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THE DISTRIBUTION OF RADIOMERCURY OF A MERCURIAL DIURETIC IN SOME OF THE BODY FLUIDS OF MAN*

By C. T. Ray, M.D.
G. E. Burch, M.D.
S. A. Threefoot, M.D.
and
F. J. Kelly, M.D.**
NEW ORLEANS, LOUISIANA

(From the Department of Medicine, Tulane University School of Medicine and Charity Hospital of Louisiana at New Orleans)

During the course of experiments[2,3,5,6,9] with Mercuhydrin† labeled with $Hg^{203,205}$, various body fluids were obtained for the purpose of studying the relationship of the concentration-time course of the radiomercury in the blood serum to that in the respective body fluids. All of the various fluids could not be studied in the same subject nor could they be studied comprehensively in many instances.

Many observations on the distribution and excretion of mercury are found in the literature[4,7,8]. However, these investigations have been concerned principally with mercury in the treatment of syphilis by inunction or injection or with mercurial poisoning. These constitute a different problem from that of an intravenously administered mercurial diuretic in that the factors of time, total dosage, rapidity of absorption, and the chemical compound containing the mercury affect its distribution and excretion. In view of the relative paucity of data on the distribution and fate of the mercury incorporated in a mercurial diuretic of the type used frequently in clinical medicine, it seems advisable to report these observations, even though the series is small and the data were obtained only incidentally to other more extensively planned investigations.

Materials and Methods. The subjects were adults who were either normal or were suffering with disease states which produced pleural, peritoneal, or edema fluids suitable in quantity for collection and study. Two cubic centimeters of the mercurial diuretic was administered intravenously, each cc. containing 39 mg. of mercury. The radiomercury had an activity such that 8 to 20 million counts per minute were introduced. In an occasional instance, the diuretic was introduced in a capsule, as previously described[6]. When possible, samples of the body fluids were collected simultaneously with those of blood, for purposes of comparison.

The various body fluids were collected in the following manner:

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** Life Insurance Medical Research Fund Fellow (1948-49), Department of Medicine, Tulane University School of Medicine and Charity Hospital of Louisiana at New Orleans.

† The Mercuhydrin (methoxy-oxymercuripropylsuccinylurea with theophylline labeled with radiomercury) was prepared in this laboratory by Messrs. Harold Krahnke, Darwin Kaestner, and Edwin Sprengler through the cooperation of Dr. H. L. Daiell of Lakeside Laboratories, Milwaukee, Wisconsin.

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1, gastric juice by means of a stomach tube in one subject;

2, sweat in vials, from the surfaces of the body of 9 subjects who rested quietly in a hot and humid room (approximately 49° C. and 75% relative humidity). The subjects entered the hot room at varying lengths of time after the injection (0-120 minutes);

3, bile from the outlet of a T-tube placed in the common bile duct for postoperative

TABLE 1.—CLINICAL DATA

Material Studied	*No. of Subjects*	*Sex*		*Color*		*Age or Age Range (Yrs.)*	*Diagnoses*
		M	*F*	*C*	*W*		
Ascitic fluid	2	2		1	1	58 & 60	2 Hepatic cirrhosis
Sputum	3	2	1	3		41 – 68	1 HCVD* with CHF** 1 ASHD*** with CHF** 1 Cholecystitis
Pleural fluid	2	1	1	2		16 & 58	1 Tuberc. with pleural effusion 1 Malignancy and scleroderma
Gastric juice	1	1		1		31	1 Postpneumonia
Pericardial fluid	1	1		1		68	1 Tuberc. pericard.
Sweat	9	6	3	9		24 – 54	3 Gastric neuroses 3 Peptic ulcers 1 Unresolved pneumonia 1 Hypertrophic arth. 1 Gonococcal arth. (recovered)
Erythrocytes	9	6	3	9		22 – 59	3 Syph. aort. insuffic. with CHF** 1 Asthma with cor pulmonale and CHF** 1 RHD**** with CHF** 1 Pylorospasm 1 ASHD*** with CHF** 1 Pneumonia 1 Hepatic cirrhosis
Spinal fluid	4	4		4		19 – 36	1 Pulmonary abscess 1 Hepatitis 1 Infectious mononucl. 1 Pneumonia All convalescent
Edema fluid	16	11	5	14	2	33 – 76	5 HCVD* with CHF** 3 Syphil. heart dis. with CHF** 1 Lymphatic obstr. 5 ASHD*** with CHF** 1 Chronic glomerulonephritis with nephrotic syndrome 1 RHD**** with CHF**
Injection into ascitic fluid	5	3	2	3	2	56 – 84	4 Hepatic cirrhosis 1 Carcinoma of stomach with peritoneal metastases
Bile	4		4	1	3	32 – 55	1 Biliary calculi 2 Postop. cholecystectomy 1 Biliary fistula (repaired)

* Hypertensive cardiovascular disease
** Congestive heart failure
*** Arteriosclerotic heart disease
**** Rheumatic heart disease

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drainage in 4 subjects and from the gall-bladder in 1 subject;

4, cerebrospinal fluid by means of lumbar puncture in 4 subjects;

5, edema fluid by means of a 20-gauge needle as used for muscle tissue pressure[1] inserted into the tissue spaces of 16 subjects;

6, ascitic fluid by paracentesis in 2 subjects;

7, saliva by expectoration in 4 subjects;

8, pleural fluid by thoracentesis in 2 subjects;

9, pericardial fluid by paracentesis in 1 subject; and,

10, erythrocytes separated from the plasma and then washed twice with a physiologic solution of sodium chloride in 9 subjects. Clinical data concerning the subjects studied are summarized in Table 1.

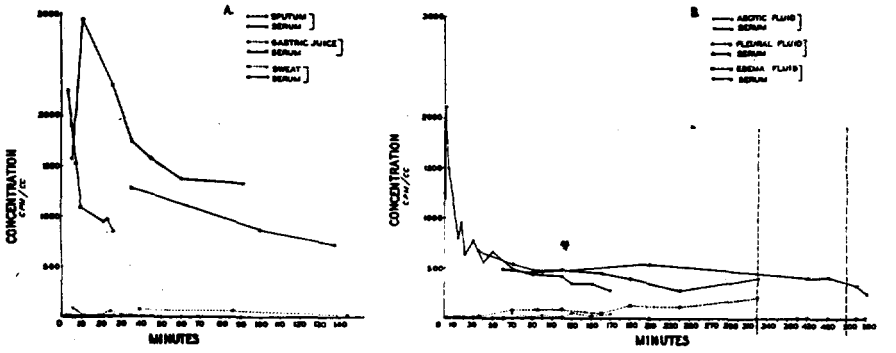

FIG. 1.—Distribution of radiomercury in various body fluids. The measurements were made on different subjects. *(A)* Relative concentrations of radiomercury in the serum, gastric juice, sputum and sweat of 3 subjects. *(B)* Relative concentrations of radiomercury in the serum, ascitic fluid, pleural fluid, and edema fluid of 3 subjects.

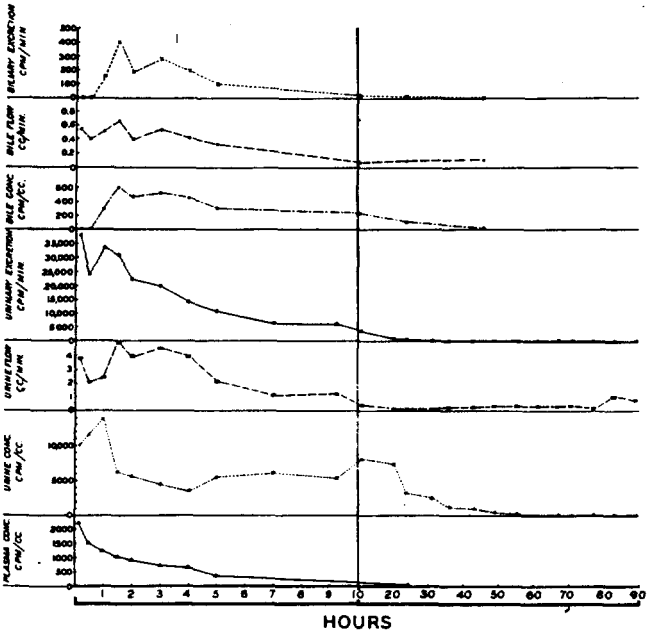

FIG. 2.—Relative concentration of radiomercury in the serum, urine and bile of 1 subject, a 49 year old colored woman with cholelithiasis and T-tube drain.

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Results. Results are summarized in Figs. 1, 2 and 3. It is evident from these illustrations that the radiomercury did not escape in high concentrations into the body fluids studied, with the exception of bile. The escape into sweat and gastric juice was essentially zero and was slow into edema fluid, sputum, ascitic fluid, and pleural fluid (Fig. 1A and B). On the other hand, the escape into bile was relatively high, though it did not reach the levels encountered for the urine (Fig. 2). The bile of 2 of the subjects was studied quantitatively for total excretion of radiomercury; in one, 7.2% of the recovered radiomercury administered orally was in the bile; 92.8% was in the urine, and in the other, 2.7% of the intravenously injected dose was excreted in the bile and 94.2% in the urine. Relative rates of excretion in the urine and bile are shown in detail in Fig. 2.

No accumulation of radiomercury was detected in the spinal fluid. Absence of transfer of measurable quantities of radiomercury into the spinal fluid was consistent for all subjects studied. The washed erythrocytes did not contain any of the isotope. The two washings could have removed radiomercury that may have been adsorbed or bound to the surfaces of the erythrocytes.

The other fluids, on the other hand, showed wide variations from subject to subject; the illustrations shown represent typical patterns. Even though the concentration varied considerably in the time-course, all the fluids except urine, blood, and bile were consistently low in concentration by comparison.

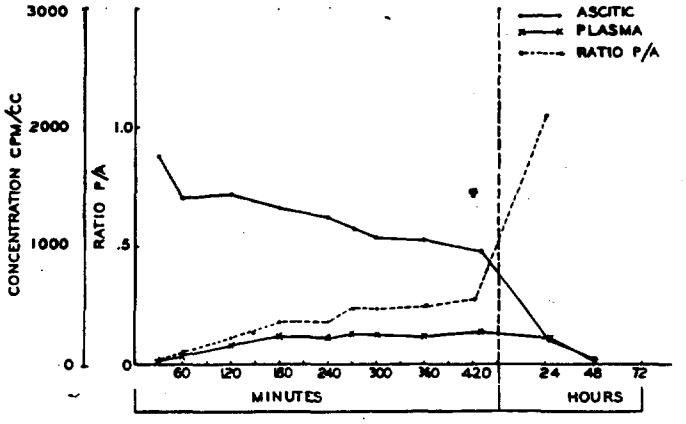

FIG. 3.—Relative concentrations of radiomercury in the plasma and ascitic fluid after intraperitoneal injection in a 53 year old white woman with Laennec's cirrhosis. The ratio of concentration of plasma to concentration of ascitic fluid is shown. The slow appearance in the plasma is apparent, 24 hours being required before the concentrations are the same.

Each of 6 subjects with ascites received 2 cc. of the labeled diuretic intraperitoneally. Results are typified by the example shown in Fig. 3. There were wide variations in absolute values of the concentrations in the blood serum and ascitic fluid which are explainable by differences in the volume of ascitic fluid among patients. All subjects showed a definite absorption of the material from the peritoneal space. One subject had none remaining in the ascitic fluid at the end of 24 hours, whereas another, followed for

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72 hours, still showed significant quantities. Most of the radiomercury was excreted in the urine.

Discussion. Since the movement of the radiomercury is a direct index of the movement of all of the mercury in the diuretic, and since there is relatively little mercury in the entire body of man, the data represent quantitatively as well as qualitatively the distribution of the mercury of a mercurial diuretic administered intravenously[9]. In one subject who received the labeled diuretic orally the pattern of the concentration-time course for the radiomercury in the bile was not significantly different from that presented in the bile by the other subjects who received the material intravenously.

The quantitative distribution of the radiomercury was not extensive, being limited primarily to the blood, urine, bile, and feces. Failure of mercury to penetrate readily the vascular barriers may be due to its tendency to be fixed fairly firmly to the protein molecules of the plasma. The rapid unidirectional removal of the mercury from the blood by the kidneys with excretion into the urine is probably responsible in part for failure of the element to enter slowly the other body fluids and reach relatively high concentrations therein.

In many of the studies counts of samples were frequently 10 to 20 above background (16 to 24 counts per minute). Such sporadically appearing values were most probably the result of statistically expected variations in counting and technique. For example, when tissue fluid is collected and a needle puncture is made, spillage of minute amounts of blood might produce such variations, especially during periods when the concentration of radiomercury in the blood is high. Although such variations are shown in the illustrations, only those points which exhibit a consistent trend can be considered significant. A good example of this type of curve is represented by that for the pleural fluid (Fig. 1). Regardless of the possible errors due to statistical factors concerned with counting and spillage of blood into the body fluids during this collection, the data indicate definitely a slight transfer of the mercury of an intravenously administered mercurial diuretic out of the blood vessels.

Data for feces are not shown because of the difficulties and uncertainties of the method from a quantitative point of view. Concentration of the radiomercury in the feces varied with its quantity and physical state. A larger amount of mercury was excreted in the feces when diarrhea existed. Furthermore, because a specimen was not passed daily, calculations of rate of excretion were disturbed. Approximately 0.01 to 26% of the intravenously administered diuretic was recovered in the feces. This has been discussed previously[4,8] for oral administration of the diuretic.

Contrary to previous reports, the sweat glands, unlike the kidneys, were found not to excrete measurable amounts of the mercurial diuretic[8]. The same is true for the glands of the stomach.

Failure of mercury to accumulate in the tissues in relatively large amounts in general arouses speculation concerning the diuretic action of the material through systemic action, although the action of a drug is not *necessarily* directly related to its concentration in a tissue.

The relatively high concentration of mercury in the bile, as compared with other body fluids, except blood and urine, is in essential agreement with previous studies. However, the total amount excreted in the bile is rela-

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tively small—2.7% in one patient. The ratio of concentration of mercury in the bile to that found in the urine and blood depends in large part on the time of sampling (Fig. 2). Thus with collections made 6 to 20 hours after injection, when the blood content of mercury was low, the concentration of bile was greater than that of the blood. Such factors as the slow rate of biliary flow and relatively low rate of clearance of mercury by the liver, as well as the large storage space in the liver and relatively slow elimination of mercury from these stores, must be evaluated. It is apparent that biliary excretion of the mercury of a mercurial diuretic is not an important route of elimination in the presence of normal kidneys. With impaired renal function and good hepatic function, biliary excretion appeared to be more significant in one subject.

Summary. The distribution of radiomercury in edema fluid, ascitic fluid, pleural fluid, bile, saliva, gastric juice, cerebrospinal fluid, sweat, and erythrocytes following intravenous administration of a single dose of a mercurial diuretic is described. No measurable quantities entered the cerebrospinal fluid, sweat, gastric juice and erythrocytes, and only low concentrations were reached in the saliva, edema, peritoneal and pleural fluids. Relatively high concentrations were attained in the bile.

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