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William M. McConahey, … , F. Raymond Keating Jr., Marschelle H. Power

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Research Article

AN ESTIMATION OF THE RENAL AND EXTRARENAL CLEARANCE OF RADIOIODIDE IN MAN

By WILLIAM M. McCONAHEY, F. RAYMOND KEATING, JR., AND MARSCHELLE H. POWER

(From the Division of Medicine, Mayo Clinic, and the Division of Biochemistry, Mayo Foundation, Rochester, Minnesota)

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The growing importance of radioiodine to clinical practice and medical research has stimulated interest in various kinetic aspects of iodine metabolism, including the renal excretion of iodide as estimated by the renal clearance of iodide (1–3). In addition, it has been suggested that the most explicit and precise measure of the iodine-accumulating function of the thyroid gland may be the clearance of iodide by the thyroid (3, 4), defined by analogy as the volume of plasma or serum cleared by the thyroid gland of its iodide content per minute, and determined from multiple observations *in vivo* of the thyroid itself compared with observations of serum. Since most of the circulating iodide eventually reaches the urine or the thyroid gland, it has also been observed (1) that a useful indirect measure of clearance of iodide by the thyroid called "extrarenal iodide clearance," may be obtained from observations on serum plus urinary excretion alone, without recourse to observations *in vivo*.

Although the foregoing concepts and methods of estimation have been discussed at length, few actual values for such clearances have been published. It is the purpose of this report to present values for renal and extrarenal clearance of radioiodide in a group of patients illustrating various states of thyroid and renal function.

METHODS

After the administration by mouth of 100 microcurie tracer doses of radioiodine, along with 100 micrograms of sodium iodide as carrier, samples of blood serum and of urine, collected at suitable intervals, were analyzed for their content of I^{131}. The methods employed for collections and analyses have been described elsewhere (1, 5). Clearances were calculated by the method described by Berkson and associates (6). The renal clearance of iodide was obtained by use of the formula $Cl = \frac{U'_t}{P'_0} r$, in which U'_t is the estimated asymptotic value of the renal excretion curve expressed as a fraction of the dose administered and r the exponential rate constant of that curve, and P'_0 is the concentration of inorganic I^{131} in the blood at zero time obtained by extrapolation. Extrarenal clearance of iodide was calculated by the use of the formula $\frac{r(1 - U'_t)}{P'_0}$, and is the difference between total clearance and renal clearance.

RESULTS

Renal clearances of iodide have been estimated for 43 individuals by the foregoing method. Fifteen of the patients studied had exophthalmic goiter, one had adenomatous goiter with hyperthyroidism, six had myxedema and 21 were euthyroid (15 with normal thyroids, two with carcinoma of the thyroid and four with adenomatous goiter without hyperthyroidism).

Twelve of the 15 patients with normal thyroid glands who were studied had severe renal insufficiency, and had been hospitalized for treatment of this condition. The various diagnoses of the renal disease among these 12 patients were glomerulonephritis, nephrosis, myeloma, cardiac decompensation and intracapillary glomerulosclerosis.

Although tests of renal function were not performed in the other 31 patients, none of them made any complaint referable to the kidneys and studies or laboratory tests were not indicative of serious renal disease. It was assumed that their renal function was normal, or at least nearly so.

Table I gives the mean values for renal clearance of iodide among the patients studied.

TABLE I

Renal iodide clearance in cubic centimeters of serum cleared per minute

Condition	Renal function*			
	Presumably normal		Definitely impaired	
	Cases	Iodide clearance	Cases	Iodide clearance
Hyperthyroidism	16	32.7 ± 1.0		
Euthyroidism	9	33.3 ± 3.1	12	8.7 ± 1.6
Myxedema	5	17.9 ± 1.6		

* The value following the ± is the standard error of the mean.

In Table II are listed the extrarenal clearances of iodide obtained. For patients who had hyperthyroidism, the mean value was 154.6 cc. of serum cleared of radioiodine per minute; for euthyroid persons with presumably normal renal function it was 26.3 cc. per minute; for euthyroid patients with impaired renal function it was 6.5 cc. per minute; and for patients with myxedema it was 4.7 cc. per minute. It should be noted that there is very little overlapping of one group by another.

COMMENT

The values for renal clearance of iodide reported here compare closely with those found by Myant and his associates (3), who, in a study in which radioiodine also was used, observed mean clearance rates of 31 cc. per minute among 11 euthyroid persons and 27 cc. per minute among 11 persons with untreated thyrotoxicosis. In studies in which large amounts of nonradioactive sodium iodide were administered, Elsom and his co-workers (7) found that the kidney of the dog cleared 9.0 cc. of plasma per minute of its iodide content, and Nelson and his associates (8) found the range of clearance of renal iodide in 13 normal men to be between 10 and 25 cc. per minute. It is of interest that the clearance of iodide in physiologic amounts (as observed in the studies in which radioiodine was used) was greater than the clearance estimated when much larger quantities of iodide were given to human beings and to dogs.

In so far as the clearance of tracer amounts of I^{131} may be taken as a valid measure of the clearance of the nonradioactive inorganic iodide of the plasma, the clearance of the latter would appear to be greater than that of other halogens, such as chloride or bromide.

TABLE II

Extrarenal clearance of iodide: 43 cases

Condition	Cases	Serum cleared per minute, cc.	
		Range	Mean*
Hyperthyroidism	16	49–479	154.6 ± 19.5
Euthyroidism with presumably normal renal function	9	10–64	26.3 ± 5.2
Euthyroidism with impaired renal function	12	3–11	6.5 ± 0.2
Myxedema	6	3–8	4.7 ± 0.7

* The value following the ± is the standard error of the mean.

The values for extrarenal clearance of iodide found in this study correspond to the thyroid clearance rates reported by Myant and his associates (3) and by Stanley (9). The former investigators found the mean thyroid clearance in 11 normal persons to be 16.0 cc. per minute and in 11 thyrotoxic patients, 486 cc. per minute. Stanley found the thyroid clearance of iodide in three normal persons to be 18.6, 7.2 and 28.7 ml. per minute. Extrarenal clearance in euthyroid and hyperthyroid persons is a close approximation of thyroid clearance but in myxedematous persons this is not so.

Extrarenal clearance was consistently lower among the patients who had impaired renal function. This inferred reduction in thyroidal iodide clearance may not necessarily imply that the thyroid glands in this group accumulated less iodine per unit of time, since the average concentration of inorganic iodide in plasma may well be higher in these cases.

SUMMARY

Doses of I^{131} were administered to 43 persons, and from samples of urine and serum collected at suitable intervals, renal clearances of I^{131} were calculated by a method described by Berkson and associates (6). Mean clearances in the individuals presumed to have normal renal function were 32.7 cc. per minute for persons who had hyperthyroidism, 33.3 cc. per minute for euthyroid persons, and 17.9 cc. per minute in patients who had myxedema. The clearances among persons who had impaired renal function were markedly decreased.

A method is also given for the determination of the extrarenal clearance of radioiodide (which is an approximation of thyroid clearance of iodide in all except hypothyroid persons). The hyperthyroid patients studied had a mean extrarenal clearance of iodide of 154.4 cc. per minute; the euthyroid persons with presumably normal function, 26.3 cc. per minute; the euthyroid persons with impaired renal function, 6.5 cc. per minute; and persons with myxedema, 4.7 cc. per minute.

Little overlap was found between any two groups. This clearance rate appears to be a sensitive index of thyroid function.

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