Smith, and Balke and Smith, was determined in concentrated sulfuric acid. A saturated solution was found to contain 8.34 g. of columbium pentoxide and 88.11% anhydrous sulfuric acid in 100 g. of solution.

2. The most favorable conditions were determined for preparing a stable and relatively concentrated solution of columbic acid in sulfuric acid. The solution must contain at least 3 *M* sulfuric acid and not more than 0.038 *M* Cb_2O_5 to remain stable for three days. A higher concentration of Cb_2O_5 may be obtained only when the concentration of sulfuric acid is greater than 3 *M*.

3. A procedure which is sensitive to 0.00032 *M* columbium solution was devised for the detection of small amounts of columbium in the presence of tantalum.

4. By using mercury, which has a high hydrogen overvoltage as a cathode, solutions of columbic acid containing 3, 6 and 10 *M* sulfuric acid were completely reduced to the trivalent state within experimental error. The apparatus devised for such reductions has been described.

This will form the basis of a volumetric method for the quantitative determination of columbium, employing a stoichiometric factor, work for which has been planned.

5. In the presence of 3 *M* sulfuric acid, a blue solution is obtained upon electrolytic reduction, while in 6 *M* and 10 *M* sulfuric acid, reddish-brown solutions were formed which became blue on dilution with water. These brown solutions turned blue upon dilution, indicating complex compounds rather than a different valence.

NEW YORK, N. Y.

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF WESTERN RESERVE UNIVERSITY]

THE DETERMINATION OF TRACES OF MERCURY. III. THE QUANTITATIVE DETERMINATION OF MERCURY IN URINE AND FECES AND THE INFLUENCE OF MEDICATION[1]

BY N. E. SCHREIBER, TORALD SOLLMANN AND HAROLD SIMMONS BOOTH

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The method for the quantitative determination of traces of mercury described by Booth, Schreiber and Zwick[2] was intended primarily for the study of the clinical excretion of mercury. The present paper deals with its applicability to urine and feces. These may introduce complications

[1] This research has been carried on in collaboration with Dr. H. N. Cole of The School of Medicine of Western Reserve University, as a preliminary to a comprehensive study of the absorption and elimination of mercury and mercury compounds by the human body.

The expenses have been met mainly by Lakeside Hospital, Cleveland, Ohio, and by a grant from the Therapeutic Research Committee of the Council on Pharmacy and Chemistry of the American Medical Association.

[2] Booth and Schreiber, THIS JOURNAL, **47**, 2625 (1925); Booth, Schreiber and Zwick, *ibid.*, **48**, 1815 (1926).

due to the presence of substances that are difficult to oxidize or to the presence of drugs which are administered to the patients. A number of these drugs were found not to interfere with the standard method, but the procedure had to be modified for iodides and large amounts of bromides, and a few drugs require such extensive modification that it appeared better to avoid their administration. The problem of the oxidation of normal urine and feces has also been satisfactorily solved.

I. Application of the Method to Normal Urine

In the previous paper[2] it was shown that the method permits the accurate determination of 5 mg. or less of mercury in a liter of water or gelatin solution with a loss of 0.01 to 0.02 mg. of mercury. To measure its availability for normal urine, small amounts of mercury were measured in the calibrated capillary buret, transferred to a 3-liter, long-necked, round-bottomed flask, dissolved in nitric acid and a liter of normal urine added. The reflux condenser was put in place and the urine oxidized, then filtered, the mercury precipitated, coagulated, filtered, decomposed, collected and measured as described in the previous paper. Table I records the result of eight analyses made after this fashion, using 0.44 to 3.26 mg. of mercury added to a liter of normal urine.

TABLE I

RESULTS ON NORMAL URINE

Mercury added, mg.	Mercury recovered, mg.	Loss, mg.	Mercury added, mg.	Mercury recovered, mg.	Loss, mg.
0.44	0.43	0.01	2.31	2.27	0.04
.98	.96	.02	2.66	2.63	.03
1.29	1.28	.01	2.98	2.97	.01
1.63	1.63	.00	3.26	3.25	.01

These results indicate that the method is applicable to the quantitative determination of small amounts of mercury in normal urines with a median loss of about 0.01 mg., that is, the same as in pure solutions of mercury salts.

II. The Effect of Standing

It is often convenient and sometimes practically necessary to keep the urines some days before analyzing. It seemed essential to make sure that this would not result in losses by gradual precipitation of the mercury on the walls of the containers. To obtain an extreme range, the mercury content was determined in the urines of several patients who were receiving mercury rubs, within twenty-four hours after the urine was voided, and again on the same urines after they had stood for six months in bottles in the refrigerator without freezing. In order to test further for the possibility of precipitation, each specimen was divided into aliquot parts. One part was measured and analyzed, while in the case of the second part the bottle was rinsed out with 10 cc. of concentrated nitric acid and this

added to the specimen. The usual procedure was followed and the mercury content determined.

TABLE II

THE EFFECT OF STANDING

Before standing Mercury, mg.	After standing for 6 months: Without nitric acid Mercury, mg.	After standing for 6 months: With nitric acid Mercury, mg.
0.35	0.34	0.35
.86	.85	.84

These results tend to show that long standing without freezing does not lessen the mercury content.

III. The Effect of Drugs on the Determination of Mercury in Urine

Before proceeding to the clinical application of the method, it appeared advisable to ascertain the possible interference of a number of drugs which are often administered to patients who are receiving mercury. Known amounts of mercury dissolved in nitric acid were therefore added to the urines of patients who were receiving these drugs, or to the normal urine to which these drugs had been added.[3] The analysis of these drugged urines showed that the intramuscular injection of neoarsphenamine, arsphenamine and of bismuth compounds, and small amounts of bromides, and the oral administration of chloral hydrate, barbital and small amounts of hexamethylenetetramine do not interfere with the standard procedure. Aromatic compounds (sodium salicylate and cinchophen) and hexamethylenetetramine if administered in large doses cannot be easily oxidized with sulfuric acid and potassium permanganate. Consequently, a considerable amount of organic matter distils over with the mercury. This can be partially prevented by washing the precipitate of mercuric sulfide and manganic hydroxide with small amounts of alcohol and ether, but the last traces of organic matter cannot be completely removed. It therefore seems better to exclude the use of these drugs from the study of mercurial medication.

Iodides, even in small amounts, and ordinary doses of bromides interfere seriously with the standard procedure. Since these drugs are often administered to patients who are receiving mercury, it was found necessary to devise a modification of the method for such cases. The interference of iodides and bromides is due partly to the formation of complex salts from which the mercury cannot be precipitated as sulfide,[4] and partly to the iodates and bromates which are formed in the oxidation. These oxidize the hydrogen sulfide and liberate free sulfur, which interferes with a complete collection of mercury.

[3] Specimens of urine from patients who received the drugs were furnished by The City Hospital and Lakeside Hospital through the kindness of Dr. H. N. Cole, Dr. J. Rauschkolb and Dr. J. Gammel.

[4] Kekulé, *Liebigs Ann., Suppl.*, **2**, 101 (1862).

The following modification avoids these difficulties by removing the iodine or bromine. When violet or brown vapors in the course of the oxidation show that the specimen contains iodide or bromide, the oxidation is continued as described under the standard method and, when complete, the condenser is carefully rinsed and removed. Small amounts of sodium nitrite are added, the solution is gently warmed and a current of air is blown through. Usually 3 to 5 g. of sodium nitrite are sufficient to liberate the iodine or bromine and render the solution colorless. A small amount of potassium permanganate is added and the solution boiled with the reflux condenser in place. This oxidizes any nitrite to nitrate. The excess of manganese dioxide is reduced with hydrogen peroxide and the standard procedure then followed.

Table III contains the results of the analyses of medicated urines or normal urines containing drugs and to which known amounts of mercury were added.

TABLE III

THE EFFECT OF MEDICATION ON THE DETERMINATION OF MERCURY IN URINE

Medication	Administration	Dosage of drug	Mercury added, mg.	Mercury recovered, mg.	Loss mg.	Remarks
Arsphenamine	Intramuscular	0.85 g.	3.16	3.13	0.03	
		1.35 g.	0.95	0.94	.01	
		1.70 g.	1.40	1.38	.02	
Barbital	Oral	0.324 g.	1.12	1.12	.00	
		0.324 g.	2.23	2.21	.02	
Bismuth salicylate	Intramuscular	1.04 g.	3.16	3.15	.01	
Bromide (sodium)	Added to urine	1 g./l.	2.08	2.07	.01	Bromine vapors removed—with sodium nitrite
			4.30	4.26	.04	
Chloral hydrate	Oral	0.324 g.	2.84	2.81	.03	
			3.92	3.90	.02	
Cinchophen	Oral	0.972 g.	Under mercurial medication			Organic matter distilled over
Hexamethylenetetramine	Added to urine	1 g./l.	0.125	0.120	.005	No organic matter distilled over
		5 g./l.	2.61	..		Organic matter distilled over
Iodide (sodium)	Added to urine	0.5 g./l.	0.81	0.79	.02	Iodine vapors removed—with sodium nitrite
			5.72	5.68	.04	
Salicylate (sodium)	Oral	1.944 g.	Under mercurial medication			Organic matter distilled over

IV. The Determination of Mercury in Feces

The determination of mercury in feces presents several difficulties not encountered with the urine.[5] The usual method of oxidation with sulfuric acid and permanganate

[5] In our earlier attempts to overcome these difficulties we enjoyed the collaboration of Dr. Karl G. Zwick.

could not be used, due to the formation of the insoluble sulfates which settle out and cause bumping before the destruction of the organic matter is complete. This difficulty was avoided by the use of concentrated nitric acid and permanganate, but this stronger oxidizing mixture oxidized the hydrogen sulfide, which is used to precipitate the mercuric sulfide, and caused a deposit of sulfur in the distillate. Proceeding upon the suggestion of Dr. W. F. Von Oettingen, a small spiral of 24-gage copper wire was partially oxidized in the flame, reduced with methyl alcohol and placed in the inner decomposition tube above the glass wool. This prevents the deposition of free sulfur and is now used as a matter of routine also for urine, although not always necessary.

Even with the use of strong oxidizing agents, the fats cannot be oxidized completely, but collect in a layer on the surface. Lomholt and Christiansen[6] filtered off the layer of fat and found that it retained no mercury. Our experiments[7] confirm this statement and the results in Table IV show that all of the mercury was recovered after the fat had been rejected. The Standard Method for the oxidation of feces is therefore as follows. A daily specimen (200 to 250 g.) is thinned, usually by the addition of 100 to 150 cc. of water, transferred to a 3-liter, long-necked, round-bottomed flask, 150 cc. of concentrated nitric acid is added and the mixture warmed on a steam-bath until foaming has ceased. Potassium permanganate tablets are then added, the reflux condenser is put in place and the mixture heated for about three hours longer. The flask is then transferred to a hot-plate, more permanganate added, as required, and the oxidation continued until the liquid is yellow and the fat has collected on the surface. The solution is cooled, the fat filtered off and washed with water and the filtrate oxidized with more permanganate until it is colorless. The excess manganese dioxide is reduced by adding a few drops of 50 vol. hydrogen peroxide, the excess boiled off and the solution cooled and filtered. The mercury is then precipitated, coagulated, filtered, decomposed, collected and measured as described under the Standard Method for the Determination of Mercury in Urine[2] with the addition of the copper spiral mentioned above.

In testing out this method, various amounts of mercury were measured in the calibrated capillary buret, dissolved in nitric acid, diluted to 200 cc. and precipitated as sulfide, since the mercury is eliminated as sulfide. Then 200 to 250 g. of feces were added and the Standard Procedure followed as described above. The result of five analyses made after this fashion, using amounts of mercury varying from 0.58 to 3.62 mg. are recorded in Table IV. The median loss is 0.02 mg., practically the same as with urines. The results of the oxidation with sulfuric acid are also added. The latter gave a somewhat large loss and the method was abandoned, mainly because of this inaccuracy.

TABLE IV

RESULTS ON FECES AND MERCURIC SULFIDE

A. Standard Method—Oxidation with Nitric Acid and Potassium Permanganate

Mercury added, mg.	Mercury recovered, mg.	Mercury loss, mg.
0.58	0.56	0.02
1.22	1.20	.02
2.07	2.06	.01
2.87	2.84	.03
3.62	3.58	.04

B. Oxidation with Sulfuric Acid and Potassium Permanganate (Abandoned)

Mercury added, mg.	Mercury recovered, mg.	Mercury loss, mg.
2.20	2.13	0.07
2.67	2.60	.07
3.09	2.71	.29

[6] Lomholt and Christiansen, *Biochem. Z.*, **81**, 356 (1917).

[7] W. A. H. Naylor, *Pharm. J.*, **4**, 12, 392 (1901).

Summary

1. With normal urines the method of Booth, Schreiber and Zwick permits the quantitative determination of mercury with a loss of about 0.01 to 0.02 mg.

2. Long standing without freezing does not alter the mercury content of the urine specimens.

3. Arsphenamine, bismuth, chloral hydrate, barbital, small amounts of hexamethylenetetramine and small amounts of bromides do not interfere with the standard procedure.

4. Aromatic compounds, such as sodium salicylate, cinchophen and large amounts of hexamethylenetetramine complicate the oxidation to such a degree that it is advisable to avoid the administration of these drugs during a study of mercurial medication.

5. Iodides and large amounts of bromides interfere seriously. A modification of the method involving the addition of sodium nitrite is described which takes care of this interference.

6. The determination of mercury in the feces is best made by destroying the organic matter with potassium permanganate and concentrated nitric acid in place of sulfuric acid, with certain modifications which have been described. This determines 2 to 3 mg. of mercury in the daily stool with a loss of 0.01 to 0.04 mg. of mercury.

CLEVELAND, OHIO

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, THE UNIVERSITY OF MINNESOTA]

A SPECIFIC REAGENT FOR THE RAPID GRAVIMETRIC DETERMINATION OF SODIUM

BY H. H. BARBER AND I. M. KOLTHOFF

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A. Blanchetière[1] made application of Streng's reagent for the detection and precipitation of sodium as the triple salt, uranyl magnesium sodium acetate. According to his statement the precipitate has the formula $(UO_2)_3MgNa(CH_3COO)_9 \cdot 9H_2O$ and is obtained water free after drying for one-half hour at 110°.

A. Kling and A. Lassieur[2] report the results of some experiments and conclude that the method of Blanchetière gives satisfactory results. A critical survey of their data shows, however, that the relative error is −6.0 to +3.0%. Crepaz[3] reports the method too inaccurate for the gravimetric determination of sodium. Recently similar results have been found by Perietzeana,[4] who states that the relative error is −3.0

[1] Blanchetière, *Bull. soc. chim.*, [4] **33**, 807 (1923).

[2] Kling and Lassieur, *Chimie et industrie*, **12**, 1012 (1924).

[3] Crepaz, *Ann. chim. appl.*, **16**, 219–224 (1926); *C. A.* **20**, 3144 (1926).

[4] Perietzeana, *Bull. soc. chim. România*, **9**, 17–19 (1927); *C. A.*, **22**, 201 (1928).