/4.8	82	
Mr J.L.	2.7	160	195	121.5	83	0.68	-	-	x
	8.3	100	128.6	128.6	126.9	0.98	-	-	
	4.7	68	96	147.5	71.9	0.48	-	-	
Mr A. McL.							1/4.2	-	x
Mr M.	0.75	100	95	95	58	0.6	1/4.4	102.4	
Mrs P.	3.1	188	248	134.3	58	0.43	1/6.8	149	
Mr Q.									x
Mr S.	5	97	85	87.5	-	-	1/4.5	87.5	
Mr H.S.	5	97	115	118	89	0.75	1/7	134	x
	2.5	64	97	151	67.5	0.46	-	171	
	15	164	247	137	114	0.84	-	155	
	6.6	105	102	97.6	64.6	0.6	-	110	
	1.6	77	85	110.7	16	0.14	-	125	
Mr D.W.									x

x Subjects in which three or more consecutive blood inulin estimations have been performed, following a single injection of inulin.

Subject: Mr A.A. Ward D.2. Eastern General Hospital, Edinburgh. Aet. 69 years.

Height: 5 ft, 2 in. Weight: 9 stone.

Surface area: 1.57 sq.metres.

Disease: Primary lateral sclerosis.

Investigations carried out:

1. Distribution of inulin in the human body.
2. Inulin clearance.
3. Inulin output.

10.45-10.52	150 c.c. inulin solution (I) intravenously.
11.50. U_1	255 c.c. urine passed.
11.50. B_1	oxylated venous blood.
12.05. B_2	oxylated venous blood.
12.20. U_2	175 c.c. urine passed.

Period of urinary secretion - 30 minutes.

Sample/

Sample	Fructose standard	Colorimeter	Dilution	Conc.
B_1	20 mg./100 c.c.	2.174 times	4 times	173.9 mg./100 c.c.
B_2	"	1.887 "	"	150.9 "
U_1	"	0.683 "	200 "	2.732 gm./100 c.c.
U_2	"	0.980 "	"	3.920 gm./"
I.	"	1.408 "	800 "	22.528 gm./"

I. Distribution of inulin in the human body.

Amount of inulin injected = $\frac{\text{Conc. I}}{100} \times \text{vol.I} =$

$\frac{22.528}{100} \times 150 = 33.792$ gm.

Amount of inulin excreted in 53 minutes =

$\frac{\text{Conc. } U_1}{100} \times \text{Vol.}U_1 = \frac{2.732}{100} \times 2^{55} = 6.960$ gm.

Amount of inulin left in body at end of 53 min. = 26.826 gm.

Blood conc. B_1 at end of 53 min. = 173.9 mg./100 c.c.

Amount of fluid in which inulin remaining in body is dissolved =

$\frac{26.826}{,1739 \times 10} = 15.5$ litres

Body weight = 57.1 kg.

Fraction/

Fraction of body weight in which inulin is distributed =

$$\frac{15.5}{57.1} = \frac{1}{3.6} \text{ B.W.}$$

2. Inulin clearance.

$$\frac{U}{B} \times V = \frac{\text{Conc. } U_2}{\text{Conc. } B_2} \times \frac{\text{Vol. } U_2}{\text{Period secr.}}$$

$$= \frac{3920}{151} \times \frac{175}{30}$$

$$= 141 \text{ c.c./min.}$$

Reduced to 1.73 sq. metres surface area =

$$\frac{\text{Inulin clearance}}{\text{Subject's surface area}} \times 1.73 =$$

$$\frac{141}{1.57} \times 1.73 = 155 \text{ c.c./min.}$$

3. Inulin Output.

Urine Flow Volume $= \frac{\text{Vol.} U_2}{\text{Period secr.}} =$

$$\frac{175}{30} = 5.8 \text{ c.c./min.}$$

Inulin output/min. at conc. of 151 mg./100 c.c.

$$= \frac{\text{Conc. } U_2}{100} \times V. = \frac{3920}{100} \times 5.8 = 228 \text{ mg./min.}$$

Subject: Mr J.B. Ward C. Eastern General Hospital, Edinburgh. Aet. 60 years.

Disease: Sub-clinical scurvy.

Investigations carried out:

1. Inulin clearance.
2. Inulin output.

11.07-11.10. 130 c.c. inulin solution (I) intravenously.

11.27 220 c.c. urine passed and discarded.

11.42 B_1 oxylated venous blood.

11.57 U_1 185 c.c. urine passed.

Sample	Fructose standard	Colorimeter	Dilution	Conc.
B_1	20 mg./100 c.c.	1.923 times	4 times	153.8 mg./100 c.c.
U_1	"	0.601 "	200 "	2.404 gm./100 c.c.

1. Inulin clearance.

$$\frac{U}{B} \times V. = \frac{\text{Conc. } U_1}{\text{conc. } B_1} \times \frac{\text{Vol.} U_1}{\text{Period secr.}} =$$

$$\frac{2404}{154} \times \frac{185}{30} = 95.1 \text{ c.c./min.}$$

2./

2. Inulin Output.

3. Urine flow = 6.1 c.c./min.

Amount of inulin excreted per min. = 147 mg./min.
at blood conc. of 153.8. mg./100 c.c.

Subject: Mr J.B. Ward C. Eastern General Hospital, Edinburgh. Aet. 60 years.

Disease: Sub-clinical scurvy.

Investigations carried out: Inulin clearance and output (2 observations)

10.55-11.00		130 c.c. inulin solution (I) intravenously.
11.15		Urine passed and discarded.
11.30	B_1.	oxylated venous blood.
11.45	U_1.	175 c.c. urine passed.
12.00	B_2.	oxylated venous blood.
12.15	U_2.	250 c.c. urine passed.

Sample	Fructose standard.	Colorimeter	Dilution	Conc.
B_1	20 mg./100 c.c.	2.439 times	4 times	195.1 mg./100 c.c.
B_2	"	1.961 "	"	156.8 mg./100 c.c.
U_1	10 mg./100 c.c.	1.418 "	200 "	2.404 gm./100 c.c.
U_2	"	1.047 "	200 "	2.094 "

1./

1. Inulin clearance.

$$\frac{U}{B} \times V. = \frac{\text{Conc. } U_1}{\text{conc. } B_1} \times \frac{\text{Vol. } U_1}{\text{period secr.}} =$$

$$\frac{2404}{195} \times \frac{175}{30} = 71.3 \text{ c.c./min.}$$

Urine flow = 5.8 c.c./min.

Amount of inulin excreted per min. = 139 mg./min.
at blood inulin of 195 mg./100 c.c.

2. Inulin clearance.

$$\frac{U}{B} \times V = \frac{2094}{156} \times \frac{250}{30} = 111.2 \text{ c.c./min.}$$

Urine flow = 8.3 c.c./min.

Amount of inulin excreted per min. = 173.8 mg./min.
at blood inulin of 156 mg./100 c.c.

Subject: Mr R.B. Ward D.4. Eastern General Hospital, Edinburgh. Aet. 31 years.

Height: 5 ft. 4 in. Weight: 9 stone, 6½ lbs.

Investigations carried out:

1. Distribution of inulin in the human body.
2. Inulin clearance.
3. Urea clearance.
4. Urea/inulin ratio.
5. Inulin output.

11.02-11.10. 150 c.c. inulin solution (I) intravenously.

12.5 U_1 135 c.c. urine passed.

12.5 B_1 oxylated venous blood.

12.20 B_2 oxylated venous blood.

12.35 U_2 55 c.c. urine passed.

Period of urinary secretion - 30min.

Sample/

Sample	Fructose standard	Colorimeter	Dilution	Conc.
B_1	20 mg./100 c.c.	1.015 times	4 times	81.2 mg./100 c.c.
B_2	"	0.837 "	"	66.96 "
U_1	"	2.410 "	200 "	9.64 gm./100 c.c.
U_2	"	1.575 "	200 "	6.3 "
I	"	1.852 "	400 "	14.816 "

1. Distribution of inulin in the human body.

Amount of inulin injected = $\frac{\text{Conc. I.}}{100}$ x Vol. I. =

$$\frac{14.816}{100} \times 150.$$

$$= 22.224 \text{ gm.}$$

Amount of inulin excreted in 55 min. =

$$\frac{\text{Conc. } U_1}{100} \times \text{vol. } U_1 = \frac{9.64}{100} \times 135 =$$

13.014 gm.

Amount of inulin left in body at end of 55 min. = 9.210 gm.

Blood conc. at end of 55 min. = 81.2 mg./100 c.c.

Amount of fluid in which inulin remaining inbody is dissolved =

$$\frac{9210}{81 \times 10} = 11.3 \text{ litres.}$$

Body/

Body weight = 60.5 kg.

Fraction of body weight in which inulin is distributed =

$$\frac{11.3}{60.5} = \frac{1}{5.3} \text{ B.W.}$$

2. Inulin clearance.

$$\frac{U}{B} \times V = \frac{\text{Conc. } U_2}{\text{Conc. } B_2} \times \frac{\text{Vol. } U_2}{\text{Period secr.}} =$$

$$\frac{6300}{65} \times \frac{55}{30} = 174 \text{ c.c./min.}$$

Reduced to 1.73 sq. metres surface area.

$$\frac{\text{Inulin clearance}}{\text{Subject's surface area}} \times 1.73 = \frac{174}{1.63} \times 1.73$$

$$= 181 \text{ c.c./min.}$$

3. Urea clearance.

$$\text{Urine flow} = V = \frac{\text{Vol. } U_2}{\text{Period of urinary secr.}} =$$

$$\frac{55}{30} = 1.8 \text{ c.c./min.}$$

Urea N. conc. U_2 = 1270 mg./100 c.c.

Urea N. conc. B_2 = 18 mg./100 c.c.

Urea clearance by maximum formula = $\frac{U}{B} \times V$

$$= \frac{1270}{18} \times 1.8 = 127 \text{ c.c.}$$

4. /

4. Urea/Inulin ratio.

$$= \frac{\text{Simultaneous urea clearance}}{\text{Inulin clearance}} =$$

$$\frac{127}{174} = 0.73 \text{ times.}$$

5. Inulin output.

Inulin output/min. at blood inulin of 66 mg./100 c.c. =

$$\frac{\text{Conc. } U_2}{100} \times V$$

$$= \frac{6300}{100} \times 1.8 = 113 \text{ mg./min.}$$

Subject: Mr F.C. Ward D.2. Eastern General Hospital, Edinburgh. Aet. 69 years.

Height: 5 ft. 9 in. Weight: 9 stone, 13 lbs.

Surface area: 1.76 sq. metres.

Disease: Alcoholic neuritis.

Investigations carried out:

1. Distribution of inulin in the human body.
2. Inulin clearance.
3. Inulin output.

10.48-11.00 150 c.c. inulin solution (I) injected.

12.15 U_1 150 c.c. urine withdrawn by catheter.

12.15 B_1 oxylated venous blood.

12.30 B_2 oxylated venous blood.

12.45 U_2 65 c.c. urine withdrawn by catheter.

Period of urinary secretion - 30 minutes.

Sample/

Sample	Fructose standard	Colorimeter	Dilution	Conc.
B_1	20 mg./100 c.c.	0.855 times	4 times	68.4 mg./100 c.c.
B_2	10 mg. "	0.810 "	7 "	56.7 "
U_1	10 mg. "	1.075 "	400 "	4.3 gm./100 c.c.
U_2	10 mg. "	0.563 "	400 "	2.252 gm./100 c.c.
I	20 mg. "	1.124 "	500 "	11.24 gm./100 c.c.

1. Distribution of inulin in the human body.

Amount of inulin injected = $\frac{\text{Conc. I}}{100}$ x vol. I =

$\frac{11.24}{100}$ x 150 = 16.86 gm.

Amount of inulin excreted in 75 minutes =

$\frac{\text{Conc. } U_2}{100}$ x vol. U_1 = $\frac{4.3}{100}$ x 150 = 6.45 gm.

Amount of inulin left in body at end of 87 min. = 10.41 gm.

Blood conc. B_1 at end of 75 min. = 68.4 mg./100 c.c.

Amount of fluid in which inulin remaining in body is dissolved =

$\frac{10410}{68 \times 10}$ = 15.308 litres.

Body weight = 63.067 kg.

Fraction/

Fraction of body weight in which inulin is distributed = $\frac{15.308}{63.067} = \frac{1}{4.1}$ B.W.

2. Inulin clearance.

$$\frac{U}{B} \times V = \frac{\text{Conc. } U_2}{\text{Conc. } B_2} \times \frac{\text{Vol. } U_2}{\text{Period secr.}} =$$

$$\frac{2252}{56} \times \frac{65}{30} = 86.8 \text{ c.c./min.}$$

Reduced to 1.73 sq. metres surface area.

$$\frac{\text{Inulin clearance}}{\text{Subject's surface area}} \times 1.73 = \frac{86.8}{1.76} \times 1.73 =$$

85 c.c./min.

3. Inulin output.

Urine flow volume = $\frac{\text{Vol. } U_2}{\text{Period secr.}} = \frac{65}{30} = 2.2$ c.c./min.

Amount of inulin excreted/min. at blood conc. of 56 mg./100 c.c. =

$$\frac{\text{Conc. } U_2}{100} \times V = \frac{2.252}{100} \times 2.2 = 49 \text{ mg./min.}$$

Subject: Mr H. Ward D, Eastern General Hospital, Edinburgh. Aet. 70 year.

Disease: Carcinoma of tongue.

Investigations carried out: Fall of blood concentration following injection of a single large dose of inulin.

Roughly 10gm. of inulin were injected intravenously, and after an hour had elapsed 4 blood samples were withdrawn for a further hour and a half.

Sample	Fructose standard	Colorimeter	Dilution	Conc.
60 min.	5 mg./100 c.c.	0.913 times	4 times	18.26 mg./100 c.c.
105 min.	"	0.784 "	"	15.68 "
120 min.	"	0.612 "	"	12.24 "
135 min.	"	0.571 "	"	11.42 "

Subject: Mr D.I. Ward 13, Eastern General Hospital, Edinburgh. Aet 31 years.

Disease: Mental defect and etitis media.

Investigations carried out: 1. Fall of blood concentration following injection of a single large dose of inulin.

130 c.c. of an inulin solution were injected intravenously and 6 blood samples withdrawn up to 2 hours.

Sample	Fructose standard	Colorimeter	Dilution	Conc.
15 min.	20 mg./100 c.c.	2.062 times	4 times	164.9 mg./100 c.c.
30 "	"	1.587 "	"	126.9 "
45 "	"	1.163 "	"	93.0 "
60 "	"			
75 "	"	0.946 "	"	75.0 "
90 "	"	0.733 "	"	58.6 "
105 "				
120 "	10 mg./100 c.c.	1.031 "	"	41.0 "

Subject: Mrs L. Ward 21, Royal Infirmary, Edinburgh. Aet. 50 years.

Height: 4 ft. 10¼ in. Weight: 48.64 kg.

Surface area: 1.39 sq. metres.

Disease: Hypertension.

Investigations carried out:

1. Distribution of inulin in the human body.
2. Inulin clearance.
3. Urea clearance.
4. Urea/Inulin ratio.
5. Inulin output.

10.35-10.43		150 c.c. inulin solution (I) intravenously.
11.43.	U_1	300 c.c. urine passed.
11.45.	B_1	venous blood.
12.05	B_2	venous blood.
12.28	U_2	255 c.c. urine passed.

Period of urinary secretion - 50 minutes.

Sample/

Sample.	Fructose standard	Colorimeter	Dilution	Conc.
B_1	20 mg./100 c.c.	2.198 times	4 times	175.8 mg./100 c.c.
B_2	"	1.724 "	"	137.9 "
U_1	"	0.855 "	200 "	3.42 gm./100 c.c.
U_2	10 mg./100 c.c.	0.806 "	200 "	1.612 "
I	20 mg./100 c.c.	1.156 "	800 "	18.496 "

1. Distribution of inulin in the human body.

Amount of inulin injected = $\frac{\text{Conc. I.}}{100}$ x vol. I.

$= \frac{18.496}{100} \times 150 = 27.739$ gm.

Amount of inulin excreted in 1 hour =

$\frac{\text{Conc. } U_1}{100} \times \text{vol. } U_1 = \frac{3.42}{100} \times 300$

$= 10.26$ gm.

Amount of inulin left in body at end of 1 hour

$= 17.479$ gm.

Blood conc. at end of 1 hour = 175 mg./100 c.c.

Amount of fluid in which inulin remaining in body is dissolved =

$\frac{17479}{175} \times 10 =$ 9.9 litres.

Body weight = 48.64 kg.

Fraction of body weight in which inulin is distributed:

$\frac{9.9}{48.64} = \frac{1}{4.8}$ B.W.

2. Inulin clearance.

$$\frac{U}{B} \times V = \frac{\text{Conc. } U_2}{\text{Conc. } B_2} = \frac{\text{Vol. } U_2}{\text{Period excr.}}$$

$$\frac{1612}{137} \times \frac{255}{45} = 66 \text{ c.c. per min.}$$

Reduced to 1.73 sq. metres surface area.

$$\frac{\text{Inulin clearance}}{\text{Subject's surface area}} \times 1.75 =$$

$$\frac{66}{1.39} \times 1.73 = 82 \text{ c.c./min.}$$

3. Urea clearance.

$$\text{Urine flow } V = \frac{\text{vol. } U_2}{\text{period of urinary secr.}}$$

$$= \frac{255}{45} = 5.7 \text{ c.c./min.}$$

Urea N conc. U_2 = 19 mg./100 c.c.

Urea N conc. B_2 = 188 mg./100 c.c.

Urea clearance maximum formula = $\frac{U}{B} \times V.$

$$\frac{\text{Urea conc. } U_2}{\text{Urea conc. } B_2} \times \frac{\text{Vol. } U_2}{\text{period of urinary secr.}}$$

$$\frac{188}{19} \times 5.7 = 56.5 \text{ c.c./min.}$$

4./

4. Urea/Inulin ratio.

$$\frac{\text{Simultaneous urea clearance}}{\text{inulin clearance}} = \frac{56.5}{66}$$

$$= 0.85 \text{ times.}$$

5. Inulin output.

$V = 5.7$

Output at blood conc. of 137 mg./100 c.c. =

$$\frac{\text{Conc. } U_2}{100} \times V = \frac{1.612}{100} \times 5.7$$

$$= 92 \text{ mg./min.}$$

Subject: Mr J.L. Student. Aet 20 years.

Investigations carried out: Three inulin clearances, urea clearances, urea/inulin ratios, inulin output.

9.50–10.00 130 c.c. inulin solution (I) intravenously, and one pint of water by mouth.

10.15. Urine passed and discarded.

10.30 B_1 oxylated venous blood.

10.45 U_1 82 c.c. urine passed

11.00 B_2 oxylated venous blood.

11.15 U_2 250 c.c. urine passed.

11.30 B_3 oxylated venous blood.

11.45 U_3 142 c.c. urine passed.

Three 30 min. periods of urinary secretion.

Sample	Fructose standard	Colorimeter	Dilution	Conc.
B_1	20 mg./100 c.c.	2.000 times	4 times	160 mg./100 c.c.
U_1	"	1.802 "	200 "	7.208 gm./100 c.c.
B_2	"	1.252 "	4 "	100.1 mg./100 c.c.
U_2	10 mg./100 c.c.	0.775 "	200 "	1.550 gm./100 c.c.
B_3	20 mg./100 c.c.	0.816 "	4 "	65.2 mg./100 c.c.
U_3	10 mg./100 c.c.	1.020 "	200 "	2.040 mg./100 c.c.

1. Inulin clearance.

$$\frac{U}{B} \times V = \frac{\text{Conc. } U_1}{\text{conc. } B_1} \times \frac{\text{Vol. } U_1}{\text{period secr.}}$$

$$= \frac{7208}{160} \quad \frac{82}{30}$$

$$= 121.5 \text{ c.c./min.}$$

2. Urea clearance.

$$\text{Urine flow} = \frac{\text{vol. } U_1}{\text{period of urinary secr.}} =$$

$$\frac{82}{30} = 2.7 \text{ c.c./min.}$$

Urea N conc. U_1 = 492 mg./100 c.c.

Urea N conc. B_1 = 16 mg. /100 c.c.

Urea clearance by maximum formula $= \frac{U}{B} \times V =$

$$\frac{\text{Urea N conc. } U_1}{\text{urea N conc. } B_1} \times \text{urine flow in c.c./min.} =$$

$$\frac{492}{16} \times 2.7 = 83 \text{ c.c./min.}$$

Urea/Inulin ratio.

$$\frac{\text{Simultaneous urea clearance}}{\text{inulin clearance}} = \frac{83}{121.5} = 0.68 \text{ times.}$$

Inulin output at blood inulin of 160 mg./100 c.c.

$$= \frac{U_1}{100} \times V_1 = 195 \text{ mg./min.}$$

2. Inulin clearance.

$$\frac{U}{B} \times V. = \frac{\text{Conc. } U_2}{\text{conc. } B_2} \times \frac{\text{Vol. } U_2}{\text{period secr.}} =$$

$$\frac{1550}{100} \times \frac{250}{30} = 128.6 \text{ c.c/min.}$$

Urea/

Urea clearance.

Urine flow $V_2 = \frac{\text{Vol. } U_2}{\text{period of urinary secr.}} =$

$\frac{250}{30} = 8.3$ c.c./min.

Urea N conc. $U_2 = 260$ mg./100 c.c.

Urea N conc. $B_2 = 17$ mg./100 c.c.

Urea clearance by maximum formula $= \frac{U}{B} \times V.$

$= \frac{\text{Urea N conc. } U_2}{\text{Urea N conc. } B_2}$ x urine flow in c.c/min .

$= \frac{260}{17} \times 8.3 = 126.9$ c.c./min.

Urea/Inulin ratio.

$\frac{\text{Simultaneous urea clearance}}{\text{inulin clearance}} = \frac{126}{128} = 0.98$ times

Inulin output at blood inulin of 100 mg./100 c.c.

$= \frac{U_2}{100} \times U_2 = 128$ mg./min.

3. Inulin clearance.

$\frac{U}{B} \times V = \frac{\text{Conc. } U_3}{\text{conc. } B_3} \times \frac{\text{Vol. } U_3}{\text{period secr.}} =$

$\frac{2040}{68} \times \frac{142}{30} = 147.5$ c.c./min.

Urea clearance.

Urine flow $V_3 = \frac{\text{Vol. } U_3}{\text{period of urinary secr.}} =$

$\frac{142}{30} = 4.7$ c.c./min.

Urea/

Urea N conc. U_3 = 260 mg./100 c.c.

Urea N conc. B_3 = 17 mg./100 c.c.

Urea clearance by maximum formula = $\frac{U}{B}$ x V.

= $\frac{\text{Urea N conc. } U_3}{\text{urea N conc. } B_3}$ x urine flow in c.c./min.

= $\frac{260}{17}$ x 4.7 = 71.9 c.c./min.

Urea/ inulin ratio.

$\frac{\text{Simultaneous urea clearance}}{\text{inulin clearance}}$ $\frac{71.9}{147.5}$ = 0.48 times

Inulin output at blood inulin conc. of 68 mg./100 c.c.

= $\frac{U_3}{100}$ x V_3 = 96 mg./min.

Subject: Mr A.McL. Ward D, Eastern General Hospital, Edinburgh. Aet. 48 years.

Weight: 50.8 kg.

Investigations carried out:
1. Fall of blood inulin.
2. Distribution of inulin in human body.

10.47-10.50 70 c.c. inulin solution (I) intravenously.

11.05 B_1 oxylated venous blood.

11.20 B_2 "

11.35 B_3 "

11.50 U_1 110 c.c. urine passed.

Sample	Fructose standard	Colorimeter	Dilution	Conc.
B_1	20 mg./100 c.c.	0.855 times	4 times	68.4 mg./100 c.c.
B_2	"	0.662 "	"	52.9 mg./100 c.c.
B_3	10 mg./100 c.c.	0.922 "	"	36.8 mg./100 c.c.
U_1	20 mg./100 c.c.	1.852 "	80 "	2.96 gm./100 c.c.
I.	"	1.087 "	500 "	10.87 gm./100 c.c.

1./

1. Distribution of inulin in the human body.

Amount of inulin injected = $\frac{\text{Conc. I}}{100}$ x vol. I. =

$$\frac{10.870}{100} \times 70 = 7.609 \text{ gm.}$$

Amount of inulin excreted in 70 minutes =

$$\frac{\text{Conc. } U_1}{100} \times \text{vol. } U_1 = \frac{2.960}{100} \times 110$$

$$= 3.256 \text{ gm.}$$

2. Amount of inulin remaining in body at end of 1 hour = 4.353 gm.

Final blood inulin concentration = 36.88 mg./100 c.c.

Volume of fluid in which 4.353 gm. of inulin must be dissolved to give concentration of 36.88 mg./100 c.c. =

$$\frac{4.353}{36 \times 100} \times 100 = 12.1 \text{ litres.}$$

Body weight = 50.8 kg.

Therefore proportion of body weight in which inulin is in solution = 1/4.2.

Subject: Mr M. Ward D.3. Eastern General Hospital, Edinburgh. Aet. 50 years.

Height: 5 ft. 2 in. Weight: 9 st. 6 lbs.

Surface area: 1.6 sq. metres.

Investigations carried out:

1. Distribution of inulin in the human body.
2. Inulin clearance.
3. Urea clearance.
4. Urea/Inulin ratio.
5. Inulin output.

11.22-11.30.		150 c.c. inulin solution (I) intravenously.
12.45	U_1	440 c.c. urine passed.
12.45	B_1	oxylated venous blood.
01.05	B_2	oxylated venous blood.
01.25	U_2	30 c.c. urine passed.

Period of urinary secretion - 40 minutes.

Sample	Fructose standard	Colorimeter	Dilution	Conc.
B_1	20 mg./100 c.c.	1.639 times	4 times	131.12 mg./100 c.c.
B_2	"	1.258 "	"	100.64 "
U_1	"	0.985 "	200 "	3.940 gm./100 c.c.
U_2	10 mg./100 c.c.	1.266 "	1000 "	12.660 gm./100
I.	20 "	1.176 "	"	23.520 " c.c

1. Distribution of inulin in the human body.

Amount of inulin injected = $\frac{\text{Conc. I}}{100}$ x Vol. I =

$\frac{23.520}{100}$ x 150 = 35.280 gm.

Amount of inulin excreted in 75 min. =

$\frac{\text{Conc. } U_1}{100}$ x Vol. U_1 = $\frac{3.94}{100}$ x 440

= 17.336 gm.

Amount of inulin left in body at end of 75 min. = 17.944 gm.

Blood conc. B_1 at end of 75 min. = 131.12 mg./100 c.c.

Amount of fluid in which inulin remaining in body is dissolved =

$\frac{17944}{131 \times 10}$ = 13.697 litres.

Body weight = 60 kg.

Fraction of body wt. in which inulin is distributed =

$\frac{13}{60} = \frac{1}{4.4}$ B.W.

2. Inulin clearance.

$\frac{U}{B} \times V = \frac{\text{Conc. } U_2}{\text{conc. } B_2} \times \frac{\text{Vol. } U_2}{\text{period secr.}} =$

$\frac{12660}{100} \times \frac{30}{40}$ = 95 c.c./min.

Reduced to 1.73 sq. metres surface area.

$\frac{\text{Inulin clearance}}{\text{Subject's surface area}} \times 1.73 = \frac{95}{1.6} \times 1.73 =$

102.4 c.c./min.

3. Urea clearance.

$$\text{Urine flow} = \frac{\text{Vol. } U_2}{\text{period of urinary secr.}} =$$

$$\frac{30}{40} = 0.75 \text{ c.c./min.}$$

Urea N conc. U_2 = 6000 mg./100 c.c.

Urea N conc. B_2 = 28 mg./100 c.c.

Urea clearance by standard formula = $\frac{U}{B} \times \sqrt{V}$

$$= \frac{\text{Urea N. conc. } U_2}{\text{urea N conc. } B_2} \times \text{urine flow in c.c./min.}$$

$$= \frac{6000}{28} \times \sqrt{75} = 58 \text{ c.c. /min.}$$

4. Urea/Inulin ratio.

$$\frac{\text{Simultaneous urea clearance}}{\text{inulin clearance}} = \frac{58}{95} =$$

.6 times.

5. Inulin output. at blood inulin of 100 mg./100 c.c. = 95 mg./min.

Subject: Mrs P. Ward 21, Royal Infirmary, Edinburgh. Aet. 59 years.

Height: 4 ft. 11 in. Weight: 60 kg.

Surface area: 1.55 sq. metres.

Investigations carried out:

1. Distribution of inulin in the human body.
2. Inulin clearance.
3. Urea clearance.
4. Urea/Inulin ratio.
5. Inulin output.

10.53-11.00 150 c.c. inulin solution (I) intravenously.

11.30 U_1 343 c.c. urine passed.

12.00 B_1 oxylated venous blood.

12.30 U_2 190 c.c. urine passed.

12.32 B_2 oxylated venous blood.

Period of urinary secretion - 60 minutes.

Sample	Fructose standard	Colorimeter	Dilution	Conc.
B_1	20 mg./100 c.c.	2.353 times	4 times	188.2 mg./100 c.c.
B_2	"	1.667 "	"	133.4 "
U_1	"	0.862 "	200 "	3.448 gm./100 c.c.
U_2	"	2.000 "	"	8.000 "
I.	"	1.626 "	800 "	25.816 "

1. Distribution of inulin in the human body.

$$\text{Amount of inulin injected} = \frac{\text{Conc. I.}}{100} \times \text{vol. I}$$

$$= \frac{25.816}{100} \times 150 = 38.724 \text{ gm.}$$

Amount of inulin excreted in 90 minutes =

$$\frac{\text{Conc. } U_1}{100} \times \text{vol. } U_1 + \frac{\text{Conc. } U_2}{100} \times \text{vol. } U_2$$

$$= \frac{3.448}{100} \times 343 + \frac{8.000}{100} \times 190$$

$$= 27.026 \text{ gm.}$$

Amount of inulin left in body at end of 90 min. = 11.698 gm.

Blood concentration B_2 at end of 90 min. = 133.4 mg./100 c.c.

Amount of fluid in which inulin remaining in body is dissolved =

$$\frac{11698 \times 10}{133.4 \times 10} = 8.73 \text{ litres.}$$

Body weight = 60 kg.

Fraction of body weight in which inulin is distributed:

$$\frac{8.73}{60} = \frac{1}{6.8} \text{ B.W.}$$

2. Inulin clearance

$$\frac{U}{B} \times V = \frac{\text{Conc. } U_2}{\text{conc. } B_1} \times \frac{\text{Vol. } U_2}{\text{period secr.}}$$

$$= \frac{8000}{188} \times \frac{190}{60} = 134.3 \text{ c.c./min.}$$

Reduced to 1.73 sq. metres surface area.

$$\frac{\text{Inulin clearance}}{\text{Subject's surface area}} \times 1.73 = \frac{134.3}{1.55} \times 1.73$$

$$= 149 \text{ c.c./min.}$$

3. Urea clearance.

$$\text{Urine flow} = \frac{\text{Vol. } U_2}{\text{period of urinary secr.}} =$$

$$\frac{190}{60} = 3.1 \text{ c.c./min.}$$

Urea N conc. U_2 = 304 mg./100 c.c.

Urea N conc. B_1 = 16 mg./100 c.c.

Urea clearance maximum formula = $\frac{U}{B} \times V$.

$$\frac{\text{Urea N conc. } U_2}{\text{urea N conc. } B_1} \times \text{urine flow in c.c./min} =$$

$$\frac{304}{16} \times 3.1 = 58.9 \text{ c.c./min.}$$

4. Urea/inulin ratio.

$$\frac{\text{Simultaneous urea clearance}}{\text{inulin clearance}} =$$

$$\frac{58.9}{134.3} = 0.43 \text{ times.}$$

5. /

5. Inulin output/ min. at blood concentration of 188 mg./100 c.c. $= \frac{U_2}{100} \times V$

$$= \frac{8000}{100} \times 3.1$$

$$= 248 \text{ mg./min.}$$

Subject: Mr Q. Ward B, Eastern General Hospital, Edinburgh. Aet 16 years.

Disease: Asthma.

Investigations carried out: Fall of blood concentration following injection of a single large dose of inulin.

90 c.c. of an inulin solution were injected intravenously and 6 blood samples withdrawn up to 2 hours.

Sample	Fructose standard	Colorimeter	Dilution	Conc.
15 min.	20 mg./100 c.c.	0.581 times	4 times	46.48 mg./100 c.c.
45 min.	10 mg./100 c.c.	1.064 "	"	21.28 mg./100 c.c.
60 min.	5 mg./100 c.c.	1.064 "	"	21.28 "
90 min.	"	0.741 "	"	14.82 "
105 min.	"	0.719 "	"	14.38 "
120 min.	"	0.612	"	12.24 "

Subject: Mr S. Ward D.4, Eastern General Hospital, Edinburgh. Aet. 70 years.

Height: 5 ft. 8 in. Weight: 61.7 kg.

Surface area: 1.73 sq. metres.

Disease: Neuritis.

Investigations carried out:

1. Distribution of inulin in the human body.
2. Inulin clearance.
3. Inulin output.

11.15-11.20. 130 c.c. inulin solution (I) intravenously.

12.05 U_1 240 c.c. urine withdrawn by catheter.

12.05 B_1 oxylated venous blood.

12.20 B_2 oxylated venous blood.

12.35 U_2 150 c.c. urine passed.

Period of urinary secretion - 30 minutes.

Sample	Fructose standard	Colorimeter	Dilution	Conc.
B_1	20 mg./100 c.c.	1.470 times	4 times	117.60 mg./100 c.c.
B_2	"	1.212 "	"	96.96 "
U_1	"	0.643 "	200 "	2.572 gm./100 c.c.
U_2	10 mg./100 c.c.	0.851 "	"	1.702 gm./100 c.c.
I	20 mg./100 c.c.	2.128 "	400 "	17.024 "

1. Distribution of inulin in the human body.

Amount of inulin injected = $\frac{\text{Conc. I}}{100}$ x vol. I.

= $\frac{17.024}{100}$ x 130 = 22.131 gm.

Amount of inulin excreted in 45 minutes =

$\frac{\text{Conc. } U_1}{100}$ x vol. U_1 = $\frac{2.572}{100}$ x 240

= 6.173 gm.

Amount of inulin left inbody at end of 45 minutes = 15.958 gm.

Blood concentration B_1 at end of 45 minutes = 117.6 mg./100 c.c.

Amount of fluid in which inulin remaining in the body is dissolved:

$\frac{15958}{117 \text{ x } 10}$ = 13.622 litres

Body weight = 61.7 kg.

Fraction of body weight in which inulin is distributed:

$\frac{13.6}{61.7}$ = $\frac{1}{4.5}$ B.W.

2. Inulin clearance.

$\frac{U}{B}$ x V = $\frac{\text{Conc. } U_2}{\text{conc. } B_2}$ $\frac{\text{Vol. } U_2}{\text{period secr.}}$ =

$\frac{1702}{97}$ $\frac{150}{30}$ = 87.5 c.c./min.

This patient has already normal standard surface area of 1.73 sq. metres.

3. Inulin excretion/min. at blood conc. of 97 mg./100 c.c. =

$$\frac{U_2}{100} \times U = \frac{1702}{100} \times 5 = 85 \text{ mg./min.}$$

Subject: Mr H.S. Ward D, Eastern General Hospital, Edinburgh. Aet. 23 years.

Height: 5 ft. 2 in. Weight: 56.2 kg.

Surface area: 1.53 sq. metres.

Disease: asthma.

Investigations carried out:

Inulin clearance.
Urea clearance.
Urea/Inulin ratio (repeated thrice)

10.00-10.05		150 c.c. inulin solution (I) intravenously.
10.10		Half pint water by mouth.
10.20		Urine passed and discarded.
10.40	B_1	oxylated venous blood.
11.00	U_1	600 c.c. urine passed.
11.15	B_2	oxylated venous blood.
11.30	U_2	200 c.c. urine passed.
11.45	B_3	oxylated venous blood.
12.00	U_3	50 c.c. urine passed.

One 40 min. and two 30 min. periods of urinary secretion.

Sample/

Sample	Fructose standard	Colorimeter	Dilution	Conc.
B_1	20 mg./100 c.c.	2.062 times	4 times	164.9 mg./100 c.c.
B_2	"	1.316 "	"	105.28 "
B_3	"	0.961 "	"	76.88 "
U_1	10 mg./100 c.c.	0.754 "	200 "	1.508 gm./100 c.c
U_2	"	0.775 "	"	1.550 "
U_3	20 mg./100 c.c.	1.333 "	"	5.332 "
I	"	1.439 "	800 "	22.924 "

1. Inulin clearance. (1st period)

$$\frac{U}{B} \times V = \frac{\text{Conc. } U_1}{\text{conc. } B_1} \times \frac{\text{Vol. } U_1}{\text{period secr.}}$$

$$\frac{1504}{164.9} \times \frac{600}{40} = 137.5 \text{ c.c./min.}$$

Reduced to 1.73 sq. meters surface area.

$$\frac{\text{Inulin clearance}}{\text{subject's surface area}} \times 1.73 = 155 \text{ c.c./min.}$$

Urea clearance.

$$\text{Urine flow} = \frac{\text{vol. } U_1}{\text{period of urinary secr.}} =$$

$$\frac{600}{40} = 15 \text{ c.c./min.}$$

Urea N conc. U_1 = 100 mg./100 c.c.

Urea N conc. B_1 = 13 mg./100 c.c.

Urea clearance by maximum formula = $\frac{U}{B} \times V$.

Urea/

$$\frac{\text{Urea N conc. } U_1}{\text{urea N conc. } B_1} \times \text{Urine flow in c.c./min.}$$

$$\frac{100}{13} \times 15 = 114 \text{ c.c./min.}$$

Urea/Inulin ratio.

$$\frac{\text{Simultaneous urea clearance}}{\text{inulin clearance}} =$$

$$\frac{114}{127.5} = 0.84 \text{ times.}$$

Inulin output at blood inulin of 164.9 mg./100 c.c. =

$$\frac{U}{100} \times V = \frac{164.9}{100} \times 15 = 247 \text{ mg./min.}$$

2. Inulin clearance (2nd period)

$$\frac{U}{B} \times V. = \frac{\text{Conc. } U_2}{\text{conc. } B_2} \times \frac{\text{Vol. } U_2}{\text{period secr.}} =$$

$$\frac{1550}{105} \times \frac{200}{30} = 97.6 \text{ c.c./min.}$$

Reduced to 1.73 sq. metres surface area.

$$\frac{\text{Inulin clearance}}{\text{subject's surface area}} \times 1.73 =$$

$$\frac{97.6}{153} \times 1.73. = 110 \text{ c.c./min.}$$

Urea clearance.

Urine flow $= \frac{\text{vol. } U_2}{\text{period of urinary secr.}} = \frac{200}{30}$

$= 6.6$ c.c./min.

Urea/

Urea N conc. U_2 = 128 mg./100 c.c.

Urea N conc. B_2 = 13 mg./100 c.c.

Urea clearance by maximum formula = $\frac{U}{B} \times V$

$$\frac{\text{Urea N conc. } U_2}{\text{urea N conc. } B_2} \times \text{urine flow in c.c./min.}$$

$$= \frac{128}{13} \times 6.6 = 64.6 \text{ c.c./min.}$$

Urea/Inulin ratio.

$$\frac{\text{Simultaneous urea clearance}}{\text{inulin clearance}} = \frac{97.6}{64.6} =$$

0.6 times.

Inulin output at blood inulin of 105 mg./100 c.c.

$$= U \times \frac{U_2}{100} = 6.6 \times \frac{1550}{100}$$

$$= 102 \text{ mg./min.}$$

3. Inulin clearance (3rd period)

$$\frac{U}{B} \times V.$$

$$\frac{\text{Conc. } U_3}{\text{conc. } B_3} \times \frac{\text{Vol. } U_3}{\text{period secr.}} = \frac{5332}{77} \quad \frac{50}{30}$$

$$= 110.7 \text{ c.c./min.}$$

Reduced to 1.73 sq. meters surface area.

$$\frac{\text{Inulin clearance}}{\text{subject's surface area}} \times 1.73$$

$$\frac{110.7}{1.53} \times 1.73 = 125 \text{ c.c./min.}$$

Urea/

Urea clearance.

$$\text{Urine flow} = \frac{\text{vol. } U_3}{\text{period of urinary secr.}}$$

$$= \frac{50}{30} = 1.6 \text{ c.c./min.}$$

Urea N conc. U_3 = 176 mg./100 c.c.

Urea N conc. B_3 = 14 mg./100 c.c.

Urea clearance by standard formula.

$$\frac{U}{B} \times V = \frac{\text{Urea N conc. } U_3}{\text{urea N conc. } B_3} \times \frac{}{\text{Urine flow in c.c./min.}}$$

$$\frac{176}{14} \times 1.6 = 16 \text{ c.c./min.}$$

Urea/Inulin ratio.

$$\frac{\text{Simultaneous urea clearance}}{\text{inulin clearance}} = \frac{16}{110} =$$

0.14 times.

$$\frac{\text{Inulin output}}{\text{of 77/mg./100 c.c.}} \text{ at blood inulin} =$$

$$\frac{U_3}{100} \times V = \frac{5332}{100} \times 1.6 = 85 \text{ mg./min.}$$

Subject: Mr H.S. Ward D, Eastern General Hospital, Edinburgh. Aet. 23 years.

Height: 5 ft. 2 in. Weight: 56.2 kg.

Surface area: 1.53 sq. metres.

Disease: asthma.

Investigations carried out:

1. Distribution of inulin in the human body.
2. Inulin clearance; urea clearance; urea/inulin ratio and inulin output.
3. As (2).

10.50-11.00.		150 c.c. inulin solution (I) intravenously.
12.00	U_1	540 c.c. urine passed.
12.02	B_1	oxylated venous blood.
12.15	B_2	oxylated venous blood.
12.30	U_2	150 c.c. urine passed.
12.45	B_3	oxylated venous blood.
1.00	U_3	75 c.c. urine passed.

Two 30 min. periods of urinary secretion.

Sample/

Sample	Fructose standard	Colorimeter	Dilution	Conc.
B_1	20 mg./100 c.c.	1.408 times	4 times	112.64 mg./100 c.c.
B_2	"	1.219 "	"	97.52 "
B_3	"	0.800 "	"	64.00 "
U_1	"	0.813 "	200 "	3.252 g./100 c.c.
U_2	10 mg./100 c.c.	1.149 "	"	2.298 "
U_3	20 mg./100 c.c.	0.971 "	"	3.884 "
I	"	1.105 "	800 "	17.68 "

1. Distribution of inulin in the human body.

Amount of inulin injected = $\frac{\text{Conc. I}}{100}$ x Vol. I =

$$\frac{17.68}{100} \times 150 = 26.52 \text{ gm.}$$

Amount of inulin excreted in 60 minutes =

$$\frac{\text{Conc. } U_1}{100} \times \text{Vol. } U_1 = \frac{3.252}{100} \times 540$$

$$= 17.56 \text{ gm.}$$

Amount of inulin left in body at end of 60 minutes = 8.96 gm.

Blood concentration B_1 at end of 60 minutes = 112.6 mg./100 c.c.

Amount of fluid in which inulin remaining in body is dissolved =

$$\frac{8960}{112.6 \times 10} = 8 \text{ litres.}$$

Body/

Body weight = 56.2 kg.

Fraction of body weight in which inulin is distributed =

$$\frac{8}{56.2} = \frac{1}{7} \text{ B.W.}$$

2. Inulin clearance (1st period.

$$\frac{U}{B} \times V = \frac{\text{Conc. } U_2}{\text{conc. } B_2} \times \frac{\text{Vol. } U_2}{\text{period secr.}}$$

$$= \frac{2298}{97} \times \frac{150}{30} = 118.5 \text{ c.c./min.}$$

Reduced to 1.73 sq. metres surface area.

$$\frac{\text{Inulin clearance}}{\text{subject's surface area}} \times 1.73 = 134 \text{ c.c./min.}$$

Urea clearance.

$$\text{Urine flow} = \frac{\text{vol. } U_2}{\text{period of urinary secr.}} =$$

$$\frac{150}{30} = 5 \text{ c.c./min.}$$

Urea N conc. U_2 = 250 mg./100 c.c.

Urea N conc. B_2 = 14 mg./100 c.c.

Urea clearance by maximum formula = $\frac{U}{B} \times V$.

$$\frac{\text{Urea N conc. } U_2}{\text{urea N conc. } B_2} \times \text{urine flow in c.c./min.} =$$

$$\frac{250}{14} \times 5 = 89 \text{ c.c./min.}$$

Urea/

Urea/Inulin ratio.

$$\frac{\text{Simultaneous urea clearance}}{\text{inulin clearance}} = \frac{89}{118.5} =$$

0.75 times.

Inulin output at blood inulin of 97 mg./100 c.c. =

$$V \times \frac{U_2}{100} = 5 \times \frac{2298}{100} = 115 \text{ mg./min.}$$

2. Inulin clearance (2nd period.

$$\frac{U}{B} \times V. = \frac{\text{Conc. } U_3}{\text{conc. } B_3} \times \frac{\text{Vol. } U_3}{\text{Period secr.}}$$

$$= \frac{3.884}{64} \times \frac{75}{30} = 151.5 \text{ c.c./min.}$$

Reduced to 1.73 sq. metres surface area.

$$\frac{\text{Inulin clearance}}{\text{subject's surface area}} \times 1.73 =$$

$$\frac{151.5}{1.53} \times 1.73 = 171 \text{ c.c./min.}$$

Urea clearance.

$$\text{Urine flow} = \frac{\text{vol. } U_3}{\text{period of urinary secr.}} =$$

$$\frac{75}{30} = 2.5 \text{ c.c./min.}$$

Urea N conc. U_3 = 324 mg./100 c.c.

Urea N conc. B_3 = 12 mg./100 c.c.

Urea clearance by maximum formula = $\frac{U}{B} \times V$

Urea/

$$\frac{\text{Urea N conc. } U_2}{\text{urea N conc. } B_2} \text{ x urine flow in c.c./min.} =$$

$$\frac{324}{12} \times 2.5 = 67.5 \text{ c.c./min.}$$

Urea/inulin ratio.

$$\frac{\text{Simultaneous urea clearance}}{\text{inulin clearance}} \qquad \frac{151.5}{67.5}$$

$$= 0.46 \text{ times.}$$

Inulin output at blood inulin of 64 mg./100 c.c.

$$= V \times \frac{U_3}{100} = 2.5 \times \frac{3884}{100} =$$

97 mg./min.

Subject: Mr D.W. Ward E.3, Eastern General Hospital, Edinburgh. Aet. 63 years.

Weight: 47 kg.

Disease: Carcinoma of tongue.

Investigations carried out:

1. Fall of blood concentration following injection of a single large dose of inulin.
2. Distribution of inulin in the human body.

11.15-11.17 60 c.c. inulin solution (I) intravenously.

11.33 B_1 oxylated venous blood.

11.47 B_2 "

12.02 B_3 "

12.18 U_1 270 c.c. urine passed.

Period of urinary secretion - 1 hour, 3 minutes.

Sample	Fructose standard	Colorimeter	Dilution	Conc.
B_1	10 mg./100 c.c.	1.653 times	4 times	66.1 mg./100 c.c.
B_2	"	1.087 "	"	43.4 "
B_3	"	0.733 "	"	29.3 "
B_4	"	0.445	"	17.7 "
U_1	10 mg./100 c.c.	2.035 "	200 "	4.07 gm./100 c.c.
I.	"	2.174 "	1000 "	21.74 "

1. Distribution if inulin in the human body.

Amount of inulin injected = $\frac{\text{Conc. I}}{100}$ x vol. I =

$\frac{21.74}{100}$ x 60 = 13.04 gm.

Amount of inulin excreted = $\frac{\text{Conc. I}}{100}$ x vol. U_1 =

= $\frac{4.07}{100}$ x 270 = 11 gm.

Amount of inulin remaining in body at end of 63 min. = 2.04 gm.

Blood concentration B_4 at end of 63 min. = 17.7

Amount of fluid in which inulin remaining in body is dissolved =

$\frac{2040}{17.7} \div 10$ = 11.5 litres.

Body weight = 47 kg.

Fraction of body weight in which inulin is distributed =

$\frac{11.5}{47}$ = 1/4.1 B.W.