mird / DOSE ESTIMATE REPORT NO. 6

SUMMARY OF CURRENT RADIATION DOSE ESTIMATES TO HUMANS FROM ^{197}Hg- AND ^{203}Hg-LABELED CHLORMERODRIN

November 1975

SUMMARY OF ESTIMATED ABSORBED DOSES FROM RADIOACTIVE MERCURY AFTER A SINGLE INTRAVENOUS ADMINISTRATION OF LABELED CHLORMERODRIN

	Absorbed dose (rads/mCi of radioactive mercury administered)			
	No "blocking dose" of meralluride		With "blocking dose" of 1 ml meralluride (39 mg Hg/ml)	
Target organ	^{197}Hg	^{203}Hg	^{197}Hg	^{203}Hg
Bladder wall	1.1	2.1	1.2	2.1
Renal cortex	12	100	9.5	55
Renal medulla	1.4	20	1.2	15
Liver	1.5	19	0.56	7.1
Ovaries	0.040	0.77	0.046	0.61
Red marrow	0.11	1.6	0.082	0.98
Testes	0.028	0.52	0.037	0.46

RADIOPHARMACEUTICAL

Chlormerodrin (3-chlormercuri-2-methoxypropylurea) is a well-known clinical diuretic. Current commercial preparations of labeled chlormerodrin contain either ^{203}Hg or ^{197}Hg at a specific activity ranging from 0.1 to 5 mCi/mg Hg. The injectable aqueous solution contains 0.9% benzyl alcohol as a preservative and may contain sodium hydroxide or acetic acid for pH adjustment. For purposes of these dose calculations the radionuclidic and radiochemical purity of the pharmaceutical have been assumed to be 100%. Preparations of ^{197}Hg-labeled chlormerodrin containing ^{203}Hg as a radionuclidic impurity will result in higher radiation doses than those calculated for a preparation with a radionuclidic purity of 100%.

To reduce the amount of radiomercury retained by the kidneys, 1 ml of the nonradioactive diuretic sodium meralluride may be administered intramuscularly 1 day before the radioactive injection. This preparation contains 48 mg theophylline and 39 mg Hg (bound to meralluride)/ml which results in a dose of 0.56 mg Hg/kg body weight for a 70-kg man.

NUCLEAR DATA

Nuclear data for ^{197}Hg and ^{203}Hg are given in Table 1 (*1*).

BIOLOGIC DATA

As a result of the marked species difference in the renal distribution of chlormerodrin, only human data were used. The human tissue distribution data for labeled chlormerodrin on which this report was based were obtained from the literature and from studies initiated by the MIRD Committee. A portion of these data was summarized by McAfee (*2*) and copies of the complete data are available from the MIRD Committee. The biologic parameters given in Table 2 and the histograms shown in Fig. 1 were derived from these data.

After the intravenous injection of chlormerodrin, it accumulates in the renal cortex with an uptake half-time of approximately 20 min. Within 2–3 hr a peak concentration of 44% of the administered activity is located in the renal cortex (two kidneys). By extrapolating the retention curve for the renal cortex back to the time of injection, 50% of the administered activity can be attributed to the renal cortex. This retention curve can be fitted by assuming that 38% of the activity passing through the cortex has a biologic half-time of approximately 8 hr, and 12% (range, 8–20%) has a biologic half-time of 30 days (range, 25–85 days).

TABLE 1. NUCLEAR DATA*

Radionuclide	^{197}Hg		^{203}Hg	
Physical half-life	65 hr		46.5 days	
Decay constant	0.0107 hr^{-1}		0.0149 day^{-1}	
Mode of decay	Electron capture		Beta minus	
Equilibrium dose constant for nonpenetrating radiation (g-rad/μCi-h)	0.1445		0.2096	
Principal photons†	E_i (MeV)	n_i	E_i (MeV)	n_i
	0.0107‡	0.502	0.0114‡	0.0567
	0.0704‖	0.717	0.0776‖	0.128
	0.0773	0.254	0.2792	0.817

* For complete compilation of nuclear data, the reader is referred to Ref 1.

† Table lists only photons with mean yield per disintegration $\geq$0.01; E_i is photon energy in MeV; n_i is mean number of photons per disintegration.

‡ Weighted mean energy of L x-rays.

‖ Weighted mean energy of K x-rays.

TABLE 2. BIOLOGIC PARAMETERS OF THE FRACTIONAL DISTRIBUTION FUNCTIONS, $\alpha_h(t)$, OF MERCURY FROM A SINGLE INTRAVENOUS ADMINISTRATION OF CHLORMERODRIN*

$$\alpha_h(t) = \sum_j \alpha_{hj} e^{-\lambda_j t} = \alpha_{h1} e^{-\lambda_1 t} + \alpha_{h2} e^{-\lambda_2 t} + \alpha_{h3} e^{-\lambda_3 t} + \alpha_{h4} e^{-\lambda_4 t}$$

Source organs r_h	α_{h1}	λ_1 (hr^{-1})	α_{h2}	λ_2 (hr^{-1})	α_{h3}	λ_3 (hr^{-1})	α_{h4}	λ_4 (hr^{-1})
No "blocking dose" of meralluride								
Blood	0.83	3.47	0.16	0.231	0.008	0.0578	0.002	0.000413
Liver	—	—	—	—	0.15	0.000722	—	—
Ovaries	—	—	—	—	0.000009	0.000413	—	—
Renal cortex (2)	—	—	0.38	0.0866	0.12	0.000963	—	—
Renal medulla (2)	—	—	—	—	0.006	0.000722	—	—
Skeletal muscle	—	—	—	—	0.03	0.000413	—	—
Skeleton	—	—	—	—	0.04	0.000413	—	—
Testes	—	—	—	—	0.00004	0.000413	—	—
Total body†	0.10	0.693	0.53	0.1155	0.10	0.00413	0.27	0.000413
With "blocking dose" of 1 ml meralluride (39 mg Hg/ml)								
Blood	0.83	3.47	0.16	0.231	0.008	0.0578	0.002	0.000413
Liver	—	—	—	—	0.055	0.000722	—	—
Ovaries	—	—	—	—	0.000009	0.000413	—	—
Renal cortex (2)	—	—	0.44	0.0866	0.06	0.000963	—	—
Renal medulla (2)	—	—	—	—	0.006	0.000722	—	—
Skeletal muscle	—	—	—	—	0.015	0.000413	—	—
Skeleton	—	—	—	—	0.02	0.000413	—	—
Testes	—	—	—	—	0.00004	0.000413	—	—
Total body†	0.10	0.693	0.67	0.1155	0.10	0.00413	0.13	0.000413

* The activity in the source region r_h at time t after administration of the radionuclide of activity A_o is given by $A_h(t) = q_h(t)e^{-\lambda t}$, where $q_h(t) = A_o \sum_j \alpha_{hj} e^{-\lambda_j t}$, α_{hj} is the initial value of of the j^{th} exponential component of the fraction of the mercury administered as chlormerodrin that appears in the source region r_h, λ_j is the biologic disappearance constant of the j^{th} exponential component, and λ is the physical decay constant of the radionuclide. The cumulated activity in the source r_h over an infinite period is given by $\tilde{A}_h(0, \infty) = A_o \sum_j \alpha_{hj}/(\lambda_j + \lambda)$.

† Values for total body include all tissues.

The distribution of radiomercury within the kidney was obtained by studying five human kidneys that were surgically removed within 24 hr after the administration of ^{203}Hg-chlormerodrin (*3*). Block specimens extending from renal capsule to papillae were sectioned in layers 2 mm thick for radioassay. The concentration of ^{203}Hg in the cortex was 5 to 13 times that in the medulla. By autoradiography, the concentration of ^{203}Hg in the cortex appeared to be relatively uniform. By radioassay, however, the maximum variation in concentration throughout different areas of cortex was approximately ±50%.

Approximately 15% of the administered radiomercury goes to the liver and has a biologic half-time of approximately 40 days. From 2 to 3% of the administered radiomercury is excreted in the bile during the first 10–12 hr. In renal disease, hepatic concentration and biliary excretion are probably important mechanisms for the elimination of this radiopharmaceutical. No quantitative concentration data

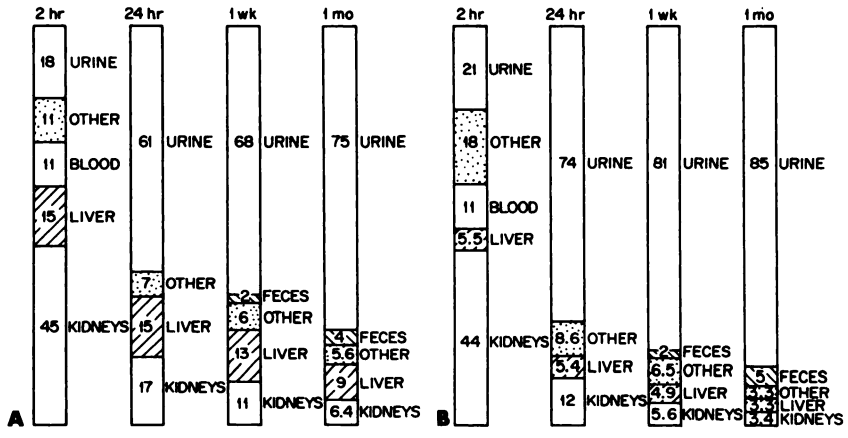

FIG. 1. Estimated percent of administered radiomercury in tissues of body at various times after single intravenous injection of ^{197}Hg or ^{203}Hg labeled chlormerodrin corrected for radioactive decay. (A) No "blocking dose" of meralluride; (B) with "blocking dose" of 1 ml meralluride (39 mg Hg/ml).

from patients with renal insufficiency are available to support this hypothesis. However, total-body counting studies have been made by Blahd on two patients with renal insufficiency which indicated an increased retention of the administered radioactivity (*2*).

Considerable data on the total-body retention of radiomercury when administered as chlormerodrin have been collected by several laboratories using excretion measurements and total-body counting. A four-component exponential function can be used to describe the total-body retention curve derived from the composite data. The biologic parameters describing distribution and retention of radiomercury in the total body and several organs are summarized in Table 2. The fraction of the administered activity excreted in the urine and feces can be estimated from Fig. 1.

The intramuscular injection of meralluride before the administration of labeled chlormerodrin serves as a "blocking dose"; however, the effectiveness of the blocking dose varies considerably among patients. In an average patient, the retention of radiomercury for the slow component in the renal cortex and for the total body is reduced to about one-half and the hepatic retention to approximately one-third of that found when meralluride is not used (*2*). There is no evidence that the "blocking dose" has any effect on the biologic disappearance constants.

ABSORBED-DOSE ESTIMATES

The values of cumulated activity $\tilde{A}$ were calculated from the biologic parameters given in Table 2 assuming instantaneous uptake of the radiomercury in the source organs. The cumulated activity for the bladder, $\tilde{A}_{BLAD}$ (*4*), was computed based on the assumption that the bladder fills at a rate of 62.5 ml/hr and empties completely five times daily at regular intervals of 4.8 hr. The bladder was assumed to be empty when the chlormerodrin was administered, which gives a maximum value for $\tilde{A}_{BLAD}$. The average dose to the bladder wall was computed using the method described by Snyder, et al (*5,6*).

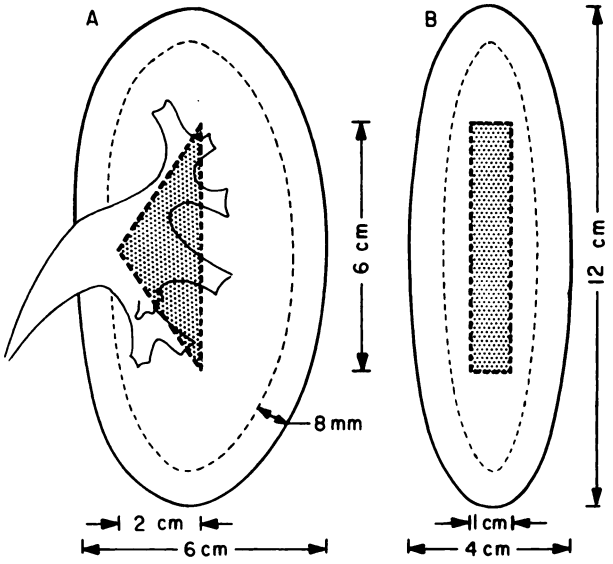

FIG. 2. Anatomic model of human kidney used for absorbed-dose calculations. Shaded area represents renal collecting system. (A) Coronal plane; (B) sagittal plane.

The cumulated activity in the renal collecting systems (geometrically wedge-shaped cavities), $\tilde{A}_w$, was calculated from the urine excretion data assuming a volume of 12 ml for the combined collecting systems and a daily urinary volume of 1500 ml. The details for computing $\tilde{A}_{BLAD}$ and $\tilde{A}_w$ are available from the MIRD Committee.

The anatomic model used for the kidneys is shown in Fig. 2 and the details are given in Refs. *2* and *4*. The absorbed fractions for the medulla, cortex, and collecting system used to compute the self-dose and dose to other regions of the kidney from penetrating radiation are given in Table 3. When the dose was computed to other organs from activity in the kidneys, the cumulated activities from the medulla, cortex, and renal collecting system were summed to give $\tilde{A}_{KID}$.

The absorbed fractions used for the dose estimate calculations in this report were obtained from special Monte Carlo computer calculations using the complete energy spectrum of penetrating and nonpenetrating radiations emitted by ^{197}Hg and ^{203}Hg in-

TABLE 3. ABSORBED FRACTIONS FOR THE COMPLETE PHOTON SPECTRUM FROM RADIOMERCURY FOR SUBREGIONS OF THE KIDNEY

Target organ (two kidneys)	Mass (gm)	Source organ (two kidneys): Cortex		Medulla		Collecting system	
		^{197}Hg	^{203}Hg	^{197}Hg	^{203}Hg	^{197}Hg	^{203}Hg
Cortex	187	0.108	0.0464	0.0456	0.0358	0.0366	0.0332
Medulla	102	0.0251	0.0206	0.107	0.0468	0.0566	0.0382
Collecting system	12	0.00217	0.00210	0.00624	0.00466	0.0762	0.0238

stead of from the interpolated values of absorbed fractions published in *MIRD Pamphlet No. 5* (*7*). The heterogeneous phantom (*8*) used for these calculations is a modification of that described in *MIRD Pamphlet No. 5* and more nearly simulates man.

REFERENCES

1. DILLMAN LT, VON DER LAGE FC: *Radionuclide Decay Schemes and Nuclear Parameters for Use in Radiation Dose Estimation, MIRD Pamphlet No 10*, New York, Society of Nuclear Medicine, 1975

2. MCAFEE JG: Problems in evaluating the radiation dose for radionuclides excreted by the kidneys. In *Medical Radionuclides: Radiation Dose and Effects*, Cloutier RJ, Edwards CL, Snyder WS, eds, AEC Symposium Series 20, CONF-691212, Oak Ridge, Tenn, Oak Ridge National Laboratory, 1970, pp 272–294

3. MCAFEE JG: Unpublished data, 1971

4. SNYDER WS, FORD MR: A dosimetric study for the administration of Neohydrin labeled with ^{203}Hg and ^{197}Hg. In *Health Physics Division Annual Progress Report*, Oak Ridge, Tenn, Oak Ridge National Laboratory, July 31, 1967, ORNL 4168, pp 267–273

5. SNYDER WS, FORD MR, WARNER GG: Estimation of dose and dose commitment to bladder wall from a radionuclide present in urine. In *Health Physics Division Annual Progress Report*, Oak Ridge, Tenn, Oak Ridge National Laboratory, July 31, 1970, ORNL 4584, pp 206–208

6. SNYDER WS, POSTON JW, WARNER GG, et al: Dose to a dynamic bladder for administered radionuclides. In *Health Physics Division Annual Progress Report*, Oak Ridge, Tenn, Oak Ridge National Laboratory, July 31, 1974, ORNL 4979, pp 13–16

7. SNYDER WS, FORD MR, WARNER GG, et al: Estimates of absorbed fractions for monoenergetic photon sources uniformly distributed in various organs of a heterogeneous phantom. MIRD Pamphlet No 5, *J Nucl Med* 10: Suppl No 3, 7–12, 1969

8. SNYDER WS, FORD MR, WARNER GG: Estimates of specific absorbed fractions for radiation sources uniformly distributed in various organs of a heterogeneous phantom. MIRD Pamphlet: to be published

ACKNOWLEDGMENTS

The work on which this report is based was performed pursuant to Contract No. FDA 223-74-6044 with the Public Health Service, Food and Drug Administration, Department of Health, Education and Welfare.

The Committee wishes to acknowledge the efforts of individuals at many medical centers for providing tissue distribution data and detailed computer analysis of this data, and to W. S. Snyder and his associates, Oak Ridge National Laboratory, for computing the absorbed fractions for ^{197}Hg and ^{203}Hg.

TASK GROUP

M. Blau, Roswell Park Memorial Institute, Buffalo, N.Y.
J. G. McAfee, Upstate Medical Center, Syracuse, N.Y.
R. H. Rohrer, Emory University, Atlanta, Ga.
W. S. Snyder, Oak Ridge National Laboratory, Oak Ridge, Tenn.
E. M. Smith, Editor of Dose Estimate Reports, Maryville, Tenn.

New MIRD Committee Publications

Pamphlet #10—Radionuclide Decay Schemes and Nuclear Parameter for Use in Radiation-Dose Estimation—Approx. 125 pp.

Provides essential radioactive decay scheme information in convenient form on more than 120 medically important radionuclides. This publication updates and supercedes Pamphlets 4 and 6 which provided data for 54 radionuclides. In loose-leaf binder format for ease of updating and adding additional radionuclides.

$8.75 with binder; $6.50 without binder.

Pamphlet #11—"S" Absorbed Dose per Unit Cumulated Activity for Selected Radionuclides and Organs—Approx. 255 pp.

The tabulated values of "S" in this publication simplify dose calculations. Instead of requiring separate consideration of each radiation of the decay scheme and its associated absorbed fraction, the "S" tabulation permits dose calculations by simply referring to a single table entry for each organ combination. This pamphlet provides "S" values for 117 radionuclides plus 6 parent and short-lived daughter combinations as a uniformly distributed source in 20 source organs irradiating 20 target organs which include ovaries, red bone marrow, testes, and total body. In loose-leaf binder format for ease of updating and adding additional radionuclides and source and target organs.

$10.20 with binder: $7.95 without binder.

Extra binders available at $3.75 each.

Please address all orders to:
MIRD Committee
404 Church Avenue, Suite 15
Maryville, Tn. 37801

CHECKS MADE PAYABLE TO THE "SOCIETY OF NUCLEAR MEDICINE" OR A PURCHASE ORDER MUST ACCOMPANY ALL ORDERS.