after being kept in the refrigerator for several days. This fluorescence was proportional in strength in the previously determined urobilinogen content, indicating the slow oxidation of the latter into urobilin which under the conditions of its solution in the cerebrospinal fluid exhibited a fluorescence greater than usual. This observation corresponds to that of Creyx, Georget and Bonnel[2] who found a fluorescence in the fresh spinal fluid of their case of Weil's disease, prompting them to establish the occurrence of urobilinorachia.

Comment. The origin of urobilinogenorachia may be explained by the diffusion of urobilinogen from the blood into the cerebrospinal fluid whenever the blood urobilinogen is sufficiently increased and the blood-cerebrospinal fluid barrier is disturbed. The conditions under which urobilinogen and bilirubin may pass the blood-cerebrospinal fluid barrier do not necessarily appear to coincide, as illustrated by Case 2 in which the cerebrospinal fluid contained 4.4 mg % urobilinogen and practically no bilirubin while the plasma bilirubin amounted to 4.5 mg %. On the other hand, Case 1 seems to indicate that diffusion of both pigments took place at a similar rate. As xanthochromic spinal fluids in jaundice are rare[8] factors other than liver damage can be assumed to be responsible for the increased barrier permeability, the most likely being infection.[9] The present cases showed severe pulmonary infection and in one instance malaria in addition.

Summary. Six cases of urobilinogenorachia have been presented in which the postmortem cerebrospinal fluid urobilinogen ranged from traces to 9 mg %.

8 Klein, N., and Szentmihalyi, S., *Dtsch. Arch. f. klin. Med.*, 1932, **173**, 234; Lickint, F., *Z. f. d. ges. Neurol. u. Psych.*, 1931, **136**, 291.

9 Malamud, W., and Rothschild, D., *Arch. Neurol. Psych.*, 1931, **24**, 348.

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Effect of Thiols on Mercurial Diuresis.

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The formation of stable complexes between mercury and thiols[1,2] led us to believe that the use of the latter compounds might yield further evidence of the mechanism of action of mercurial diuretics as well as the mechanism of the normal transport of water across the renal tubule. Peters[3] and his associates have presented ample evidence that many of the physiologic actions of the trivalent arsenicals may be explained by the reaction of the arsenical with essential sulfhydryl groups of certain enzymes, thereby inactivating the enzyme. Barron and Singer[4] have demonstrated that organic mercurials are also powerful inhibitors of some enzymes containing sulfhydryl groups.

This report concerns the effect of several compounds that contain sulfhydryl groups on mercurial diuresis.

Methods. The basal urine output of female dogs with inlying catheters was measured; the mercurial diuretic was then given intravenously, and the diuresis curves (Fig. 1) were obtained by recording 20-minute urine volumes over a period of about 3 hours.

1 Gilman, A., *Fed. Proc.*, 1946, **5**, 285.

2 Braun, H. A., Lusky, L. M., and Calvary, H. O., *J. Pharmacol.*, Suppl., 1946, **87**, 119.

3 Peters, R. A., Stocken, L. A., and Thompson, H. S., *Nature*, 1945, **156**, 616.

4 Barron, E. S. G., and Singer, T. P., *J. Biol. Chem.*, 1945, **157**, 221.

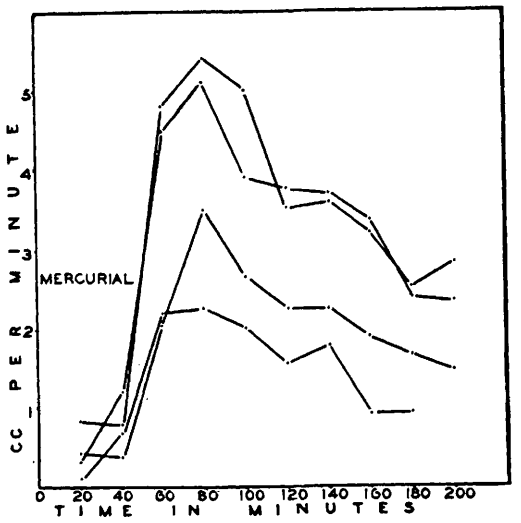

FIG. 1.
Mercuhydrin diuresis curves.

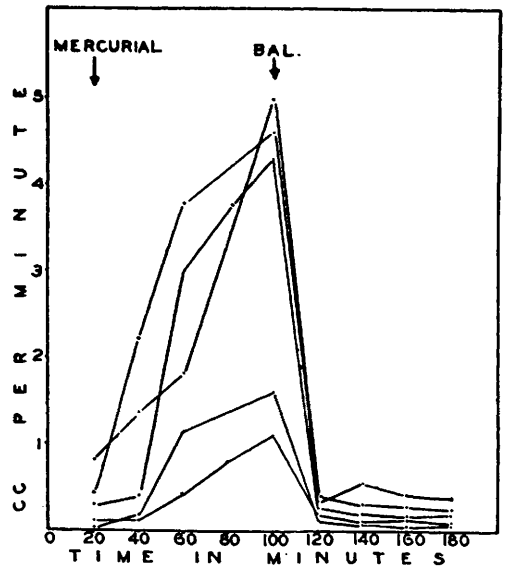

FIG. 2.
Antagonism of mercurial diuresis by Bal.

1-(methoxy-oxymercuri-propyl) - 3 - succinyl urea* (Mercuhydrin) and Mersalyl, U.S.P., were used. With these agents, in a dosage of 10 mg per kg given intravenously, maximal diuresis appears in about one hour in dogs. Diuresis usually continues for many hours. In another group of dogs, one of the thiols was administered intravenously during maximal diuresis.

Results. Fig. 2 shows that 2,3-dimercaptopropanol (Bal) immediately returns the urine output to the prediuretic level. The effect of Bal is permanent, although another dose of mercurial will again produce diuresis which, in turn, may be abolished by Bal. If Bal is injected before, or soon after, the mercurial, no diuresis develops. Thioglycolic acid has a similar action, but the effective dose is much larger. Methylene blue and glutathione temporarily inhibit mercurial diuresis while cysteine is ineffective in the dosage employed. Hematuria was sometimes observed when Bal and thioglycolic acid were administered after the mercurial diuretics, indicating that the thiol-mercury complexes may produce kidney damage. None of the thiols had any influence on water diuresis or normal urine output, but the diuresis produced by mercuric chloride was rapidly abolished by Bal.

Discussion. The demonstration that certain thiols effectively counteract the acute toxic effects of organic mercurial compounds[5] and abolish the diuretic action, furnishes additional evidence that both toxicity and diuresis from these agents are due to the liberation of free mercury. Bal, the most effective antagonist, forms a stable complex with mercury.

A study of kidney enzymes inhibited by the mercurial diuretics should yield information on the enzyme systems concerned in the reabsorption of water by the renal tubules. We are investigating this possibility.

Summary. The diuretic action of organic mercurials or inorganic mercury compounds is prevented or abolished by certain thiols. Of the compounds tested, Bal was the most effective, followed by thioglycolic acid, glutathione, and methylene blue in decreasing order of activity. Cysteine had very little effect.

* Kindly supplied by Dr. E. L. Foreman of the Lakeside Laboratories.

[5] Long, W. K., and Farah, A., *Science*, 1946, **104**, 220.