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Internal Dosimetry Studies of Radiopharmaceuticals; II. Sodium Iodohippurate ^{131}I[1]

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The distribution and effective half-life of Sodium Iodohippurate ^{131}I was determined in two species, namely rats and cats. These data were then extrapolated to man to calculate the radiation dose delivered during the diagnostic use of Sodium Iodohippurate ^{131}I.

This communication will show the levels of radiation expected, on the basis of rat and cat data, following the intravenous administration of Sodium Iodohippurate to man. Radiation levels reported are based upon the administration of a 30 μc dose. This dose represents an upper level currently being used in the determination of renal function (1).

This communication will also compare the radiation dose delivered during the diagnostic use of Sodium Iodohippurate ^{131}I with maximum permissible occupational exposure limits as recommended by the National Committee on Radiation Protection (2) and the International Commission on Radiological Protection (3).

MATERIALS AND METHODS

The distribution of Sodium Iodohippurate ^{131}I was studied in adult rats and cats. Tissue concentrations of ^{131}I were determined by completely digesting tissues or organs in aqueous sodium hydroxide and counting aliquots of resulting solutions in a sodium iodide well scintillation counter. Effective half-life was determined using a Packard-Armac scintillation detector. Due to the size of the detector chamber, it was necessary to use kittens instead of adult cats to determine effective half-life in the cat.

Formulae used in calculating radiation dose were taken from the report of I.C.R.P. Committee II (4) as follows: $q = \frac{2.8 \times 10^{-3} mR}{f_2 \Sigma}$ where: q represents the body burden of the radionuclide in microcuries, f_2 is the fraction of radionuclide in organ of that in total body, R is the dose rate in rems per week, m is the mass, in grams, of the organ of reference, and Σ is the effective energy per disintegration of the radionuclide.

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[1]Hippuran®-131, Abbott Laboratories, North Chicago, Illinois, & Oak Ridge, Tennessee.
[2]Nucleonics Laboratory, Abbott Laboratories.

TABLE I

PHYSICAL CONSTANTS USED FOR CALCULATION OF EFFECTIVE ENERGY, Σ (7)

Emissions	*Energy, mev*	*Fraction f*	*Tissue Absorption Coefficient*	*Internal Conversion K shell*
β_1	.250	.028		
β_2	.335	.093		
β_3	.608	.872		
β_4	.815	.007		
γ_1	.722	.028	.033	.0028
γ_2	.637	.093	.034	.0037
γ_3	.364	.872	.033	.018
γ_4	.164	.007	Ignored	

Binding energy, η, for product nuclide, Xe, = .035 mev.

TABLE II

TISSUE DISTRIBUTION OF SODIUM IODOHIPPURATE ^{131}I IN RATS

% of Total Recovered Radioactivity

Organ	*5 min*	*5 min*	*20 min*	*1 hr*	*4 hr*	*6 hr*	*24 hr*
Thyroid	—	—	0.03	0.06	0.31	0.15	.78*
Liver	8.07	9.4*	1.6	0.37	0.15	0.06	1.36
Spleen	0.13	0.15*	0.035	0.01	—	0.001	—
Heart	1.24*	0.43	0.07	0.02	—	0.002	.01
Testes	0.28	0.45*	0.092	0.03	0.001	0.006	—
G.I. Tract	4.68	4.82	2.3	5.98*	4.19	1.75	.88
Carcass	67.55	66.8	23.3	14.05	6.89	1.28	2.2
Kidneys	10.42	14.96	1.6	0.18	—	0.05	—
Bladder and Urine	7.62	2.96	70.7	79.30	88.46	96.70	94.71
Kidneys and Urine	18.04*	17.92					
% of Injected Dose Recovered	82.0	105.0	107.0	96.9	91.6	97.9	105
Animal Weight (gm)	230	190	230	242	245	230	240

*Highest concentration found

By rearranging, simplifying and integrating from zero to infinity, the above equation becomes:

$$\text{Total Dose } \beta + \gamma \text{ (rems)} = \Sigma \times \frac{357}{7} \times \frac{qF_2}{m} \times \frac{T}{.693}$$ where: T = effective half-life, in days, of the radionuclide.

For the case where the radionuclide is not disappearing at a constant rate, this equation would then become:

$$D\beta + \gamma \text{ (rems)} = \Sigma \times \frac{357}{7} \times \frac{qF_2}{m} \left(f_a \frac{Ta}{.693} + f_b \frac{T_b}{.693} \text{ etc.} \right)$$

Here f_a, f_b, T_a, T_b represent fractional parts and effective half-lives of each component part of the disappearance curve.

The effective energy per disintegration, Σ, can be calculated according to empirical equations given in the report of the I.C.R.P. Committee II (4). This effective energy term is dependent upon the decay scheme of the radionuclide, tissue absorption coefficients, effective radius of the body organ, etc. Pertinent physical data used in calculation of ϵ are shown in Table I and calculated values of Σ for ^{131}I are shown for various organs in Table IV.

For purposes of calculating radiation dose, the highest concentration found in any organ, rat or cat, was used as the initial concentration, $\frac{qF_2}{m}$. Initial whole body retention was assumed to equal 100 per cent of the injected dose. Radiation dosages were calculated from the total body effective half-life as determined

TABLE III

TISSUE DISTRIBUTION OF SODIUM IODOHIPPURATE ^{131}I IN CATS

	% of Injected Radioactivity	
Organ	*13 min*	*24 hrs*
Thyroid	0.009	0.017*
Heart	0.805*	0.082
Lungs	0.995*	0.085
Liver	4.51*	0.605
Spleen	0.295*	0.029
Testes	0.048*	0.019
G. I. Tract	3.95*	1.20
Kidneys	17.27*	3.12
Bladder and Urine	7.89*	3.30
Kidneys and Urine	25.16*	

*Highest concentration found

TABLE IV

DATA SUMMARY USED IN CALCULATION OF RADIATION DOSAGE
(q = 30 μc Sodium Iodohippurate ^{131}I)

Organ	*Highest Fraction of Dose* F_2	*Amt present with 30 μc Hippuran-131* qF_2 (μc)	*Organ Wt Man* m (gm)	*Concen μc/gm* $\frac{qF_2}{m}$	Σ	*Fraction of Total Dose and Effective Half-Life*			
						f_a	T_a	f_b	T_b
Whole Body	1.0	30	70000	.0004285	.445	.755	.01 days	.245	.22 days
Thyroid	.0078 rat	0.234	20	.0117	.236	"	"	"	"
Liver	.094 rat	2.82	1700	.001659	.310	"	"	"	"
Spleen	.00295 cat	.0885	150	.00059	.274	"	"	"	"
Kidneys + Urine	.2516 cat	7.548	300	.02516	.274	"	"	"	"
Heart	.0124 rat	.372	300	.00124	.274	"	"	"	"
Testes	.0045 rat	.135	40	.00337	.236	"	"	"	"
G.I. Tract	.0598 rat	1.794	2000	.0009	.445	"	"	"	"
Lungs	.00995 cat	.2985	1000	.000298	.310	"	"	"	"

in the rat. Effective half-life in individual body organs was assumed to be the same as total body half-life. Strictly speaking, the effective half-life of Sodium Iodohippurate ^{131}I in individual body organs might be different from total body half-life, although organ data shown in Table II do not indicate any great such difference, with the exception of the thyroid. Thyroid concentration of metabolized iodide might be expected to approach maximum at approximately 24 hours.

Due to the extremely rapid clearance of Sodium Iodohippurate ^{131}I, we made the assumption that the initial concentration in the kidneys was equal to the highest concentration found in the kidneys per se *plus* the amount excreted in the urine during that time interval.

RESULTS

A. *Concentration or Tissue Distribution*

1. Rats: Seven male rats (avg wt 230 gm) were intravenously injected with 1 μc (2.32 μg) Sodium Iodohippurate ^{131}I (lot no. Hr-169-12) in 0.7 ml 5% Dextrose solution.

Animals were sacrificed at 5 and 20 minutes and 1, 4, 6 and 24 hours and tissue concentrations determined. Table II summarizes these distribution studies.

2. Cats: Two male adult cats (wts 3.1 and 3.4 kg) were intravenously injected with 12.3 μc (.024 mg) and 13.5 μc (.026 mg) of Sodium Iodohippurate ^{131}I (lot no. Hr-226-9). Animals were anesthetized with 30 mg/kg sodium pentobarbital[1] intraperitoneally in order to facilitate intravenous injection. These animals were sacrificed at 13 minutes and 24 hours and tissue concentrations of ^{131}I determined. Table III summarizes these distribution studies.

B. *Turnover Studies*

1. *Rats:* Eight male rats (avg wt 225 gm) were intravenously injected with 0.5 μc (1.26 μg) Sodium Iodohippurate ^{131}I and each was counted periodically via a liquid scintillation detector to determine rate of disappearance of drug. The average values for the eight animals are shown in Fig. 1. Electrical stimulation of testes was used to cause rats to void urine just prior to counting.

Graphic resolution of the observed disappearance curve (Fig. 1) into its component parts yielded two components with initial fraction of total dose and effective half-lives as follows: $f_a = .755$, T_a (effective) = 0.01 days; $f_b = .245$ T_b (effective) = 0.22 days.

2. Cats: One female kitten (wt 695 gm) and one male kitten (wt 650 gm) were intravenously injected with 0.5 μc (.002 mg) and 0.26 μc (.001 mg) of Sodium Iodohippurate, respectively.

An indwelling catheter was fixed in the bladder so that the bladder could be rinsed just prior to counting the animal in an Armac liquid-scintillation detector. The animals were anesthetized with 30 mg/kg sodium pentobarbital intraperitoneally in order to place the catheter and to facilitate injection.

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[1]Nembutal®, Abbott Laboratories, North Chicago, Illinois.

Figure 2 shows the disappearance of ^{131}I in the kittens. The curve was resolved into its components as previously described, yielding two components with initial fraction of total dose and effective half-lives as follows: $f_a = .778$, T_a (effective) = 0.01 days; $f_b = .222$, T_b (effective) = 0.09 days. These values are not greatly different from those obtained in rats and it is doubtful that differences are significant, since only two kittens were used.

Data used in calculation of total radiation dose from the use of 30 μc Sodium Iodohippurate ^{131}I are summarized in Table IV. Data used in these calculations were purposely chosen so that radiation dosage would represent maximum values, *i.e.*, calculations are made using highest tissue concentrations found and greatest effective half-life factor. Table IV accounts for approximately 45 per cent of total dose in cited organs and over 90 per cent of dose is excreted within 6 to

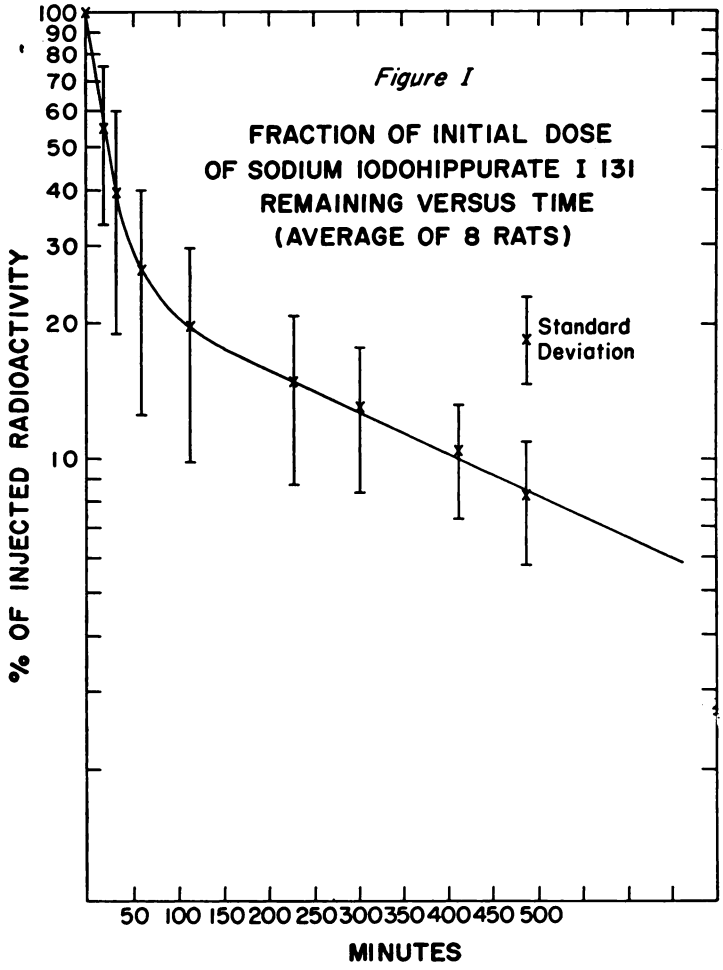

Fig. 1. Fraction of Initial Dose of Sodium Iodohippurate ^{131}I Remaining Versus Time (Average of 8 rats).

24 hours. To our knowledge there are no other sites where ^{131}I is significantly concentrated.

Representative radiation doses that might be expected in man during the diagnostic use of 30 μc of Sodium Iodohippurate ^{131}I are shown in Table V. Table VI gives maximum permissible occupational exposure limits, as recommended by the N.C.R.P. (2) and I.C.R.P. (3), in addition to a comparison of these limits to the radiation dose delivered during the diagnostic use of Sodium Iodohippurate ^{131}I.

DISCUSSION

The estimated radiation dose to man from a 30 μc diagnostic dose of Sodium Iodohippurate ^{131}I is low even when the most adverse data is used to make calculations, *i.e.* highest tissue concentrations found and longest effective half-life. It should be noted that the animal data agree favorably with reported in man.

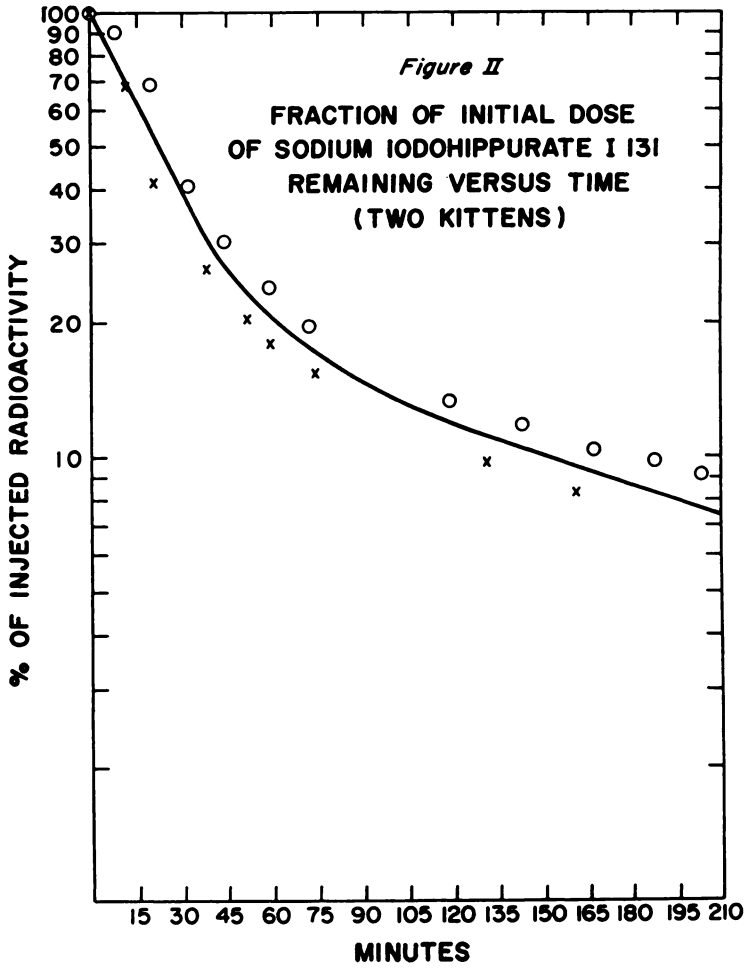

Fig. 2. Fraction of Initial Dose of Sodium Iodohippurate ^{131}I Remaining Versus Time (Two Kittens).

For example, Meade and Shy (5) report 67.7 per cent excretion of Sodium Iodohippurate ^{131}I within 30 minutes and Boyd and Murdock (6) report 55 per cent excretion of injected dose within 20 minutes.

In terms of radiation dosage, Sodium Iodohippurate ^{131}I might be considered an ideal radiopharmaceutical in that desired diagnosis is achieved rapidly and the radioactivity is rapidly excreted with even the longest effective half-life component being considerably less than one day. The rate of excretion in patients with kidney disease would be slower, resulting in a longer effective half-life and a greater radiation dose. Efforts are being made in these laboratories to evaluate

TABLE V

ESTIMATED TOTAL RADIATION DOSAGE IN MAN FROM DIAGNOSTIC USE OF 30 μC OF SODIUM IODOHIPPURATE—^{131}I

Organ	$D_{\beta+\gamma}$ *mrems*
Whole Body	0.9
Thyroid	12.5
Liver	2.3
Kidneys	31.2
Spleen	0.7
Heart	1.5
Testes	3.6
G. I. Tract	1.8
Lungs	0.4

TABLE VI

MAXIMUM PERMISSIBLE OCCUPATIONAL EXPOSURE LIMITS AND COMPARISON WITH ESTIMATED RADIATION DOSE FROM 30 μC SODIUM IODOHIPPURATE ^{131}I

Organ	*Maximum permissible weekly occupational exposure limit (mrems)*	*Ratio-delivered dose (Iodohippurate) to weekly exposure limit*
Total Body	100	.009
Thyroid	600	.020
Liver	300	.008
Kidneys	300	.104
Spleen	300	.002
Heart	300	.005
Testes	100	.036
Lungs	300	.001

most of the radiopharmaceuticals as to amounts of internal radiation delivered (8).

In Table VI a comparison of radiation dose delivered versus suggested exposure limits clearly demonstrates that a 30 μc diagnostic dose of Sodium Iodohippurate ^{131}I does not even exceed suggested weekly exposure limits. Theoretically, such a diagnostic procedure could be used repeatedly during a given year without exceeding even occupational exposure limits. It is universally agreed, however, that unnecessary exposure to radiation should be avoided so that, as with any radiopharmaceutical, use should be consistent with the concept of adequate diagnosis and minimum radiation.

SUMMARY

The distribution and effective half-life of Sodium Iodohippurate ^{131}I has been studied in both rats and cats. These data have been extrapolated to man to estimate the radiation dose delivered during diagnostic use for determination of renal function. Radiation dosage calculations indicate that the radiation hazard from a 30 μc dose of Sodium Iodohippurate ^{131}I would seem to be minimal, and that this dose would deliver less radiation than suggested weekly exposure limits to radiation workers.

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