7564 P

Renal Excretion of Inulin, Creatinine and Xylose in Normal Dogs.

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During the course of studies of the properties of the renal tubule of amphibia we had occasion to search for a substance which, introduced into the tubule, would not be expected to be absorbed from it into the blood, either actively or by diffusion. Among those tried was the polysaccharide inulin, chosen because of its high molecular weight and because it is not hydrolyzed by enzymes or tissues of vertebrates. After having found that inulin is much less rapidly diffusible than either creatinine or glucose; that it is filterable through collodion membranes which are impermeable to protein and through the glomerular membranes of amphibia; and also that it is not excreted by the aglomerular kidney (toadfish) after intravenous injection, it seemed desirable to study its rate of excretion in mammals. Given intravenously to dogs or rabbits it is excreted in the urine rapidly, and, insofar as a few experiments show, completely. Concentration ratios, U/P, as high as 150 have been observed. It became obvious that some of the considerations developed by Jolliffe, Shannon and Smith[1] upon which they based their advocacy of plasma clearance of xylose in preference to that of creatinine as a true measure of the volume of glomerular filtration could equally well be made the basis of similar advocacy of inulin clearance for the same purpose; with this advantage, that the low diffusibility of inulin, much lower than that of creatinine, of xylose and of the other 2 non-metabolized sugars tested by them (sucrose, raffinose) could be expected to minimize a difference between plasma clearance and rate of glomerular filtration, provided such a difference exists and is the result of back diffusion of the substance studied. Accordingly, a series of preliminary experiments has been made, admittedly not perfect, in which the simultaneous plasma clearances of inulin and creatinine have been determined in unanesthetized female dogs. The results, which seem sufficiently convincing to put on record, indicate that the plasma clearance of inulin given intravenously is slightly higher than, but of the same order as that of creatinine.

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[1] Jolliffe, N., Shannon, J. A., and Smith, Homer W., *Am. J. Physiol.*, 1932, **100**, 301; **102**, 534.

A year later a similar series was made in which simultaneous clearances of inulin and xylose were determined. The results indicate that inulin clearance is significantly higher than that of xylose.

Inulin was given intravenously: 1 to 4 gm. before beginning the experiment; slow continuous infusion during it. Creatinine was given intraperitoneally, xylose by mouth.

Urine collection periods varied from 12 to 52 minutes; average, 27. Blood from the jugular vein was taken one minute before the beginning and one minute before the end of each period. Urine was collected by catheter.

Inulin and xylose in plasma and urine were determined by the Shaffer-Somogyi method[2] applied to the properly diluted fluids (a) before hydrolysis, (glucose + xylose); (b) before hydrolysis, after fermentation with washed yeast (xylose); (c) after hydrolysis with 0.1 N HCl (glucose + xylose + inulin). Urines were diluted to make the reducing powers approximately the same as those of the corresponding plasmas.

Creatinine was determined by Folin's method as used by Holten and Rehberg.[3]

Twenty-three comparisons of inulin and creatinine clearances were obtained in 10 experiments on 5 normal dogs in June and July, 1933; 11 more in 5 experiments on 4 dogs in July, 1934.

Twenty-five comparisons of inulin and xylose clearances were made in 11 experiments on 4 normal dogs in May, June and July, 1934. In any single experiment clearance of only 2 of the 3 substances was measured.

Average plasma concentrations of inulin ranged from 60 to 346; of creatinine, from 3.3 to 26.0; of xylose, from 30 to 233 mg. %. Rates of urine excretion varied from 0.44 to 5.8 cc. per min.

The results, given as clearance ratios, were as follows:

A. *Inulin clearance/Creatinine clearance:* 0.64, 0.64, 0.73, 0.84, 0.85, 0.87, 0.92, 0.92, 0.96, 0.97, 1.00, 1.00, 1.01, 1.02, 1.03, 1.03, 1.05, 1.05, 1.08, 1.11, 1.11, 1.14, 1.14, 1.14, 1.15, 1.16, 1.18, 1.20, 1.20, 1.21, 1.36, 1.38, 1.46, 1.53. Mean, 1.06.

B. *Inulin clearance/Xylose clearance:* 0.85, 0.89, 0.93, 1.03, 1.08, 1.09, 1.11, 1.16, 1.16, 1.16, 1.23, 1.25, 1.27, 1.33, 1.35, 1.35, 1.39, 1.41, 1.43, 1.47, 1.49, 1.49, 1.59, 1.59, 1.67. Mean, 1.27.

The difference between the 2 groups of results seems significant.

No correlation was found between inulin clearance and plasma concentration of inulin or rate of urine flow.

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[2] Shaffer, P. A., and Somogyi, M., *J. Biol. Chem.*, 1933, **100**, 695.

[3] Holten, C., and Rehberg, P. B., *Acta Med. Skand.*, 1931, **74**, 479.

The concentrations of inulin in the urine were astonishing: in one experiment 35.8%; in another 32.3; in another 22.4. In one instance the concentration ratio, U/P, was 150; in another 132.

It must be stated that in more than half the experiments undesirably large variations in the plasma concentrations of the substances studied (particularly of inulin) occurred, due presumably to the methods of administration. Exclusion of these from consideration does not, however, alter the conclusion drawn from the series as a whole, *viz.*, that the plasma clearance of injected inulin is of the same order as that of injected creatinine and higher than that of xylose. We are inclined to ascribe this difference to greater diffusion of xylose than of inulin from the renal tubule.

One main purpose of this publication is to call attention to the possible usefulness of inulin in connection with renal studies.

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Occurrence of Non-Motile Leucocytes.

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Sabin, Cunningham, Doan and Kindwall[1] observed that when supravital counts were made on blood drawn every 15 minutes there appeared "showers of non-motile cells" at approximately hourly intervals. They interpreted these as being due to degenerating polymorphs which were actually dying in the blood stream. Beard and Beard[2] confirmed the existence of these showers, and were able to increase their magnitude without altering their rhythm by the injection of sodium citrate. More recent workers (Smith and McDowell,[3] Jones, Stephens, Todd, and Lawrence[4]) have been unable to confirm these observations, and find that the non-motile cells occur at irregular intervals and are probably artefacts.

If the non-motile cells are really dying polymorphs, most of them should be old cells, as determined by the criterion of the number of lobes in the nucleus (Cooke and Ponder[5]), whereas if they are

[1] Sabin, Cunningham, Doan and Kindwall, *Johns Hopkins Hosp. Bull.*, 1925, **37**, 14.

[2] Beard and Beard, PROC. SOC. EXP. BIOL. AND MED., 1927, **24**, 614.

[3] Smith and McDowell, *Arch. Int. Med.*, 1929, **43**, 68.

[4] Jones, Stephens, Todd and Lawrence, *Am. J. Physiol.*, 1933, **105**, 547.

[5] Cooke and Ponder, The Polynuclear Count, 1927, London.