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Filtration and Secretion of Exogenous Creatinine in Man.

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Jolliffe, Shannon and Smith[1] have presented evidence that the excretion of xylose and other non-metabolized sugars can be used to measure glomerular filtration in the dog, and by simultaneous xylose and creatinine clearances they have demonstrated the tubular secretion of creatinine in that animal. The use of xylose for measuring glomerular filtration has been confirmed by Clark and Smith[2] in the elasmobranch, *Squalus acanthias* and by Marshall[3] in the frog, *Rana catesbiana*.

A comparison of the excretion of xylose and creatinine in man is of particular interest, since the latter substance has been widely used on Rehberg's[4] recommendation as a measure of glomerular filtrate.

The subjects of this investigation were healthy, male, medical students between the ages of 20 and 30; xylose, creatinine and urea clearances were measured in the morning after no breakfast or a light meal in which milk, tea, coffee and protein were excluded.

Xylose (50 gm.) and creatinine (10 gm.) were administered separately with varying amounts of water 90 and 60 minutes respectively prior to the start of the first urine collection period. Three or more consecutive 20-minute periods were observed; in most of these the rate of urine flow was above the lower figure (1.7) given as the augmentation limit of urea.[5] Blood samples were withdrawn at 30-minute intervals and plasma concentrations were interpolated to the middle of each urine period. Plasma and urine (diluted to the expected U/P ratio) were analyzed by the methods described by Shannon, Jolliffe and Smith.[6]

The average clearances (UV/P.S.A.) expressed as cc. per minute per square meter of body surface are: urea, 35.1; xylose, 51.3, and

[1] Jolliffe, N., Shannon, J. A., and Smith, H. W., *Am. J. Phys.*, 1932, **100**, 301.

[2] Clarke, R. W., and Smith, H. W., *J. Comp. and Cell. Phys.*, 1932, **1**, 131.

[3] Marshall, E. K., Jr., *J. Comp. and Cell. Phys.*, 1932, **2**, 349.

[4] Rehberg, P. B., *Biochem. J.*, 1926, **20**, 447.

[5] Moller, E., McIntosh, J. F., and Van Slyke, D. D., *J. Clin. Invest.*, 1928, **6**, 427.

[6] Shannon, J. A., Jolliffe, N., and Smith, H. W., *Am. J. Phys.*, 1932, **102**, 534.

creatinine, 89.1. The average creatinine/xylose ratio was 1.74, and the average urea/xylose ratio was 0.684. The creatinine/xylose ratio for man (1.74) is thus somewhat higher than was reported for the dog (1.40). Accepting the xylose clearances as measuring the glomerular filtrate, it appears that a considerable quantity of creatinine is removed from the blood by some mechanism other than glomerular filtration, amounting to about 75% of the filtered creatinine, or 43% of the total creatinine excreted. It is inferred that this moiety is removed from the blood and excreted into the urine by tubular secretion.

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Metabolism of d- and l-Methionine.

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Previous investigation of the physiological rôle of methionine in the animal organism led the writers to conclude that "methionine, like cystine, is capable of unmistakably stimulating growth in albino rats subsisting on a basal diet poor in cystine.[1, 2] It was pointed out[2] that this observation immediately raised various questions relative to the intermediary metabolism of methionine. Referring to one of these problems, we stated: "It is obvious, of course, that, since the addition of methionine (*dl*) to the diet of animals subsisting on the regimen previously described leads to growth stimulation, the study of the physiological behavior of . . . . . the separate optically active forms of methionine becomes important." These compounds have been investigated with the following results.

Methionine was synthesized and resolved according to the methods of Windus and Marvel.[3, 4] *d*-Methionine as well as the naturally occurring *l*-methionine stimulates growth in the rat ingesting our cystine-methionine deficient diet. (*cf.*, the results of similar experi-

[1] Jackson, R. W., and Block, R. J., *Science*, 1931, **74**, 414.
[2] Jackson, R. W., and Block, R. J., *J. Biol. Chem.*, 1932, **98**, 465.
[3] Windus, W., and Marvel, C. S., *J. Am. Chem. Soc.*, 1930, **52**, 2575.
[4] Windus, W., and Marvel, C. S., *J. Am. Chem. Soc.*, 1931, **53**, 3490.