

VALIDITY OF THE UREA METHOD FOR ESTIMATING TOTAL BODY-WATER IN MALNUTRITION

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OF the substances used for the estimation of total body-water, urea has the advantages of being non-toxic, and easy to administer and estimate. Criticisms have been levelled against the two assumptions inherent in the method—that the rate of endogenous urea formation is constant throughout the experimental period, and that the diuresis induced by the ingestion of large amounts of urea does not significantly affect the results. Antipyrin and deuterium have been suggested as being more suitable. Kornberg and Davies (1952), however, using small amounts of radioactive urea, obtained values for total body-water which agreed closely with those obtained by other methods, including the use of non-isotopic urea. Studies in man, using labelled urea, have yielded results closely approximating to those obtained by the use of deuterium (San Pietro and Rittenberg 1953). These studies indicate that the urea method is reliable, at least in normal subjects.

Gopalan et al. (1953) and Holmes et al. (1954) have used the urea method for the estimation of total body-water in severely malnourished and oedematous patients, and obtained values for total body-water as high as 87-90% of the body-weight. Commenting on these high values, Widdowson (1956) has suggested that urea nitrogen might be utilised by protein-depleted tissues, and that this might result in overestimation of total body-water in malnutrition when the urea method is used. If this suggestion is correct, apart from the fundamental implications involved, it follows that the urea method is unsuitable for the estimation of body-water in severe malnutrition.

As Widdowson pointed out, the methods by which the above suggestion could be put to test would be:

(a) To compare the values obtained for total body-water in protein-deficient persons by the urea method with those obtained by the use of some other substance such as antipyrin.

(b) To give urea to patients with protein malnutrition, subsisting on low-protein diets, and to follow the retention of nitrogen in these subjects by means of balance experiments. Both these methods are being applied here for the elucidation of this question. Here we present the results of simultaneous determination of total body-water by the urea method and the antipyrin method in normal people and severely malnourished and oedematous patients.

Material and Methods

The subjects of this investigation were five apparently normal adults and five adult patients with severe malnutrition associated with protein-deficiency oedema. The patients were similar to the patients with nutritional oedema investigated earlier by Gopalan et al. (1952), though generally less severely undernourished.

The total body-water of all subjects was estimated by the simultaneous use of urea and antipyrin. 20 g. of urea was given orally, and 1 g. of antipyrin in 50 ml. of 5% glucose solution intravenously over a period of five minutes. Samples of blood were obtained 2, 3½, and 5 hours after the injection in the normal subjects and 5, 7, and 8 hours after the injection in the oedematous patients. The urine voided during each interval was collected under toluene. Urea, in the serum and urine, was determined by the method of van Slyke and Cullen (1914). Antipyrin was estimated as the 4-nitroso-antipyrin using a spectrophotometer at 350 mμ (Brodie 1951). Total plasma-proteins were estimated (by the microkjeldahl technique) in order to apply the necessary corrections to the water space.

Results

Expressed as percentage of body-weight, the total body-water, estimated by use of urea, ranged from 52.6

SIMULTANEOUS ESTIMATION OF TOTAL BODY-WATER BY UREA AND ANTIPYRIN METHODS IN FIVE NORMAL ADULTS AND FIVE MALNOURISHED PATIENTS WITH OEDEMA

Case		Total body-water (as % of body-weight)		Urea/antipyrin ratio × 100
		Urea method	Antipyrin method	
Normal adults	1	61.1	58.7	104.0
	2	61.4	59.6	103.0
	3	61.4	65.2	94.4
	4	52.6	48.8	108.0
	5	55.3	57.0	97.1
} 101.3				
Malnourished patients	1	77.8	81.6	95.3
	2	65.1	64.5	100.9
	3	75.3	73.2	102.9
	4	76.8	73.5	104.4
	5	89.3	86.3	96.7
} 101.4				

to 61.4 (mean 58.4) in the normal people, and from 65.1 to 89.3 (mean 75.8) in the oedematous patients (see table). Values, by the antipyrin method, ranged from 48.8 to 65.2 (mean 57.9) in the normals and from 64.5 to 86.3 (mean 75.8) in the oedematous patients. The urea values were slightly higher in three of the five normals and four of the five oedematous patients. The mean value for the urea/antipyrin ratio was, however, practically identical in the two groups—1.013 in the normals and 1.014 in the malnourished subjects. No correlation was observed between the percentage of body-water and the urea/antipyrin ratio.

Discussion

The results indicate that urea tends to give values slightly higher than does antipyrin in both normal and malnourished subjects. But the differences between values in the urea and antipyrin methods are no higher in the malnourished patients than in the normal controls. This would indicate that under conditions obtaining in the estimation, urea is not being used to any significant extent for purposes of nitrogen metabolism in the malnourished subjects. These results need not necessarily be considered inconsistent with the reported observations pointing to the possible use of urea by protein-deficient tissues (Holt and Snyderman 1956). It is possible that urea cannot be used by the tissues when administered alone as it was here, but can be used when given with a low-protein diet in malnourished patients. This question is being further explored and the results of the study will be published in detail later.

It may, however, be concluded from the present study that the urea method in malnourished subjects does not lead to any significant overestimation of total body-water. The results, therefore, seem to put the urea method on a firmer footing as a simple and reliable method for the determination of total body-water, not only in normal subjects, but also in severely malnourished and oedematous patients.

Summary

Total body-water was estimated in five normal adults and five malnourished oedematous patients. The differences in the results obtained by the urea and antipyrin methods were small and no more in the patients than in the normal people. These results indicate that the urea method is suitable for the estimation of total body-water even in malnourished patients.

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