diabetes were used as test animals in this study. They were force-fed a medium carbohydrate diet. Two synthetic estrogens were tested, each of which represents a chemically different series of compounds than have previously been tested for diabetogenicity. Substance I was 2,4-di(p-hydroxyphenyl)-3-ethyl hexane, and Substance II was 1,2-dimethyl-2-carboxy-7-methoxy - 1,2,3,4,9,10-hexahydrophenathrene. Substance I caused exacerbation of the diabetes in 5 out of 6 test animals. The sixth rat did not have a spontaneous glycosuria and failed to respond to the estrogen. Substance II intensified the glycosuria in all 6 test animals and appeared to be the more potent of the two compounds. When the injections were stopped the glycosuria decreased to its pre-injection level or below.

16052

BAL Inhibition of Mercurial Diuresis in Congestive Heart Failure.*

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This study was undertaken to evaluate the effect of 2,3 dimercaptopropanol[1] (dithiopropanol),—commonly known as British Antilewisite or BAL—upon the diuresis induced by the organic mercurials with the view of gaining further information regarding the mechanism of mercurial diuresis, as well as controlling some of the untoward sensitivity reactions[2,3] encountered when these substances are employed. 1 - (methoxy - oxymercuri - propyl) - 3 - succinylurea—generally known as Mercuhydrin—which contains 39 mg of mercury in organic combination with 48 mg of theophyllin per cc of aqueous solution, was the sole mercurial studied. The preparation known as BAL in oil (10% 2,3 dimercaptopropanol in benzyl benzoate and peanut oil) was used.

The subjects selected were cardiac patients in chronic congestive failure who were known to respond to organic mercurial injection with diuresis and weight loss. The experience with 7 patients comprises this report. Five patients had hypertensive arteriosclerotic heart disease; one was a rheumatic cardiac and the other suffered from heart failure of undetermined etiology. Regular sinus rhythm was present in 6 of 7 of these subjects at the time of the study.

So far as feasible, the patients were maintained on the usual therapeutic cardiac regimen consisting of incomplete bed rest, salt-poor diet, containing less than 2 g of NaCl in 24 hours, no fluid restriction, and in most instances the administration of some digitalis preparation.

When it appeared that they had attained a relatively constant weight under such management, BAL in oil was introduced for a period of 24 to 36 hours. It was administered intramuscularly every 6 hours in doses of 2.5 mg per kilo of body weight. After receiving BAL in oil for 24 hours, Mercuhydrin was injected intramuscularly in 2 cc doses. The BAL in oil was then continued for a period of 12 hours.

Table I contrasts the weight changes occurring in patients receiving BAL in oil for about 24 hours, prior to the administration of Mercuhydrin with those who received the mercurial only.

The individaul weight loss 48 hours after

* Work done under a grant from the Joseph and Helen Yeamans Levy Foundation in memory of Miriam Levy Finn.

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

2 Brown, G., Friedfeld, L., Kissin, M., Modell, W., and Sussman, Ralph M., *J. Am. Med. Assn.*, 1942, **119**, 1004.

3 Long, W. K., and Faran, A., *Science*, 1946, **104**, 220.

TABLE I.
Weight Change.

Subject	BAL with Mercurial		Mercurial	
	24 hr	48 hr	24 hr	48 hr
J.D.	— ¾	+ ¾	—3¼	—5¼
S.S.	+ ½	+1½	—4¼	—3¾
H.G.	0	+1	—4	—3½
E.G.	— ½	— ¼	—3½	
F.S.	— ¾	— ½	—2¾	—3¾
G.N.	0	+1	—3¾	—2¾
N.R.	— ¼	+1	—1¾	—3¼
Avg	— ¼	+ ⅗	—3⅓	—3⅔

the administration of the mercurial, alone, was somewhere between 2¾ and 5¼ lb, whereas, patients receiving BAL in oil with the mercurial, in most instances gained weight, only 2 having lost ½ lb or less.

Some observations made by varying the period of BAL administration preliminary to mercurial injection indicate that at least 4 doses of 2.5 mg per kilo body weight injected at intervals of 6 hours must be given prior to the introduction of the 2 cc of the mercurial in order to inhibit diuresis completely. It is also evident from this investigation that within 48 hours after the last injection of BAL in oil, diuresis can again be anticipated from another adequate injection of mercurial. Patients who were observed for several days following the cessation of BAL in oil injections displayed no evidence of diuresis from the mercurial administered simultaneously with the dithiopropanol. It may, therefore, be concluded that BAL in oil completely annuls the diuretic action of the mercury and does not merely delay it.

Notes made on the side-reactions experienced with BAL in oil coincide with earlier pharmacologic observations. Thus, transient rise in blood pressure, local reaction, nausea, vomiting, warmth, paraesthesias and chill were all observed.[4]

In 2 hypertensive patients, alarming elevation of systolic and diastolic blood pressures coincided with the administration of BAL in oil and persisted for at least 4 hours. In one patient the symptoms were interpreted as being due to "hypertensive encephalopathy".[5]

Considerable local pain was experienced at the site of injection and the administration of 0.5 cc of 1% procaine in the syringe with each injection relieved one patient considerably without in any way diminishing the anti-diuretic effect of the dithiopropanol.

No cases of organic mercurial sensitivity were available at the time of study, so that no remarks regarding the response of such patients to BAL can be made.

Unless differences in species reaction occur, it is thought that the mechanism of BAL inhibition of mercury diuresis results from the formation of a stable mercury-thiol complex,[6,7] binding free mercury, and that BAL is not, itself, an anti-diuretic substance.

These findings further substantiate the notion that the diuresis from organic mercurials is due to the systemic effect of free mercury.

Since this study was completed, an important communication from Handley and La Forge has appeared and has established that BAL injected intravenously into dogs inhibits mercurial diuresis in that animal.[8] Their findings in the normal dog are in complete accord with our observations in humans suffering from heart failure.

Conclusions. 1. BAL in oil completely annuls the diuretic effect of the organic mercurial known as Mercuhydrin.

2. A period of priming with BAL in oil was necessary to inhibit the diuresis completely.

3. Procaine may be added to BAL in oil without in any way affecting the anti-diuretic effect.

4. BAL in oil may intensify pre-existing hypertension in the presence of heart failure.

4 Modell, Walter, Gold, Harry, and Cattell, McKeen, *J. Clin. Invest.*, 1946, **25**, 480.

5 Fishberg, A. M., *Hypertension and Nephritis*, Chapter X, Lea & Febiger, 4th edition, 282.

6 Barron, E. S. G., and Kalnitsky, G. (quoted by Longcope, W. T., and Luetscher, J. A.), *J. Clin. Invest.*, 1946, **25**, 557.

7 Gilman, Alfred, Allen, Roberta P., Philips, Frederick S., and St. John, Ellen, *J. Clin. Invest.*, 1946, **25**, 549.

8 Handley, Carroll A., and La Forge, Marguerite, PROC. SOC. EXP. BIOL. AND MED., 1947, **65**, 74.